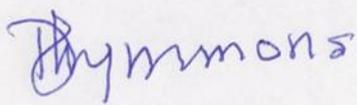


Standard Operating Procedure

Number:	UM/UoM Clinical Trial Authorisation/SOP07/6.0		
Title:	Preparation and Submission of a Clinical Trial Authorisation		
Version:	6.0 (March 2018)	Effective Date	March 2018
Author:	Dr Mohammed Zubair/ Victoria Sheard	Review Date	March 2020
Reviewed by:	Dr Mohammed Zubair		Approved By: Prof Deborah Symmons
Position:	Research Governance, Ethics and Integrity Manager		Position: Chair of Clinical Trials Management Group
Signature:	 		

Version	Date	Reason for change
2.0	January 2013	Update of web links and office details
3.0	May 2014	Addition of version control statement for SOP
4.0	October 2015	Update of web links and office details
5.0	August 2016	Update of changes, web links and office details
6.0	March 2018	Updated to reflect current processes

When using this document please ensure that the version you are using is the most up to date either by checking on the **Research Governance, Ethics and Integrity** Team website (<http://www.staffnet.manchester.ac.uk/services/rbess/governance/>) for any new versions or contacting the author to confirm the current version.

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1.0 Background

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”).

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.

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.

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.

All proposed research which falls under the above stated regulations, requires a Sponsor (Confirmation of Sponsorship SOP). A research Sponsor takes responsibility for the initiation, management and financing (or arranging the financing) of a trial. It is the Sponsor’s role to seek authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA). The UK Clinical Trial Regulations, Part 3, Reg 17, state that the request for a clinical trial “...shall be in writing and signed by or on behalf of the Sponsor.”

The request in writing seeking authorisation to conduct a clinical trial is termed a Clinical Trial Authorisation (CTA) application. A CTA is required for any clinical trial involving a medicinal product.

Where there is doubt if a clinical trial falls under the regulations, and may require regulatory approval by the MHRA, the Principal Investigator should refer to the [clinical trial](#) algorithm. If, after using the clinical trial algorithm, there is uncertainty about whether or not the proposed clinical trial does come under the Regulations, then an email, including a copy of the protocol, should be sent to the MHRA Clinical Trial helpline (clintrialhelpline@mhra.gov.uk) **marked ‘Scope - protocol review’ followed by the study title** (shortened) in the subject line, requesting an opinion on the status of the study. The Research Governance, Ethics and Integrity team can also be contacted for clarification.

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2.0 Purpose

This SOP relates to CTIMPs – (i.e. all Trials which come under the Regulations, in which The University of Manchester has accepted the role of Sponsor or co-sponsor), and describes the procedure for applying for a CTA. The requirements of this SOP should be applied as a minimum to such trials and in conjunction with all applicable University policies and procedures and the policies and procedures of the relevant NHS Trust.

3.0 Roles and responsibilities

The Chief Investigator, in liaison with the Sponsor, will prepare and submit the application for a CTA to the MHRA, in line with the specific delegated responsibility by the Sponsor. The Chief Investigator cannot submit the application for a CTA until the Sponsor has reviewed and approved the application in writing. In addition, written confirmation of full Sponsorship needs to be obtained prior to application submission. All [fees](#) associated with the CTA application are to be met by the Chief Investigator.

4.0 Procedures

4.1 Obtaining a EudraCT Number

EudraCT is a database of all clinical trials of medicinal products commencing in the EU. The EudraCT number is the unique reference given to each trial. This number must be included on all CTA applications, and other relevant documents relating to the trial. A EudraCT number can be applied for at: <https://eudract.ema.europa.eu/index.html>.

4.2 Completing the CTA form

The CTA application is an electronic process and is usually completed in parallel with the ethics application online through the Integrated Research Application System (IRAS), where guidance notes on the completion of the form can also be found (<https://www.myresearchproject.org.uk/>).

In order for an application to be considered valid by the MHRA, a submission should also contain the following supporting documentation via the copy and paste functionality as described on the MHRA website: (<https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk>):

- a covering letter (when applicable, the subject line should state that the submission is for a Phase I trial and is eligible for a shortened assessment time, or if it is submitted as part of the notification scheme)
- a clinical trial application form in PDF and XML versions

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- a protocol document
- an investigator's brochure (IB) or document replacing the IB
- an investigational medical product dossier (IMPD) or a simplified IMPD
- a non-investigational medicinal product dossier (if required)
- a summary of scientific advice from any Member State or the European Medicines Agency (EMA), if available
- manufacturer's authorisation, including the importer's authorisation and Qualified Person declaration on good manufacturing practice for each manufacturing site if the product is manufactured outside the EU
- a copy of the EMA's decision on the paediatric investigation plan and the opinion of the paediatric committee, if applicable
- the content of the labelling of the investigational medicinal product (IMP) (or justification for its absence)

4.3 Submission of the CTA form

Once the CTA application form has been completed online, the submission of the CTA application form has to be done electronically via the Common European Submission Portal ([CESP](#)).

The MHRA have produced [guidance on common errors found in CTA applications](#) which in turn can delay the validation process at the MHRA.

The MHRA will not accept paper documents.

4.4 Following Submission of the CTA form

A complete CTA application will be assessed by the MHRA and an initial response given within 30 days.

If the MHRA approve the CTA application, a letter of acceptance will be sent to the named applicant in Section C of the form (usually the Chief Investigator). The Chief Investigator must also obtain relevant approvals from the main REC, NHS Trust and sponsor green light before recruiting the first patient to the clinical trial.

4.5 Amendments to the CTA

The Chief Investigator must maintain a record of all non-substantial amendments made to the CTA following authorisation from the MHRA and notify the Sponsor via the annex associated with SOP09: Substantial and non-Substantial Amendments. Where amendments are considered to be substantial, following consultation with the Sponsor, a request must be made to the MHRA (and the REC if appropriate) seeking approval for the amendment. All amendments submitted to the MHRA should be done electronically. Please view the [MHRA guidance on amendments to the CTA](#). Please also see the University of Manchester SOP on Substantial and non-Substantial Amendments.

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A protocol amendment can only be implemented after receiving authorisation from the MHRA, the main REC and HRA Approval as appropriate.

Urgent amendments to a protocol can be made at any time and do not require prior MHRA and main REC approval if the safety of one or more study participants is at risk (see SOP on Urgent Safety Measures). The Chief Investigator must inform the MHRA, the main REC and the sponsor as soon as possible.

4.6 End of Trial Notification

A 'Declaration of the end of a Clinical Trial' form (<https://eudract.ema.europa.eu/>) should be sent to the MHRA at the end of the clinical trial. This form should be submitted by the Chief Investigator within 90 days of the trial's conclusion as defined by the protocol.

5.0 References:

- Directive 2001/20/EC
- Directive 2005/28/EC
- The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 1031)
- The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 (SI 1928)

The above can be accessed via/ downloaded from the MHRA website:

- <http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/IsaclinicaltrialauthorisationCTArequired/index.htm>
- Clinical Trials Toolkit information on 'Substantial Protocol Amendments', which can be accessed via/downloaded from <http://www.ct-toolkit.ac.uk/routemap/substantial-amendments/>
- UK Policy Framework for Health and Social Care Research

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