ECTU Central Office SOP ECTU_OP_09: Study Document and Amendments

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Authorship and Approval

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<th>Author/Reviewer/ Approval</th>
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Document Revision History

<table>
<thead>
<tr>
<th>Version No</th>
<th>Date</th>
<th>Summary of Revisions</th>
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<tbody>
<tr>
<td>1.0</td>
<td>15th May 2017</td>
<td>Initial creation/new document</td>
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<tr>
<td>2.0</td>
<td>05th Sep 2019</td>
<td>Updated at scheduled review. Document moved to new template. Updated 3.10 to reflect GCP training may not be mandatory for all studies. Update to section 3.1.6. clarifying that the fully signed protocol should be retained in the TMF. Updated reference to the General Data Protection Regulation in section 3.2.2. Updated section 3.4 DMC. Added CTIMP/Non-CTIMP Protocol, PIS/Consent Form, GDPR PIS Templates to the supporting documents.</td>
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1. PURPOSE

Study documents demonstrate the compliance of the investigators, sponsor and the monitor with all applicable regulatory requirements and the principles of Good Clinical Practice (GCP), assist with the successful management of a study, and confirm the validity of the conduct of a study and integrity of data collected.

Documentation can be grouped into two sections, before the clinical phase of a study commences and during the conduct of a study. At the study set up stage the investigator, in consultation with the sponsor, will design the study protocol and trial-related documents. During the conduct of the study, trial-related documents will facilitate the collection of trial-related data and demonstrate compliance.

This Standard Operating Procedure (SOP) describes the procedure for preparing study documents in accordance with ICH-GCP E6 (R2) principles and applicable regulatory requirements. This SOP also describes procedures for amending the study protocol and consent documents.

2. SCOPE

This Standard Operating Procedure (SOP) applies only to studies where the Sponsor does not provide their own SOP for this task. Where a Sponsor SOP is available, this will supersede this SOP.

This SOP applies to clinical researchers designing and participating in studies managed by ECTU.

3. PROCEDURE

3.1 Protocol

3.1.1 The nature and conduct of a study will be described in a clear and detailed protocol. Protocols will be written in accordance with the principles of Good Clinical Practice (GCP) and will describe the objective(s), design, methodology, statistical considerations and organisation of a study. Protocols must be carefully designed to safeguard the health and safety of the participants, as well as answer specific research questions. Templates for CTIMP and non-CTIMP protocols are available.

3.1.2 Investigators leading Clinical Trials of Investigations Medicinal Products (CTIMPs) must create a study protocol.

3.1.3 Investigators leading Non-CTIMP studies should also create a study protocol however it is not mandatory.

3.1.4 All protocols must be version controlled with the version number and date on the title page and all subsequent pages.

3.1.5 Investigators planning to undertake a clinical investigation of a medical device should design their clinical investigation plan/protocol in accordance with ISO 14155.

3.1.6 For CTIMP and regulated Clinical Investigation of Medical Device (CIMD) studies, the protocol, and amendments, will be signed by the representative of the sponsor(s) and the Chief Investigator (CI) to denote agreement to conduct the study according to the protocol. Furthermore, if there is (a) study statistician(s), the lead statistician, or designee, will sign the protocol to verify that the statistical plan and statistical rationale for the study are correct. Similarly the protocol, and amendments, will be signed by Principal Investigators (PIs) at investigator sites. A fully signed protocol should be retained in the Trial Master File (TMF).

3.1.7 For non-CTIMP studies involving the use of a clinical investigational agent (e.g medications being administered as part of an assessment) it is recommended that the protocol, and amendments, be signed by the CI, sponsor representative and lead statistician, or designee,
where a statistician has been appointed. Furthermore, it is recommended that the protocol, and amendments, be signed by the PI at each investigator site.

3.2 Consent Documents and GP letters

3.2.1 All consent documents and GP letters must be version controlled with the version number and date on all pages. These must be created by the Chief Investigator or designee. Templates are available.

3.2.2 Informed consent, from study participants, will be captured in an informed consent form.

3.2.3 Details of the nature of the study will be described to potential participants, in lay language, via a Participant Information Sheet (PIS). To fulfil transparency requirements under the General Data Protection Regulation (GDPR), details of how participants personal data will be used and what their rights are under the law should be described in the PIS or in a separate Data Protection Information Sheet.

3.2.4 If the participant agrees, their GP will be informed of their participation in the study by the investigator, in the form of a letter.

3.2.5 All protocols, consent forms, PISs and GP letters, once authorised by the sponsor, must be submitted for approval from the applicable Research Ethics Committee (REC), approval from the competent authority (e.g. the MHRA), if required, and NHS R&D management approval for the participating NHS sites.

3.3 Adverse Event (AE) Log

3.3.1 Adverse Events (AEs) must be recorded, unless otherwise stated in the study protocol. An AE log may be used to collate and record AEs.

3.3.2 Investigators will record all AEs in the AE log. The AE Log will be based on a template provided by ECTU.

3.4 Data Monitoring Committee (DMC) Charter

3.4.1 Data Monitoring Committees will be established, if required, to review safety data arising during the study.

3.4.2 Investigators leading studies with a DMC must create a DMC charter, based on template and guidance to be found in ECTU Central Office SOP ECTU_TM_12 Preparing for a Data Monitoring Committee (DMC).

3.4.3 It is the Sponsor’s responsibility to ensure that a Charter is in place for the DMC when it is established.

3.5 Site Signature and Delegation Log

A list of appropriately qualified persons, to whom the Principal Investigator (PI) has delegated significant study-related duties, must be initiated and maintained by the PI.

3.6 Subject Pre-Screening Log

The PI will be responsible for maintaining a list of subjects who entered pre-study screening.
3.7 Consent and Subject Status Log

The PI will be responsible for maintaining a list of subjects who consented to take part in the study and subjects who enrolled in the study. Entries will be made in a chronological fashion.

3.8 Monitoring Visit Log

The monitors will enter the necessary details of each site monitoring visit into the monitoring visit log. The PI or designee will countersign each entry.

3.9 Paper Case Report Form (CRF) Version Tracker

Before an updated version of a paper CRF (pCRF) is released for use, the version tracker must be updated by the Trial Manager or Chief Investigator (CI). For CTIMPs or medical device trials, Sponsor’s approval must be given. Monitors will review the CRF tracker during monitoring visits and at other times if requested.

3.10 Study Specific Training Record

The PI is responsible for ensuring that members of the investigator site research team are qualified to undertake their delegated tasks, fully informed of the study protocol and study specific procedures and have completed GCP training (if GCP training applicable). Training will be recorded in the study specific training record.

3.11 Consistency, Review and Distribution

The study Case Report Forms (CRFs), the PIS and any other relevant study information must be consistent with the protocol. The CI, or designee, will ensure that the latest, approved versions of study documents are provided to all PIs, together with any relevant explanatory information. PIs will ensure that local investigator site study team members are fully cognisant with the study protocol and are working with the latest versions of study documents.

3.12 Amendments

3.12.1 Any substantial amendments made to the protocol must be submitted for the required approvals. Amendments cannot be enacted until the required approvals have been granted.

3.12.2 The CI will ensure that study documents are amended to reflect any new study procedures.

3.12.3 The CI will ensure that any new/amended documents are not followed/used before approval has been received from the sponsor(s) and that all of the required approvals have been received e.g. REC, competent authority, local NHS R&D. The notion of substantial amendments and specific examples that require approval are described in section 3 of the European Commission CT-1 communication (2010/C 82/01).

4. RELEVANT DOCUMENTS AND REFERENCES

ECTU Central Office SOP ECTU_TM_12 Preparing for a Data Monitoring Committee (DMC)
ECT Unit/SOPs/Finalised SOP and WPD/TM/SOPs/Current pdf version for use
Protocol Template CTIMP
Protocol Template Non-CTIMP
Patient Information Sheet/Consent Form Template
Data Protection Information sheet
GP Letter Template
Adverse Event Log Template
Delegation Log Template
Screening Log Template
Consent Subject Screening Log Template
Monitoring Visit Log Template
CRF Version Tracker Template
Study Specific Training Record Template

ECT Unit/SOPs/Finalised SOP and WPD/OP/Supporting Document and Templates