Imperial College London

Research Governance and Integrity Team

Imperial College Healthcare NHS Trust

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Writing a Protocol to Good Clinical Practice (GCP)

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Version	Date	Reason for Change
Version 1.0	14 Sep 2006	1st Edition
Version 2.0	25 Jun 2007	Annual review
Version 3.0	27 Jun 2008	Annual review
Version 4.0	08 Feb 2010	Formation of Joint Research Office
Version 5.0	14 Jul 2011	Annual Review
Version 6.0	30 Nov 2012	Annual Review
Version 7.0	18 Feb 2015	Scheduled Review
Version 8.0	25 Oct 2017	Scheduled Review
Version 9.0	10 Jan 2019	Updated in line with Feedback Errors
Version 10.0	24 Jan 2020	Addition of info and requirement on incidental findings. Updated wording from NHS litigation to NHS Resolution within appendix 2
Version 11.0	19 Oct 2020	Scheduled Review Template removed and administrative changes to SOP. JRCO name change to RGIT.
Version 12.0	05 Mar 2024	Scheduled Review

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1. PURPOSE

This SOP describes writing a research protocol to Good Clinical Practice (GCP) as required by the Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments where applicable incorporating elements of International Conference on Harmonisation Good Clinical Practice (ICH GCP E6 R2). The primary focus of the SOP is clinical trials of investigational medicinal products (CTIMPs) that fall under this legislation. It is also relevant for any project involving humans, their tissue and/or data.

2. INTRODUCTION

A research protocol is the *legal* document that outlines the study plan for a clinical trial. The plan 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.

It is expected that the RGIT protocol template in Appendix 1 is used for Clinical Trials of Investigational Medicinal Products (CTIMPs). Whilst any deviation from this template should be discussed with RGIT.

Appendix 2 contains a template protocol for non CTIMP studies.

The procedures described in this SOP will focus mainly on studies of CTIMPs; for all other types of studies, disregard non-applicable sections.

Any amendment to the REC/HRA and MHRA (for CTIMPs) approved protocol must be reviewed and approved by the Research Governance and Integrity Team (RGIT) following the completion of the amendment tool before the amendment is submitted to the ethics committee and/or MHRA, as changes may affect the terms of sponsorship and insurance cover. For further information, refer to Amendments to Healthcare Research RGIT_SOP_006.

3. PROCEDURE

As per ICH GCP, the contents of a CTIMP study protocol should include the following topics in line with ICH Harmonised Tripartite Guideline E6: Guideline for Good Clinical Practice section 6

3.1. 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.

3.2. Background Information

- Name and description of the investigational product(s).
- A summary of findings from non-clinical studies that potentially have clinical significance and from clinical trials which 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, 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.

3.3. Study Objectives and Purpose

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

3.4. Study 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 subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any and a description of what constitutes end of study (i.e. last participant, last visit).
- 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.
- Maintenance of trial treatment randomisation codes and procedures for breaking codes.
- 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.

3.5. 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.

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.

3.6. 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 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.

3.7. Assessment of Efficacy

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

3.8. 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 inter-current illnesses.
- The type and duration of the follow-up of subjects after adverse events.
- Reporting of incidental findings if applicable, including review of results, management of review and notification of findings.

All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting.

Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.

3.9. Statistics

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

3.10. 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, IRB/IEC review, and regulatory inspection(s), providing direct access to source data/documents.

3.11. Quality Control and Quality Assurance
Description of procedures to maintain quality control and quality assurance.

3.11.1. **Critical process and data identification**: During protocol development, the sponsor should identify those processes and data that are critical to ensure human subject protection and the reliability of trial results.

3.11.2. Risk control: Risk reduction activities may be incorporated in protocol design and implementation.

3.12. Ethics/HRA
Description of ethical considerations and applicable regulations relating to the trial.

3.13. Data Handling and Record Keeping
Description of data management procedures.

3.14. Finance and Insurance
Financing and insurance if not addressed in a separate agreement.

3.15. Publication Policy
Publication policy, if not addressed in a separate agreement.

4. REFERENCES

ICH Harmonised Tripartite Guideline for Good Clinical Practice E6R2 (cited 19 May 2023)

EU COMMISSION DIRECTIVE 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of (cited 19 May 2023)

Amendments to Healthcare Research RGIT_SOP_006

5. APPENDICES

The following Appendices list the following Templates associated to this SOP which can be found on the SOP, Associated Documents & Templates page.

Appendix 1: Template Protocol for CTIMPs – RGIT_TEMP_026
Appendix 2: Template Protocol for non-CTIMPs - RGIT_TEMP_027