St George's University Hospitals NHS
NHS Foundation Trust

Standard Operating Procedure (SOP)

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Signature of Authorisor			

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Standard Operating Procedure (SOP)
Protocol Design

SOP Chronology		
SOP Version Number:	**Reason for Change:**	**Author:**
V1.0	Original Version	Lucy H H Parker
V 2.0	Updated Logo and Trust Name – reference to SPIRIT guidelines & inclusion of randomisation/code-breaking	Fran Mautadin

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1. Background

A research protocol is the legal document that outlines the procedure to answer the aims and objectives defined in the study. The protocol must be carefully designed to safeguard the health and safety of the participants, as well as answer specific research questions. A protocol describes who the participants are in the study; the schedule of tests, procedures, medications, and dosages; and the length of the study. While enrolled in a clinical trial, participants following a protocol are seen regularly by the research staff to monitor their health and to determine the safety and effectiveness of their treatment.

Any proposed amendment to the protocol version approved by REC must be reviewed and approved by the Joint Research and Enterprise Office (JREO) before the amendment is submitted to the ethics committee and/or MHRA where relevant as changes may affect the terms of sponsorship and insurance cover. Refer to JREOSOP0011 Management of Amendments.

2. Joint Research and Enterprise Office (JREO) Policy

All JREO SOPs will be produced and approved in accordance with the JREO SOP on SOPs and must be used in conjunction with local NHS Trust and St George's policies and procedures.

The JREO acts as the representative of both St George's University of London (SGUL) and St George's University Hospitals NHS Foundation Trust (SGHT). St George's will be the official name used on all SOPs to represent both institutions acting as Sponsor.

3. Scope

This SOP describes writing a research protocol to Good Clinical Practice (GCP) as required by the Medicines for Human Use (Clinical Trials) Regulations 2004, incorporating GCP amendments (2006) and the Research Governance Framework 2005. It is relevant for any project involving humans, their tissue and/or data.

4. Definitions

SPIRIT – Standard Protocol Items : Recommendations for Interventional Trials.

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5. Responsibilities

It is the responsibility of the Chief Investigator (CI) of the study to ensure that the study protocol adheres to the contents as laid out by International Conference on Harmonisation Good Clinical Practice (ICH GCP)

It is the responsibility of the JREO to ensure that the protocol templates designed by the JREO adhere to ICH GCP and incorporate the essence of the SPIRIT 2013 statement..

6. Procedure

The JREO has produced a library of protocol templates to suit the most common research questions at St George's

CTIMP protocol template (which must be used for CTIMP studies that will be sponsored by St George's)
Clinical Investigation plan for the use of a Medical Device (currently generic)
non- CTIMP protocol template that still requires Investigational Product management by Pharmacy
A non-CTIMP non-pharmacy protocol template
An observational/ questionnaire study template
Retrospective data protocol template

Each template also incorporates a synopsis table which will contain fields that are representative of data required by publicly available databases such Clinicaltrials.gov which are aimed to assist in the registration process. Refer to JREOSOP0022 Publicly Accessible Databases

As per GCP, the contents of a study protocol should include the following topics.

6.1 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 (if applicable)

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- Name and title of the investigator(s) who is (are) responsible for conducting the trial, and the address and telephone number(s) of all participating 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) (if applicable)
- 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. (if applicable)

6.2 Background Information

- A summary of findings from non-clinical studies that potentially have clinical significance and from clinical studies which are relevant to the study.
- 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, GCP and the applicable regulatory requirement(s).
- Description of the population to be studied.
- References to literature and data that are relevant to the study and that provide background for the study .

Specific to CTIMP/ Device trials:

- Name and description of the Investigational Medicinal Product(s)(IMPs)/medical device
- Description of and justification for the route and mode of administration, dosage, dosage regimen, and treatment period(s) / application or use
- Description of any Non Investigational Medicinal Products (NIMPs), name, dose, route and mode of administration that the patient will be co-prescribed but may not be the IMP(s) under investigation

6.3 Study Objectives and Purpose

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

6.4 Study Design

The scientific integrity of the study and the credibility of the data from the study 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 study .

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- 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.
- The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.
- Definition of end of trial (normally last participant, last visit)
- The identification of any data to be recorded directly on the CRFs (i.e. no prior written or electronic record of data), and to be considered to be source data.

Specific to CTIMPS/ Device:

- 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). Source or brand name PL number where applicable or for device studies CE number
- A description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial and entire trial
- Maintenance of trial treatment randomisation codes and procedures for breaking codes (if applicable)
- Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.
- Storage of the IMP, administration, any incompatibilities to be considered.

6.5 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:
    i. When and how to withdraw subjects from the trial/ investigational product treatment (if applicable) including wash out procedure if required
    ii. The type and timing of the data to be collected for withdrawn subjects.
    iii. Whether and how subjects are to be replaced.
    iv. The follow-up for subjects withdrawn from investigational product treatment/trial treatment (if applicable)

Details of recruitment of subjects

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6.6 Treatment of Participants

Specific to 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 subjects for each investigational product treatment/trial treatment group/arm of the trial (if applicable)
- Randomisation procedure – who is responsible, level of blinding, who is to remain blind and unblinding in event of emergency
- NIMPs/Medication(s)/treatment(s) permitted (including rescue medication) and Concomitant medication not permitted before and/or during the trial.
- Procedures for monitoring subject compliance.
- Clear description of each visit with timings, frequencies and tests to be performed. Acceptable visit windows should be defined.
- Incidental findings and the onward management

For other studies

- Detailed methodology of what will happen to participants

What instruments/questionnaires will be used

6.7 Assessment of Efficacy (if applicable)

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

6.8 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.
- Clearly define what does/does not need reporting i.e expected and related
- Death reporting requirements
- Clearly defined process and responsibilities
- Considerations specific to vulnerable subjects, such as chaperoning for participants who are minors

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6.9 Statistics

- A description of the statistical methods to be employed, including timing of any planned interim analysis(es). Depending on the nature of the study, the inclusion of advice from a statistician would be expected.
- Randomisation codes And lists- who and how they are generated- general details on treatment ratios- protocol should not detail randomisation block sizes this will be in a separate document- any stratification.
- The number of subjects planned to be enrolled, with statistical rationale. 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 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).

6.10 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)/host site institution(s) must permit trial-related monitoring, audits, REC review, and regulatory inspection(s), providing direct access to source data/documents, even personal documents, as long as the participant consents to this.

6.11 Quality Control and Quality Assurance

Description of procedures to maintain quality control and quality assurance.

6.12 Ethics

Description of ethical considerations relating to the trial.

6.13 Data Handling and Record Keeping

Description of data management procedures. Including a description of how long the study records will be archived for.

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6.14 Finance and Insurance

Financing and insurance if not addressed in a separate agreement.

6.15 Publication Policy

Publication policy, if not addressed in a separate agreement.

7. References

ICH GCP (1996)

http://www.spirit-statement.org/

Research Governance Framework 2nd Edition 2005

8. Appendices

No appendices associated with this SOP.

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