University of Hertfordshire

WRITING RESEARCH PROTOCOLS

Clinical Trials Support Network (CTSN)

Standard Operating Procedure for Writing GCP Compliant Research Protocols intended for University of Hertfordshire Sponsored/Co-sponsored or CTSN adopted Clinical Studies

SOP Number: gSOP-14-02	**Effective Date:** 28th July 2022
Version Number: 2.0	**Review Date**: 3 years (or as required)

1. BACKGROUND

This is a University of Hertfordshire (UH) standard operating procedure (SOP).

A research protocol is an essential document which provides the research team with a plan for undertaking the study. It is a legal document that, once approved by regulatory and ethical bodies, all parties and organisations involved in the study agree to comply with.

This document sets out the procedures to be followed for all staff involved in the preparation of Protocols for clinical research studies which are UH sponsored/co-sponsored or adopted by the UH CTSN. Where there are potential conflicts between different collaborating organisations' SOPs, project level working instructions should be developed, to determine precedence.

It provides guidance on what a research protocol should contain, who should be involved in its formulation and what level of review it must undergo to ensure compliance with UH research policies.

This guidance can be used for any clinical trial. External sponsors may require use of their own SOPs and this will be specified in site agreements. It is the responsibility of the local Principal Investigator (PI) to ensure that study specific SOPs can be operated without conflict to this SOP and in accordance with all organisational polices related to research.

2. PURPOSE

The aim of the protocol (a document that outlines the study plan) is to ensure the safety of the participants whilst answering the specific research questions being investigated.

The protocol should describe the study background and rationale, the study objectives, the design, the participants, trial procedures, the treatment schedule,medications and dosages, safety, data management, monitoring, audit & inspection, ethical and regulatory considerations, the statistical considerations and the study organisation.

3. APPLICABLE TO

All individuals involved with writing, advising on or authorising clinical research protocols that are UH sponsored/co- sponsored or adopted by the UH CTSN and to their collaborators and co-investigators, including Chief Investigators (CI),PIs, consultants, clinical trial pharmacists, research managers, research nurses,research assistants, allied health professionals, trial coordinators, data managers and students.

4. RESPONSIBILITIES

The CI or delegate is responsible for the design and development of research protocols. CIs are also responsible for ensuring that the approved protocol is complied with by both participants and the research team.

The investigators should sign and date the signature page of the current protocol and organisations should refer to the protocol in their agreements about the study.

5. PROCEDURE

The Health Research Authority (HRA), in collaboration with others, have developed a number of tools (including protocol templates) to assist researchers and sponsors in making high quality applications and to navigate the regulatory landscape. For more information visit the HRA website.

For guidance with protocols for interventional studies, please see: http://www.spirit-statement.org/

Please refer to protocol template CTSN TP-70 and the qualitative protocol template CTSN TP-71.

For studies adopted by the UH CTSN, the UH CTSN need to be involved in the development of the protocol. Where the UH CTSN has been delegated to write the research protocol, the UH CTSN protocol template may be used. (CTSN TP-70). The procedure will be as defined in the local working practice documentation.

The protocol should be version controlled (gSOP-39 Version control of Study Documents). Version numbers and dates should be allocated during the drafting process. The final protocol that is submitted to the REC/Ethics committee should be numbered as Version 1.0 with the date of finalisation.

If protocol amendments are made, the protocol version number and date must be updated.

The protocol and amendments must be signed by the Sponsor.

5.1 General Information

The following points should be included in the protocol document:

- Protocol title, Protocol number (Sponsor to have input into this number), Integrated Research Application System (IRAS) number and date. Any amendment(s) should also bear the amendment number(s) and date(s).

- Name and address and outline of the division of responsibilities for the Sponsor/Co-Sponsor and

Monitor (if other than the Sponsor).

- Name and title of the person(s) authorised to sign the protocol and the protocol amendment(s) for the sponsor.
- For clinical trials of investigational medicinal products (CTIMPs), the Name, title, address, and telephone number(s) of the Sponsor's medical expert (or dentist when appropriate) for the trial.
- Name and title of the Investigator(s) who is (are) responsible for conducting the trial, and the address and telephone number(s) of the trial site(s).
- For CTIMPs, the Name, title, address, and telephone number(s) of the qualified physician (or dentist, if applicable), who is responsible for all trial-site related medical (or dental) decisions (if other than Investigator).
- Name(s) and address(es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

5. 2 Background Information

- Summary of the known and potential risks and benefits, if any, to human subjects.
- A statement that the trial will be conducted in compliance with the protocol, Good Clinical Practice (GCP) and the applicable regulatory requirement(s).
- Description of the population to be studied.
- References to literature and data that are relevant to the trial, and that provide background for the trial.
- Rationale for why the research question(s) being asked is important.

For CTIMPs the following additional information should be provided;

- Name and description of the investigational product(s).
- A summary of findings from nonclinical studies that potentially have clinical significance and from clinical trials that are relevant to the trial.

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- Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).

5.3 Trial Objectives and Purpose

A detailed description of the objectives and the purpose of the study.

5.4 Trial Design

The scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design. A description of the trial design, should include:

- A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.
- A description of the type/design of trial to be conducted (e.g., double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages.
- A description of the measures taken to minimise/avoid bias, including randomisation and blinding.
- A description of the trial intervention(s). For CTIMPs this should include the dosage and dosage regimen of the investigational product(s). Also include a description of the dosage form, packaging, and labelling of the investigational product(s).
- The expected duration of participant's participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.
- A description of the "stopping rules" or "discontinuation criteria" for individual participants, parts of trial and entire trial.
- For CTIMPs, accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.
- Maintenance of trial treatment randomisation codes and procedures for breaking codes.
- The identification of any data to be recorded directly on the Case Report Forms (CRFs) (i.e., noprior written or electronic record of data), and considered to be source data.

5.5 Selection and Withdrawal of Participants

- Methods by which participants will be identified and recruited.
- Participant inclusion criteria.
- Participant exclusion criteria.
- Participant withdrawal criteria (i.e., terminating investigational product treatment/trialtreatment) and procedures specifying:

  (a) When and how to withdraw participants from the trial/investigational product treatment.
  (b) The type and timing of the data to be collected for withdrawn participants.
  (c) Whether and how participants are to be replaced.
  (d) The follow-up for participants withdrawn from investigational product treatment/trial treatment.

5.6 Treatment of Participants (CTIMPs)

- The treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for participants for each investigational product treatment/trial treatment

group/arm of the trial.

- Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.

- Procedures for monitoring participant compliance.

5.7 Intervention of participants (other clinical studies)

- The intervention to be delivered, including the follow-up period(s) for participants for each group/arm of the trial.

- Contraindications for participation.

- Procedures for monitoring participant compliance.

5.8 Assessment of Efficacy/Effectiveness

- Specification of the efficacy/effectiveness parameters.

- Methods and timing for assessing, recording, and analysing of efficacy/effectiveness parameters.

5.9 Assessment of Safety

- Specification of safety parameters.

- The methods and timing for assessing, recording, and analysing safety parameters.

- Procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses.

- The type and duration of the follow-up of participants after adverse events.

ICH GCP requires that both investigators and sponsors follow specific procedures when reporting adverse events/reactions in clinical trials involving IMPs. These procedures should be described un-ambiguously in the safety section of the protocol and may require additional documents that should be referred to in this section e.g.:

- The trial safety management plan (SmPC),
- Reference Safety Information (RSI),
- The Sponsor is responsible for providing this information for this section.

5.10 Statistics

- A description of the statistical methods to be employed, including timing of any planned interim analysis(ses).

- The number of participants planned to be enrolled. In multicentre trials, the numbers of enrolled participants projected for each trial site should be specified. Reason for choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification.

- The level of significance to be used.
- Criteria for the termination of the trial.
- Procedure for accounting for missing, unused, and spurious data.
- Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in the protocol and/or in the final report, as appropriate).
- The selection of participants to be included in the analyses (e.g., all randomised participants, all dosed participants, all eligible participants, evaluable participants).

5.11 Direct Access to Source Data/Documents

The Sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, Institutional Review Board/ Independent Ethics Committee (IRB/IEC) review, and regulatory inspection(s), providing direct access to source data/documents.

5.12 Quality Control and Quality Assurance

Description of procedures to maintain quality control and quality assurance.

5.13 Ethics & Study Administration

- Description of ethical considerations relating to the trial, including details of review body (REC or UH Ethics).
- Arrangements for the day-to-day management of the study.

Methods by which the participants' interests will be safeguarded. For example; the process of risk limitation; how confidentiality or anonymisation of participants' data will be maintained.

- State whether there has been user involvement in design of the study, and whether user involvement will be incorporated as an ongoing aspect of the research.
- State who is funding the research study and what interest they have in its outcome.
- Confirm the sponsorship arrangements for the study.

5.14 Data Handling and Record Keeping

Description of data management procedures.

5.15 Finance and Insurance

Financing and insurance if not addressed in a separate agreement.

5.16 Publication Policy and dissemination of results

Publication policy, if not addressed in a separate agreement including considerations for future studies, translational work and conversion of findings into evidence based work. Describe how you will disseminate results to participants (how has this been addressed in the IRAS application form, if applicable). State when and how the trial results will be made public (e.g., poster presentation at conferences, publication in mainstream journal, publicly assessable database etc.).

5.17 Archiving of study records and data

Location and period of archiving.

6.0 RELATED SOPS & DOCUMENTS

- gSOP-02-Adverse Event Reporting (Sponsored/Co-sponsored)
- gSOP-05-Adverse Event Reporting (Hosted)
- gSOP-23 -Audit and Inspection
- gSOP-04- Informed Consent
- gSOP-06- Trial Master File/Site File
- gSOP-07- Research Training
- gSOP-09- Amendments
- gSOP-10- Serious Breaches
- gSOP-11- Sponsor Oversight
- gSOP-13- Research Applications
- gSOP-15- Designing a Case Report Form
- gSOP-16- DSURS
- gSOP-17- Archiving
- gSOP-21- End of Trial Procedures
- gSOP-22- End of Trial Reports
- gSOP-28- Management of Source Data
- CTSN TP-70 Protocol Template

7.0 APPENDICES

- Appendix 1 – Definitions
- Appendix 2 – Protocol Design Flowchart

8.0 VERSION HISTORY

Version Number	Effective Date	Reason for Change
2.0	28th July 2022	Review of content Expanding scope to all clinical trials not just CTIMPs

9.0 AUTHORSHIP & APPROVAL

Author

Signature: 	**Date:** **16 June 2022**

Pro-Vice Chancellor (Research & Enterprise) Approval

Signature: Prof J M Senior 	**Date:** **16 June 2022**

10. AGREEMENT (MOVE ON TO SEPARATE SHEET BEFORE PRINTING)

Please detach and retain within <u>your training files</u>

I have read and understood the contents and requirements of this SOP (ref gSOP-14-02) and accept to follow University policies implementing it.

Recipient

Signature: ……Date: ……..

Name & Position: ……

Appendix 1: Definitions

Case Report Form (CRF)
A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the Sponsor on each trial subject.

Chief Investigator (CI)
A registered Physician, Dentist, Pharmacist or Nurse who has overall responsibility for the conduct of the trial.

Clinical Trial
A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or control) to evaluate the effects of those interventions on health outcomes.

Clinical Trial of Investigational Medicinal Product (CTIMP)

A study that looks at the safety or efficacy of a medicine/food stuff/placebo in humans as defined by the Medicines for Human Use Regulations (2004).

Good Clinical Practice (GCP)
As defined in the Regulations.

International Conference on Harmonisation (ICH)
The ICH produced a series of guidelines in 1996, E6 being the guideline on Good Clinical Practice, otherwise known as (ICH-GCP).

Investigational Medicinal Products (IMP)
A pharmaceutical form of an active substance or placebo being tested, or used as a reference in a clinical trial. This includes a medicinal product which has a marketing authorisation but is, for the purposes of the trial -
(a) used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation,
(b) used for an indication not included in the summary of product characteristics under the authorisation for that product, or
(c) used to gain further information about the form of that product as authorised under the authorisation

Principal Investigator (PI)
A registered Physician, Dentist, Pharmacist or Nurse who has responsibility for the conduct of the trial at a host site.

The Medicines & Healthcare products Regulatory Agency (MHRA)
UK competent authority responsible for regulation of clinical trials.

The Regulations
Medicines for Human Use (Clinical Trial) Regulations 2004 transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031. This became effective on the 1st May 2004. An amendment to implement Directive 2005/28/EC was made to the Regulations as Statutory Instrument 2006 no 1928.

Appendix 2
Protocol Design Flowchart