WRITING RESEARCH PROTOCOLS

Research & Development

Standard Operating Procedure for Writing Research Protocols Intended for West Hertfordshire Hospitals NHS Trust Sponsored Trials

SOP Number : SOP-14-05	**Effective Date:** October 2021
Version Number: v05	**Review Date:** 2 - 3 years

1.0 BACKGROUND

This document sets out the procedures to be followed by all West Hertfordshire Hospitals Trust (WHHT) staff who are involved in the preparation of protocols for research studies which are sponsored by WHHT.

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 Trust's research policies.

2.0 PURPOSE

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

All research protocols must receive Research Ethics Committee (REC) approval, Medicines and Healthcare products Regulatory Agency (MHRA) approval (if appropriate) and Health Research Authority (HRA) approval (confirmation of Capacity and Capability, if required). Other approvals should be sought where appropriate, for example, Administration of Radioactive Substances Advisory Committee (ARSAC) approval. For an overview of protocol design see Appendix 2.

WHHT require that the HRA protocol templates are used. There are separate templates available for Clinical Trial of an Investigational Medicinal Product (CTIMP) and for qualitative research. These can both be found on the HRA website via at the following link: Protocol - Health Research Authority

(hra.nhs.uk)

3.0 APPLICABLE TO

Any relevant Trust employee involved with research sponsored by WHHT including, but not limited to, Unit Heads, Chief Investigators (CI), Principal Investigators (PI), Co-investigators, Consultants, Research Fellows, Clinical Trial Pharmacists, Research Managers, Statisticians, Research nurses, Allied Health Professionals, Trial Coordinators, the Research & Development Steering Group (RDSG) & Data Managers.

4.0 RESPONSIBILITIES

The CI or Delegated Individual (DI) is responsible for the design and development of research protocols. The CI is also responsible for ensuring that the approved protocol is complied with by both participants and the Research Team.

5.0 PROCEDURE

The HRA, in collaboration with others, have developed a number of tools to assist researchers and Sponsors in making high quality applications and to navigate the regulatory landscape. For more information visit their link: www.hra.nhs.uk/hra-training/tools/

5.1 General Information

- Protocol title, protocol identifying number, and date. Any amendment(s) should also bear the amendment number(s) and date(s)
- Name and address of the 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
- 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)
- 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

- Name and description of the investigational product(s) where applicable
- 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 of IMP, dosage, dosage regimen, and treatment period(s) where applicable
- 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) where applicable. Also include a description of the dosage form, packaging, and labelling of the investigational product(s)
- The expected duration of subject 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 subjects, parts of trial and entire trial
- Accountability procedures for the investigational product(s), including the placebo(s) and

comparator(s), if any, where applicable

- 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. no prior written or electronic record of data), and to be considered to be source data.

5.5 Selection and Withdrawal of Participants

- Subject inclusion criteria

- Subject exclusion criteria

- Subject withdrawal criteria (i.e. terminating investigational product treatment/trial treatment) and procedures specifying:

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

5.6 Recruitment and Treatment of Participants

- Details of the informed consent process that will be undertaken; can consent be obtained via the telephone or is written consent required.

- 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 subjects 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 subject 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 subjects after adverse events

5.9 Statistics

- A description of the statistical methods to be employed by the trial statistician, who will detail this ensuring they have included timings of any planned interim analysis(ses)

- The number of subjects planned to be enrolled. In multicentre trials, the numbers of enrolled subjects 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 subjects to be included in the analyses (e.g. all randomised subjects, all dosed subjects, all eligible subjects, evaluable subjects)

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 patients (how has this been addressed in the Integrated Research Application System (IRAS) application form).

6.0 RELATED DOCUMENTS

- SOP-02- SAEs (Sponsored)
- SOP-04- Informed Consent
- SOP-06- Trial Master File (Sponsored)
- SOP-07- Research Staff Training
- SOP-08- Role of CI, pharmacy, nuclear medicine and R&D
- SOP-09- Amendments
- SOP-10- Serious Breaches (Sponsored)
- SOP-11- Sponsor Oversight
- SOP-13- Research Applications
- SOP-16-DSURs (Sponsored)
- SOP-17- Archiving of Essential Documents
- SOP-21- Study Closure
- SOP-28- Management of Source Data

7.0 APPENDICES

Appendix 1.0 - Definitions
Appendix 2.0 - Protocol Design Flowchart

8.0 VERSION HISTORY

Revision Chronology:		
Version Number	**Effective Date**	**Reason for Change**
SOP-14-05	**October 2021**	1. Change from general Standard Operating Procedures (gSOP) to SOP 2. Removal of the '10.0 Agreement' from the template - all agreement signatures will be collated on a new 'SOP Signature Sheet Document' 3. Other minor amendments and clarification of terms following review, including the link to the HRA protocol templates
gSOP-14-04	**10/2017**	Minor amendments following review
gSOP-14-03	**07/05/2014**	Minor amendments following review
gSOP-14-02		SOP modified for implementation at ENHT/WHHT
gSOP-14-01 (MVCC)		SOP modified for implementation at MVCC

9.0 AUTHORSHIP & APPROVAL

Author

Signature  **Date** 28/10/2021

R & D Steering Group Approval

Signature  **Date** 28/10/2021

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)
The investigator with overall responsibility for the research. In a multi-site study, the CI has co-ordinating responsibility for research at all sites. All applications for ethical review should be submitted by the CI. For Trust sponsored trials, the CI had been delegated the pharmacovigilance responsibility for identification, recording and reporting of safety events, including submission of Development Safety Update Reports (DSURs) to the MHRA and REC.

Clinical Trial
A clinical study in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic, or other types of interventions. A Study Type.

Good Clinical Practice (GCP)
Good Clinical Practice is a set of internationally recognised ethical and scientific quality requirements which must be observed for designing, conducting, recording and reporting clinical trials that involve the participation of human subjects.

International Conference on Harmonisation (ICH)
International Conference for Harmonisation, a collaboration between regulators and the pharmaceutical industry in Europe, the United States and Japan to establish common standards for clinical trials. ICH GCP is a widely recognised standard for Good Clinical Practice in clinical trials.

Principal Investigator (PI)
The investigator responsible for the research site. There should be one PI for each research site. In the case of a single-site study, the chief investigator and the PI will normally be the same person.

The Medicines & Healthcare products Regulatory Agency (MHRA)
The MHRA is the competent authority for the UK in relation to the Directive 2001/20/EC and the Clinical Trials Regulations, and for Medical Devices, the competent authority in relation to the Medical Devices Regulations 2002.

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 (with responsibilities)