Technology, Infrastructure and Environment Directorate Clinical Research Governance Team

Standard Operating Procedure

Protocol development and maintenance for University of Liverpool Sponsored studies

SOP037

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1. Introduction

The research protocol is an essential document for any research project. The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 mandate adherence to the trial protocol for Clinical Trials of Investigational Medicinal Products (CTIMPs).

It is a full description of the research study and will act as a 'manual' for members of the research team to ensure everyone adheres to the methods outlined. As the study gets underway, it can then be used to monitor the study's progress and evaluate its outcomes.

The protocol should include as much detail about the research project as possible including the objective(s), design, methodology, inclusion and exclusion criteria for participants, monitoring, publication policy, statistical considerations and organisation of a study. This enables any review bodies to fully understand your study and ensure the research is carried out consistently throughout the life of the study.

The protocol should be kept up to date as the research evolves and include a version number and approval history.

2. Scope of Procedure

This SOP describes the requirements for protocol development and maintenance for University of Liverpool Sponsored studies.

3. Who

This SOP is aimed at Chief Investigators (CI), students, trial coordinators and other members of University Staff involved in University Sponsored research.

This SOP is also applicable to members of the Technology, Infrastructure and Environment Directorate (TIED) who are involved in sponsorship.

4. When

This SOP should be referred to when developing a protocol for a University Sponsorship application, and throughout the study lifecycle, particularly when modifications are required or where study activity does not comply with the protocol.

5. Protocol template requirements

The University of Liverpool Sponsorship team has developed a Non-CTIMP protocol template (TEM006) with regard for the Health Research Authority Qualitative Protocol Development Tool. It is expected that all investigators applying for University of Liverpool Sponsorship utilise TEM006. This is to ensure that all required information is provided, and standard statements, in particular for

compliance, are included. The latest version of TEM006 can be found on the Clinical Research Governance intranet page[1] or requested from the Sponsor team via sponsor@liverpool.ac.uk.

Where a study is being managed by a Clinical Trials Unit (CTU) such as the Liverpool Clinical Trials Centre (LCTC) it is acceptable for their CTU template protocol to be utilised, however the Sponsor reserve the right to request changes to specific information where required.

Whilst a grant application will inform the study design, it is not acceptable to submit a grant application as a study protocol. Any Sponsorship applications submitted utilising a grant application will be rejected.

The Sponsorship approval letter will detail the version and date of the protocol that has been reviewed and approved by Sponsor. This version **must** be submitted to Research Ethics Committees and regulatory bodies for approval. If a substantially different protocol is reviewed by Research Ethics Committees or regulatory bodies this may impact the Sponsorship approval and require full re-review by the relevant Sponsorship Committee.

Substantial changes such as changes to the template, participant pathway or procedures, removal of or change to key Sponsor or governance information or change to study design must be submitted to the Sponsor for review. Depending on the changes made, the protocol may need to be re-reviewed by the relevant Sponsorship Committee.

Minor changes such as correction of typos, addition of clarifications, change of contact details can be made without notifying the Sponsor.

6. End of Study/Trial Definition

The protocol must contain a definition of the end of the study/trial that is appropriate to the study design. This must be considered carefully as this is the point at which you will be expected to submit an End of Study Declaration. For international studies, this is the end of study in all participating countries, not just in the UK. Overall, it is important to ensure that once closed the final summary report can be provided within 12 months, so the analysis for the primary objective must be completed.

For studies involving human tissue, the analysis of the samples should be undertaken as part of the data collection **before** the end of study is declared.

Any change to the end of study definition after approval has been given for the research should be notified as a modification to the appropriate review bodies.

Example end of Study definitions;

- Last visit of the last participant
- Completion of any follow-up monitoring and data collection
- Completion of analysis of human material samples required for study/trial endpoints

[1] https://www.liverpool.ac.uk/intranet/health-and-life-sciences/clinical/clinical-research-governance/sponsorship/

- Database lock - data cleaning, reviews, and verifications are complete, signalling that the data is ready for final analysis

Sponsor recommend that database lock is the most suitable end of study/trial definition for most research as this ensures that all data is collected and complete and ready for analysis, but each study/trial must be considered based on the requirements for that piece of research.

7. Considerations for International research

In addition to UK based research, the University also sponsors Human Health related based studies across several countries. It is still expected that TEM006 is utilised for these studies, however it is acknowledged that each country may have specific requirements. Where it is known that another country mandates the use of a local template, this should be utilised from the beginning of the application process to prevent delays during the Sponsor Permission to Proceed process.

If the research will be conducted across several countries it is acknowledged that some sections will need to be localised to meet local requirements. Sponsor recommend creation of a "Master" protocol that contains all overarching study details including the study design and outcomes, with country-specific appendices detailing local arrangements. This will negate the need for ethics committees to review multiple local arrangements. The Sponsor team can work with research teams to establish to best way to manage this where required.

8. Version Control requirements

Protocols must be maintained using stringent version control mechanisms.

The first draft should be labelled DRAFT version 0.1 and dated. Subsequent drafts will have an increase of 0.1 in the version number e.g. 0.2, 0.3, 0.4 etc. and dated. The version number and date must be documented on the footer of the protocol. Care should be taken to ensure the version control for the template used is not removed. Each draft version of the document should be saved and clearly identified by its file name

A 'draft' water mark should be used on all draft versions to provide clarity and avoid ambiguity. The watermark must be removed once the document is finalised.

Once finalised the protocol is assigned v1.0. In general, v1.0 is submitted with the Sponsorship Application.

It is accepted that modifications are usually required to the protocol during a study; version changes should be tracked during this process. Subsequent drafts will have an increase of 0.1 in the version number (e.g. 1.1, 1.2, 1.3 etc) and dated. Once approved the document will be assigned the next sequential number (e.g. 2.0). This process should be repeated for every revision made to a document. See SOP018 "Procedure for the Submission of Modifications" for further details of the modification process.

A copy of the finalised and approved protocol should be filed in the appropriate section of the trial/study master file with superseded versions also retained and clearly marked as superseded.

Each final approved version of the protocol must be signed by the Sponsor representative (usually the Senior Clinical Research Governance Manager) and the Chief Investigator. This will be undertaken in line with SOP034 "Provision of Electronic Signatures for Key Study/Trial Documentation".

9. Use of Artificial Intelligence (AI)

It acknowledged that Generative AI can be a useful tool in drafting documentation for studies, and it has the potential to improve health and social care research and, ultimately, patient care by:

- facilitating creativity and the development of ideas
- supporting neurodivergence
- reducing language barriers

AI may be used to assist in drafting study documentation including the protocol; however, this must be utilised with care to ensure that the protocol is factually accurate and does not contain any information that is:

- confidential and used without consent
- falsified
- fabricated
- plagiarised
- misrepresented

In line with research funder expectations researchers should be transparent where they have used generative AI tools in the development of a protocol or study documentation.

Examples of substantive use that could be declared:

- assisting idea generation or development of hypotheses
- interpreting, analysing or summarising data and text
- comparing literature sources
- generating an abstract

Researchers must not use generative AI tools to generate an entire protocol, or sections of a protocol, without human involvement.

The CI remains responsible for the content of their protocol; this responsibility does not change with the use of AI.

10. Roles and Responsibilities

The Chief Investigator is responsible for;

- Leading the creation and maintenance of the research protocol, ensuring all required information is accurately captured and explained
- Acknowledging any use of AI to aide development of the protocol and ensuring all information generated by AI is reviewed and checked for accuracy
- Submission of the research protocol for approval by Sponsorship, Research Ethics Committees and other regulatory bodies as required
- Ensuring the study is conducted strictly in accordance with the approved protocol, Good Clinical Practice (GCP), and applicable regulations
- Ensuring the protocol is subject to stringent version control throughout the research lifecycle

The Sponsor Responsible Officer is responsible for;

- Reviewing the protocol upon initial submission and subsequent modifications, ensuring that TEM006 has been utilised (unless another template has been agreed to be used)
- Ensuring governance and sponsorship related information is accurate
- Reviewing protocol details to ensure consistency with the information provided in the Sponsorship application form and other study documentation (such as Participant Information Sheets, Consent Forms etc.)

11. Abbreviations

AI Artificial Intelligence

CI Chief Investigator

CTIMP Clinical Trial of Investigational Medicinal Product

CTU Clinical Trials Unit

GCP Good Clinical Practice

LCTC Liverpool Clinical Trials Centre

TIED Technology, Infrastructure and Environment Directorate

12. Associated Documents and References

UK Policy Framework for Health and Social Care Research

The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025

TEM006 - Non-CTIMP protocol template

SOP018 - Procedure for the Submission of Modifications

SOP034 - Provision of Electronic Signatures for Key Study/Trial Documentation

13. Training and Resources

CIs, students, trial coordinators and other members of University Staff involved in University Sponsored research should be aware of and familiar with this SOP. Training can be provided by the Clinical Research Governance Team upon request.

14. Monitoring and Audit

An internal audit of Technology, Infrastructure and Environment Directorate Clinical Research Governance SOPs will be conducted at a minimum of every two years.