MANCHESTER 1824
The University of Manchester

Standard Operating Procedure

Number:	UoMCTSOP07/2025/V8.0		
Title:	Preparation and Submission of a Clinical Trial Authorisation (CTA)		
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Version	Date	Summary of Changes
2.0	January 2013	Update of web links and office details.
3.0	May 2014	Addition version control statement for SOP and contractual obligations (Appendix I)
4.0	October 2015	Update of weblinks and office details
5.0	August 2016	Update of weblinks and office details
6.0	March 2018	Updated to reflect current processes
7.0	February 2025	Updates to reflect changes to MRHA submissions, following Brexit
8.0	March 2026	Introduce “old rules” vs “new rules” trial status based on submission date relative to 28 April 2026, and apply MHRA transitional arrangements guidance;

		Reference SI 2025/538 (in force 28 April 2026) and implementation of ICH E6(R3) alongside the updated UK framework; Update “amendments” section to “Modifications” with categories and link to UoM SOP09 Modifications v9.0 approach; Add requirement to offer a public-understandable summary of results to participants for CTIMPs submitted from 28 April 2026, normally within 12 months of end of trial (unless waiver/deferral).

1.0 Introduction

The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) govern CTIMPs in the UK. The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 (SI 2025/538) were made in April 2025 and came into force on 28 April 2026. The Regulations include the implementation of the latest international Good Clinical Practice guideline ICH E6(R3).

Clinical trial authorisation (CTA) submitted before 28 April 2026 are treated as ‘old rules clinical trials’, and those submitted on or after 28 April 2026 are treated as ‘new rules clinical trials. This classification is based on the submission date, not the route of submission.

All proposed research which falls under the above stated regulations requires a Sponsor (Confirmation of Sponsorship SOP03). 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."

Where there is doubt if a clinical trial falls under the regulations, and may require regulatory approval by the MHRA, the Chief Investigator (CI) should refer to the competent authority's latest version of the clinical trial algorithm. When and where necessary further clarification as to whether a proposed study is considered to meet CTIMP/Medical Device criteria can be sought from the Research Governance, Ethics and Integrity (Clinical Trials) team.

2.0 Scope

This SOP applies to Clinical Trials of Investigational Medicinal Products (CTIMPs) and combined IMP/device trials in which The University of Manchester has accepted the role of Sponsor or co-sponsor.

It describes Sponsor and CI responsibilities for preparing and submitting a CTA (as part of a combined review application via the Combined Review process, which is the standard route from 28 April 2026), and for managing post-authorisation notifications relevant to the CTA.

This SOP should be applied in conjunction with other Sponsor SOPs (e.g., Sponsorship; Modifications; Urgent Safety Measures) and relevant MHRA/HRA guidance.

All CTIMPs and combined IMP-Device trials conducted under this SOP must comply with the ethical standards set out in the Declaration of Helsinki, as required under the amended Medicines for Human Use (Clinical Trials) Regulations 2025, except where provisions conflict directly with UK regulation.

3.0 Responsibilities

The CI, in liaison with the Sponsor, will prepare the CTA and supporting documentation and request Sponsor review/approval in line with delegated responsibilities.

The CI must not submit the CTA (or combined review application) until the Sponsor has reviewed and approved the submission package in writing, and written confirmation of sponsorship/green light requirements are met as applicable.

Fees associated with the CTA process (where applicable) must be budgeted for and met by the CI/trial funding.

The Sponsor retains overall responsibility for trial initiation, management, and regulatory authorisation as required under the Medicines for Human Use (Clinical Trials) Regulations and provide written authorisation for submission before the CI may proceed.

Financial Responsibilities
All fees associated with MHRA assessment, REC review, or other regulatory processes (such as Combined Review or fast-track routes under the 2026 reforms) must be included in trial budgeting and are to be covered by the CI or project funding.

4 Procedures

4.1 Applying for Ethical and Regulatory Approvals

All new CTIMPs and combined IMP-Device trials **must** use the Combined Review approvals route. This is the standard process for MHRA + REC review, under the amended Medicines for Human Use (Clinical Trials) Regulations 2025.

The Health Research Authority (HRA) provides a system that lets researchers apply for ethics and regulatory approval as part of a single application.

The documents that must be submitted as part of a valid ethics and CTA application are listed on the HRA and MHRA website
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4.2 Registertion of a CTIMP

All clinical trials including CTIMPs must be registered on a publicly available database (e.g. ISRCTN or ClinTrials.gov) before recruitment begins. The HRA automatically registers new clinical trials with ISRCTN Registry as one of the steps to ensure research transparency.

4.3 Completing the CTA form

The CTA application is an electronic process and is to be completed in parallel with the ethics application online system provided by the HRA.

The HRA system includes a list of documentation to submit for a combined review an application. The following provides some further guidance on the content of some of the specific MHRA documents:

- covering letter: When applicable, the subject line should state that the submission is for a Phase I healthy volunteer trial and is eligible for a shortened assessment time, or if you are using risk proportionate approaches to the conduct of the study. Your covering letter should clearly highlight your Purchase Order (PO) number; this will help us to invoice and allocate your payments promptly and efficiently
- investigational medical product dossier (IMPD): please note that an active substance master file (ASMF) is not acceptable as a substitute for an IMPD.
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- manufacturer's authorisation (GMP licence), 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.
- content of the labelling of the investigational medicinal product (IMP): where this has not been provided, please provide a justification for its absence

4.4 Submission of the CTA form

CTIMP submissions (initial applications, substantial amendments, end of trial notifications and annual safety reports must be submitted only to the MHRA via MHRA Submissions. If any ethical issues are identified by the MHRA when they receive these reports, they will liaise with they no longer need to be sent to Research Ethics Committees (RECs). The guidance for how you complete the annual report and how to submit should always be checked against the latest MHRA guidance on Annual Safety Reports
The MHRA will not accept paper documents.

4.5 Following Submission of the CTA form

For every approved CTA application, the MHRA will provide a letter of acceptance. 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.

4.6 Modifications to the CTA

The Chief Investigator must maintain a record of all non-substantial modifications made to the CTA following authorisation from the MHRA and notify the Sponsor via the annex associated with SOP09: Substantial and non-Substantial Modifications, using the HRA system. Where modifications 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 modification. All modifications submitted to the MHRA must be done electronically.
Please view the MHRA guidance on modifications to the CTA. Please also see the University of Manchester SOP09 on Substantial and non-Substantial Modifications.

A protocol modification can only be implemented after receiving authorisation from the MHRA and HRA Approval as appropriate.

Urgent modificaitons 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 SOP11 on Urgent Safety Measures). The Chief Investigator must inform the MHRA, the main REC and the sponsor as soon as possible.

4.7 End of Trial Notification

An end-of-trial notification must be submitted to the MHRA at the end of the trial as and as described in the protocol. The mechanism for submission of such a notification is through the HRA system, and an acknowledgement will be issued. Note that the MHRA and the ethics committee expect details of where the results have been published (in a public registry) and that it must be within 12 months of the end of the trial

The only exception is certain paediatric trials using authorised medicines (see specific guidance).

In some instances, a trial may end early. In which case the following process has to be followed:
If the trial ends early (before the protocol-defined date/event)

The licensing authority will review your end-of-trial declaration and may request further information.

Once they have everything they need, they will confirm that your declaration is accepted.

You must still send the licensing authority and ethics committee the details of public-registry results within 12 months of the trial ending, except for the same paediatric exceptions.

5 References

The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031).
The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 (SI 2025/538) (in force from 28 April 2026).
MHRA: Clinical trials regulations: transitional arrangements.
HRA: Clinical trials regulations reform (definitions and modification terminology).
HRA: Offering to share a summary of results with participants.

ICH: Guideline for Good Clinical Practice E6(R3) (Principles and Annex 1).

- 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

Related SOPs:

- UoMSOP03: UoM Sponsorship
- UoMSOP09: Modifications
- UoMSOP11: Urgent Safety Measures