

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 Managed Clinical Studies

SOP Number: gSOP-14-01	Effective Date: 26 th April 2018
Version Number: 1.0	Review Date: 3 years (or as required)

1. BACKGROUND

This is a University of Hertfordshire standard operating procedure. University of Hertfordshire (UH) acknowledges West Hertfordshire Hospitals Trust (WHHT) R&D which has allowed UH to use the SOPs developed by WHHT where possible, modified for local implementation.

This document sets out the procedures to be followed for all staff involved in the preparation of Protocols for clinical research studies which are sponsored/co-sponsored or managed by the University of Hertfordshire (UH). 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 the University of Hertfordshire research policies.

This SOP is specifically for CTIMPs, however in the absence of a documented procedure can be used as guidance for any other clinical study.

External sponsors may require use of their own SOPs and this will be specified in site agreements. It is the responsibility of the local PI to ensure that study specific SOPs can be operated without conflict to this SOP and in accordance with all organisational policies 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 objectives, the design, the participants, the treatment schedule, medications and dosages, the statistical considerations and the study organisation.

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3. APPLICABLE TO

All individuals involved with writing, advising on or authorising clinical research protocols sponsored/co-sponsored or managed by UH and to their collaborators and co-investigators, including Chief Investigators, Principal Investigators, consultants, clinical trial pharmacists, research managers, research nurses, research assistants, allied health professionals, trial coordinators, data managers and students.

4. RESPONSIBILITIES

The Chief Investigator (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.

5. PROCEDURE

The Health Research Authority, 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/>

HRA templates for trial protocols are available from the HRA website.

5.1 General Information

- Protocol title, 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 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

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5.2 Background Information

- 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
- Summary of the known and potential risks and benefits, if any, to human subjects
- Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s)
- 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

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 treatment(s) and 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
- 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

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- The identification of any data to be recorded directly on the Case Report Forms (CRFs) (i.e. no prior written or electronic record of data), and considered to be source data

5.5 Selection and Withdrawal of Participants

- Participant inclusion criteria
- Participant exclusion criteria
- Participant withdrawal criteria (i.e. terminating investigational product treatment/trial treatment) 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

- 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 Assessment of Efficacy

- Specification of the efficacy parameters
- Methods and timing for assessing, recording, and analysing of efficacy parameters

5.8 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

5.9 Statistics

- A description of the statistical methods to be employed, including timing of any planned interim

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analysis(es)

- 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)

5.10 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.

5.11 Quality Control and Quality Assurance

Description of procedures to maintain quality control and quality assurance.

5.12 Ethics

Description of ethical considerations relating to the trial.

5.13 Data Handling and Record Keeping

Description of data management procedures.

5.14 Finance and Insurance

Financing and insurance if not addressed in a separate agreement.

5.15 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). 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.).

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6.0 RELATED SOPS & DOCUMENTS

- gSOP-02-Adverse Event Reporting (Sponsored/Co-sponsored)
- gSOP-05-Adverse Event Reporting (Hosted)
- gSOP-03 -Trial Auditing
- 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- Study Closure
- gSOP-22- End of Trial Reports
- gSOP-28- Management of Source Data

7.0 APPENDICES

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

8.0 VERSION HISTORY

Version Number	Effective Date	Reason for Change

9.0 AUTHORSHIP & APPROVAL

Author

Signature:	Date:
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Pro-Vice Chancellor (Research & Enterprise) Approval

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

Please detach and retain within your training files

I have read and understood the contents and requirements of this SOP (ref gSOP-14-01) and accept to follow University policies implementing it.

<p>Recipient</p> <p>Signature:Date:</p> <p>Name & Position:</p>
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Please retain copy of the signed form for your reference in your training file

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 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).

Principal Investigator (PI)

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

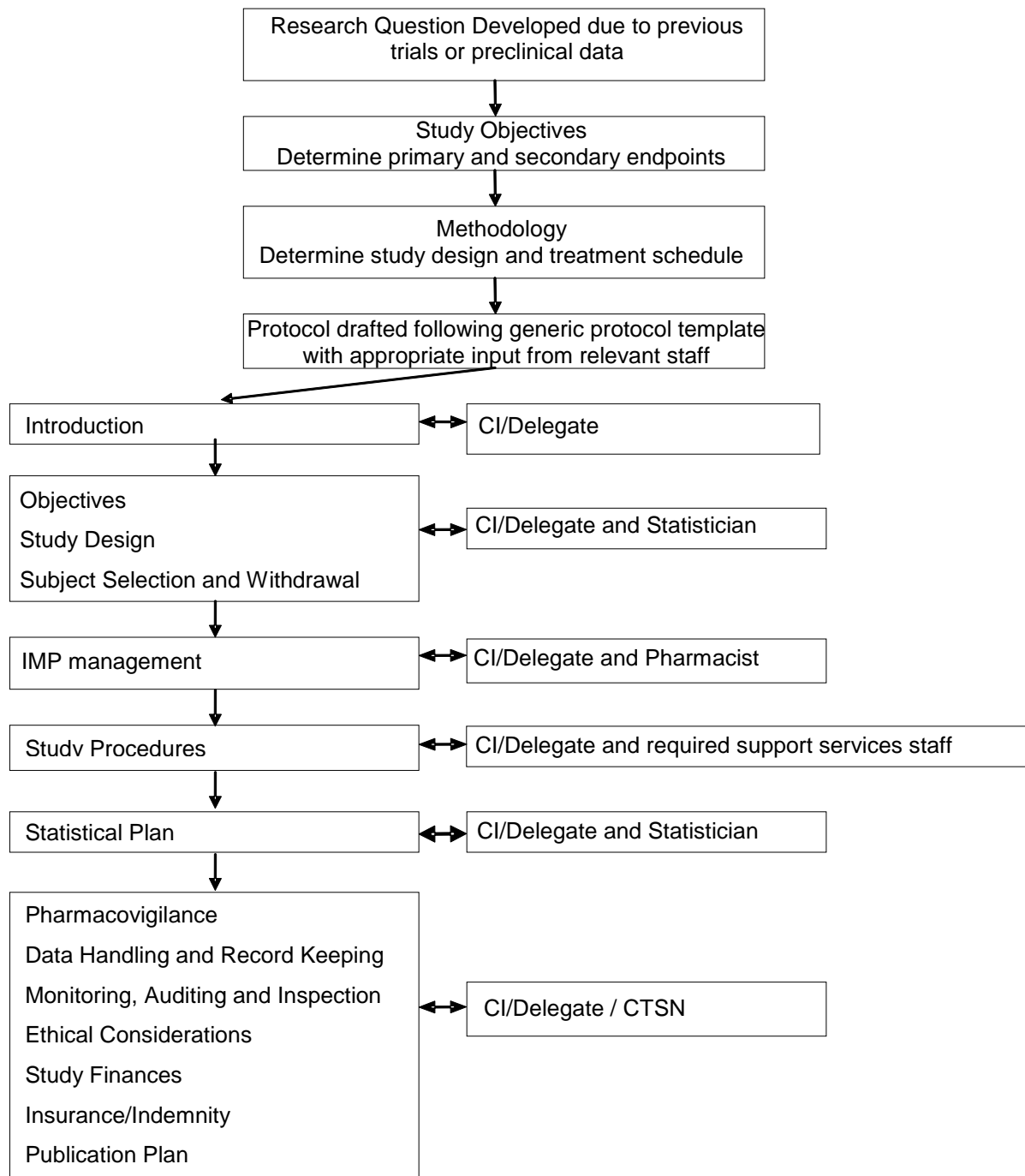
The Medicines & Healthcare products Regulatory Agency (MHRA)

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



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