Essential documents

Contents:

What are the Essential Documents?

According to the ICH Good Clinical Practice Guidelines E6 (R2) see section 3 essential documents are;

"Those documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements".

Where are these located?

Essential documents are filed at the site/master files which are generated at the beginning of the study, at investigator's/ institution and sponsor's site. Depending on the amount of the essential documents, these files may be split across numerous regulatory ring binders. These must be kept in locked offices and have restricted access.

Why are they important?

Good Clinical Practice requires that all clinical research study information shall be recorded, handled and stored in such a way that it can be accurately reported, interpreted and verified.

According to the ICH GCP Guidelines E6 (R2), essential documents serve the purpose of:

- Demonstrating the compliance of the investigator, sponsor, and the monitor with all applicable regulatory requirements and GCP.
- Assisting in the successful management of the study by the investigator, sponsor, and monitor.
- Confirming the validity of the conduct of the clinical investigation and the integrity of the data collected.

Which documents need to be compiled?

The list of essential documents will vary, depending on the design of the study and its risk and complexity. As a general guide, the following should be found in an investigator's site file (for any queries, the study sponsor can be contacted at the first instance as they would hold all essential documents in their Master file):

- Trial Management contact list
- Investigator's Brochure – clinical trials only (including version updates)
- Protocol (including signature page and version updates)
- Case Report form template (including version updates)
- Patient documents (Patient Information Sheet (PIS), Informed Consent Form (ICF), GP letter etc. including version updates)
- Insurance certificate
- Signed agreement between all parties
- Relevant regulatory approvals (HRA, REC etc.)
- IRAS form
- Local confirmations
- Caldicott approval
- Confirmation of Portfolio adoption
- Funding arrangements
- Delegation log, training log, CV and GCP certificates for all study personnel
- Lab normal values and reference ranges. Accreditation certificates (including. revisions)
- Calibration certificates (including revisions)
- IMP related documents
- Evidence of study monitoring
- Correspondence
- Signed ICFs
- Safety reporting documentation
- Annual reports – end of study report
- Audit certificates, screening, recruitment, randomisation logs
- Close out/archiving documentation
- Evidence of professional registration status for all medical and NMAHP staff

- Confirmation of Letters of Access, Honorary Clinical Contracts and Honorary Research Contracts

Hints and tips:

1. There can be multiple versions of various essential documents (e.g. several protocol versions, patient information leaflets, informed consent forms). The current version of the approved documents should be on file and previous versions should be marked as superseded but still be kept in the Investigator file.
2. Some essential documents require signatures. It is not adequate for a document to be filed without a required signature.
3. Signed CVs of study team members should be dated within the last 2 years and be reviewed and re-signed regularly.
4. Financial disclosure forms (e.g. for CTIMPs) must be completed by all delegated clinical members.
5. NuTH accepts GCP certificates if training was received within the last 3 years. These are to be reviewed regularly and updated certificates to be filed in a timely manner.
6. All study members and associated activities listed on the delegation log must be signed off by the Principal investigator. Any changes/additions to delegated tasks must also be signed off by the PI. The log must be kept up-to-date when current staff leave the study or new staff join the study.
7. Training records must be kept up-to-date when a study member receives training.
8. Where essential documents are missing or not applicable, a file note should be filed instead, giving a brief explanation why the document is not there.

When are documents completed?

The timeframe of completion will vary, as some documents are required/generated at different points during the research project lifecycle (before commencement of clinical phase, during clinical phase and at completion/termination of study).

The sponsor/monitor/regulatory authorities and IRB(s)/IEC(s) will prompt the investigator's site for relevant documents.

They must be filed in a timely manner as soon as approved copies are received.

Where/when would the documents be used?

They would generally be used for the conduct of the study (e.g. the investigator and study team member will be referring to the protocol to check the eligibility criteria for participant inclusion or the schedule of procedures, patient documents during recruitment and delegation log when staff members join or leave the investigator's study team).

They would also be used for safety reporting, during monitoring visits by the study sponsor, during study audits (internal or independent) or during inspections by regulatory authorities for confirming the validity of the trial conduct and integrity of the data collected.

Who requires documents and when?

Essential documents will need to be provided to different people/departments/agencies at various points during the set-up, running of the study or study closure:

- Health Research Authority during study set-up to carry out the assessment of governance, risk and legal compliance prior to issuing their HRA approval.
- Research Ethics Committee (REC) during study set-up to issue their independent ethical opinion.
- Local R&D department during study set-up to confirm investigator's site's capacity and capability and for auditing/ governance purposes during the conduct/closure of the study.
- Study team members at investigator's site during the conduct of the study in order to have up-to-date versions of study/patient documents, data collection tools and reporting forms / logs, training records.
- Study sponsor during the project lifecycle for study set up / management/closure and for monitoring purposes.
- Regulatory agencies during the project lifecycle until study documents destruction for study inspection purposes.

The above list is just indicative, as other review bodies may ask for essential documents depending on the design of the research study and how questions have been answered on the IRAS application.

Revisions/Updates of Documents

Version controlled documents assessed by review bodies (e.g. HRA, REC, R&D):

When version controlled documents are being reviewed during the conduct of the study, all review bodies who carried out initial assessments of such documents will need to be notified of these amended documents in order to confirm their approval of any changes.

Once all approvals are in place, the team should be notified/trained and updated versions of documents should be filed in the investigators site file and previous versions should be marked as superseded.

Non version controlled documents:

Any other documents which fall in this category (e.g. GCP certificates, insurance certificates) should be filed in the site file as soon as a new document becomes available.

Closing the Study

A close-out of a research study will be performed when the study monitor has reviewed both investigator/institution and sponsor files and confirmed that all necessary documents are in both the investigator site file and master file.

The study close letter/sponsor's correspondence will then be notified to the local R&D office (including Finance R&D so that they can close the study account) who will confirm that the study can be closed and archived according to the site agreement.