



CORE STANDARD OPERATING PROCEDURE

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SOP Title: Registration, Applications, Amendments and Reporting

SOP Number

011

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Registration, Applications, Amendments and Reporting

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1. PURPOSE

The purpose of this SOP is to describe the procedures for the registration, submission and maintenance of clinical research information including end reporting to the Competent Authority (CA), Research Ethics Committee (REC), and other relevant organisations.

2. INTRODUCTION

Clinical research requires approval from organisations, depending on the nature of the research, location, personnel and resources involved:-

- Competent Authority - Any clinical trial which falls within the scope of relevant national regulations usually requires authorisation from the Competent Authority or national equivalent.
- Research Ethics Committee – For most clinical studies in human participants, the approval of a Research Ethics Committee (REC) must be sought. In certain jurisdictions, Competent Authority approval may include ethical approval.
- Country / Regional specific approval e.g. Health Research Authority (HRA) and Health and Care Research Wales (HCRW) in the NHS in England and Wales.
- Host organisation – Studies involving participants, data, staff or facilities may require local approval of the host organisation.

Research transparency is essential so that participants and patients are protected from unnecessary research and patients benefit from improved outcomes and are informed by high quality research. All clinical trials should be registered in a publicly accessible database and it is a condition of a favourable ethical opinion to do so. For all other research studies, it is a good practice expectation.

During the conduct of the research, there is an obligation to report on its progress and safety. Once the research is ended there is also an ethical or in some cases regulatory obligation to make the results publically available. Reports should be such that they are complete and transparent and written in line with internationally endorsed standards.

As the process and regulatory environment are variable across different geographies, this SOP aims to reflect considerations which are generally applicable. As the requirements of individual bodies are variable, it is essential to refer to their specific requirements.

3. SCOPE

The scope of this procedure is for all clinical research studies sponsored by the University of Oxford, but may also be used for other clinical research studies at the discretion of the unit.

4. DEFINITIONS

Competent Authority / National Equivalent

National regulatory body responsible for review, comment and approval of clinical trials, where applicable.

Research Ethics Committee (REC)

Independent body responsible for ensuring the protection of the rights, safety and wellbeing of participants in clinical research, and for review, comment and approval of clinical research. The equivalent body in the United States of America would be referred to as the Institutional Review Board (IRB).

Health Research Authority (HRA) and Health and Care Research Wales (HCRW)

Organisations that work together in the UK to regulate different aspects of health and social care research. HRA and HCRW approval is required for all study-based research in England and Wales that involves NHS organisations where the NHS organisation has a duty of care to participants, either as patients/service users or NHS staff/volunteers. References to participants include people whose data or tissue is involved in a research project.

NB: Studies with sites in Northern Ireland or Scotland are supported through existing UK-wide compatibility systems where each country accepts relevant centralised assurances from national coordinating functions to avoid duplication.

Host Organisation

The Organisation/Institution (e.g. hospital, clinic, general practice) responsible for the facility/site where the clinical research is to be conducted.

EudraCT

Central database of clinical trials conducted in any European member state, hosted by the European Medicines Agency.

Substantial Amendment

An amendment to the terms of the application, or to the protocol or any other supporting documentation, that is likely to affect to a significant degree:

- the safety or physical or mental integrity of the participants of the study;
- the scientific value of the study;
- the conduct or management of the study; or
- the quality or safety of any IMP used.

Non-Substantial Amendment

Any amendment not falling within the definition of a substantial amendment will be considered to be non-substantial.

Annual Progress Report (APR)

A progress report that should be submitted annually to the Research Ethics Committee (REC) which gave the favourable opinion.

There are separate forms for different types of research, these are available on the HRA website.

Development Safety Update Report (DSUR)

For Clinical Trials of an Investigational Medicinal Product (CTIMPs), this is a legally required, annual safety report submitted to the Competent Authority, REC, and other parties as applicable.

The DSUR should take into account all new available safety information received during the reporting period for all trials with the same IMP and sponsored by the same organisation.

5. RESPONSIBILITIES

Chief Investigator or Delegate

Preparation, quality review and submission of the protocol and all required supporting documents and any subsequent amendments. Following Sponsor approval, submission of these documents to relevant bodies. Submission of Annual Progress Reports (APR) and Development Safety Update Reports (DSUR) to Sponsor and relevant bodies. Report to Sponsor any stoppage in study activity in any form which is anticipated to be or proves to be longer than 1 month and may result in the need to implement a formal temporary halt.

Sponsor

Review and approval of submitted documentation, together with continued oversight of progress.

6. SPECIFIC PROCEDURE

6.1 Registration

All interventional clinical trials must be registered on a publicly accessible database before recruitment of the first participant to meet the relevant Research Ethics Committees condition of approval. More information on suitable registries is available at <http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html>. Registration must be in compliance with any requirements of the funder of the research. For CTIMPs conducted in the EU, a EudraCT number must be obtained. This reference should then be used in all applications.

6.2 Applications

Applications should be in compliance with applicable local laws and regulations.

The relevant organisation applications and associated documents should be checked for consistency and coherence, and approved by the Sponsor before being signed by the Chief Investigator or delegate.

All documents must be appropriately version controlled. See University of Oxford Core SOP 014 – Version Control.

6.3 Submission package

The requirements of each relevant body with regard to submission package will vary, and each body should be consulted accordingly, both in terms of content and submission procedures. See <https://www.hra.nhs.uk/planning-and-improving-research/research-planning/prepare-study-documentation/> and <https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk> for further information.

The package will typically (but not exhaustively) include:-

Application form

Study-specific documentation, e.g. protocol.

Information relating to the IMP, e.g. Investigational Medicinal Product Dossier (IMPD), Investigator's Brochure (IB) or Summary of Product Characteristics (SmPC).

Patient-facing documents, e.g. Participant Information Sheet, Informed Consent Form.

6.4 Response, Notifications and Approvals

Favourable opinions or approvals (authorisations) must be received in writing from all relevant bodies before study-related procedures may begin. The exception to this is if a change is related to an Urgent Safety Measure (see University of Oxford Core SOP 010 – Urgent Safety Measures). Any queries or requirements by any appropriate body should be resolved to the satisfaction of the relevant body and the Sponsor. Such opinions and approvals must be filed appropriately in the Trial Master File, and maintained and updated in the event of subsequent amendments.

6.5 Amendments

Following review and approval by the Sponsor, submission of a notification of a substantial amendment must be made to the relevant bodies. Also required will be a description of, and reasons for, the amendment, and copies of the amended documents. Further information is available on the websites of relevant bodies.

Non-substantial amendments should be recorded and reviewed by the Sponsor, and notified to the REC and/or country/regional specific approval body (e.g. HRA and HCRW in England and Wales) according to current guidance on the IRAS amendments help page. The host organisation may also need to be notified according to local requirements.

6.6 Reporting

The CI shall submit throughout the study, and on request, progress reports to the relevant bodies and the Sponsor according to their requirements. These may include Annual Progress Reports (APRs) and Developmental Safety Update Reports (DSURs) (see University of Oxford Core SOP 003 – Safety Reporting).

The CI shall report to Sponsor any stoppage in study activity in any form which is anticipated to be or proves to be longer than 1 month and may result in the need to implement a formal temporary halt, following the amendment procedure in section 6.5.

6.7 At the end of the study

An End of Study notification or early termination report will be submitted to the relevant bodies including Sponsor in compliance with country-specific requirements and timelines.

A final report and/or publication will be submitted to relevant bodies including Sponsor according to their country-specific requirements and timelines.

For all CTIMPs conducted in the EU, results must be uploaded to the EudraCT database within 1 year of the end of trial declaration (6 months for paediatric trials). For all interventional trials, information on registries should also be updated during and at the end of the study. Any updates should be documented within 1 year, or less if specified by the registry.

7. RELATED DOCUMENTS

University of Oxford Core SOP 003 – Safety Reporting
 University of Oxford Core SOP 010 – Urgent Safety Measures
 University of Oxford Core SOP 014 – Version Control

8. REFERENCES

EudraCT: <https://eudract.ema.europa.eu/>
 ICH Tripartite Guideline For Good Clinical Practice, 1996 and revision
 EU Clinical Trial Directive 2001/20/EC
 Health Research Authority: <https://www.hra.nhs.uk/>
 IRAS amendments help page:
<https://www.myresearchproject.org.uk/help/hlpamendmentsresearch.aspx>
 Registries information: <http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html>.

9. CHANGE HISTORY

Version No.	Effective Date	Significant Changes	Previous Version No.
1.0	02 July 2015	First version of SOP	n/a
2.0	16 July 2018	Changes to the front page and scope to align with updated core SOP template. Addition of HRA and information on temporary halts	1.0
3.0	See first page	Change of SOP title to include Registration. New paragraph added to Introduction. Changes to HRA definition, addition of APR and DSUR definitions. The addition of a new section for registration requirements. Updated guidance on processing non-substantial amendments. The expansion of end of study report requirements in 6.7 and reference to Core SOPs on safety reporting, urgent safety measures and version control. Change to Authoriser job title.	2.0