Archiving Clinical Research Documents

NJRO-GEN-SOP-012

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1. Background/Introduction

Research study documentation must be retained so that the data is accessible after a trial has been completed. The need for robust archiving of documentation is essential for ensuring a Trial is able to be reconstructed in its entirety. Also future studies may suggest a further period of follow-up, or investigations into any allegations of fraudulent behaviour, or in the event of concerns about side effects and research participants need to be contacted.

Appropriate arrangements for archiving research documentation should be in place before the research starts including the proposed location, accessibility and any potential cost for the entire archiving period.

The EU Good Clinical Practice (GCP) Directive 2005/28/EC and subsequent enabling legislation set out the standard for archiving clinical trial essential documentation.

2. Purpose

This Standard Operating Procedure (SOP) describes the procedure for archiving research documentation for all research studies, particularly those sponsored by The Newcastle upon Tyne Hospitals NHS Foundation Trust (NUTH FT).

3. Scope of Document

This SOP is mandatory for all research projects classified as Clinical Trials of Investigational Medicinal Products (CTIMPs) and Advanced Therapy Investigational Medicinal Products (ATIMPs) where it is a regulatory requirement under the Medicines for Human Use (Clinical Trials) Amended Regulations 2006.

This SOP covers the archiving of essential documents held in paper and electronic format. It does not cover records management systems.

Non-CTIMPs must comply with the UK policy framework for health and social care research and, although compliance with GCP and legislation cannot be enforced, the same general principles apply. If the Chief Investigator (CI)/ Principal Investigator (PI) are able to provide suitable storage for the entire archiving period, this is permissible. Where no suitable storage facility is available the CI/PI must contact the Research & Development (R&D) team within the Newcastle Joint Research Office (NJRO) for advice.

4. Procedure

The study documents must be archived at the end of the study:

- For NuTH FT sponsored CTIMPs this is considered to be once the final report has been submitted (which must be submitted within 1 year of the end of trial as defined in the protocol).
- For studies where NuTH FT is not Sponsor, the study is deemed complete at site once notified following the close out visit by the study Sponsor.

Clinical study documentation should be archived by the CI or their delegate. For individual sites, the responsibility for archiving these documents falls to the local PI or delegate.

The investigator has a responsibility to allow the Sponsor access to the archived documents upon request and the documents may also be inspected by Regulatory Authorities. The PI may delegate the management of the trial documentation and Investigator Site File (ISF) to another member of the research team but the PI retains overall responsibility.

4.1. Archivist

For CTIMPs it is a legal requirement that the Sponsor appoints a named individual (archivist) within the organisation to be responsible for archiving the documents which are, or have been, contained in the Trial Master File (TMF) and that access to these documents shall be restricted to those appointed individuals, auditors and/or inspectors.

In particular the archivist is responsible for:

- Controlling access to the archive
- Ensuring that orderly storage and retrieval of materials is facilitated
- Ensuring that movement of material in and out of the archives is properly controlled and documented
- Ensuring that material submitted for archiving corresponds to that described in chain of custody documentation

In NuTH FT the archivist role is delegated to the Research Governance Manager (RGM) with a deputy appointed from the Research Management & Governance (RM&G) Manager Team. The archivist will have overview and access to all archived research files. In the event that the RGM role is vacant, the Head of the Joint Research Office will be trained and fulfil the role in the interim.

Investigator teams may arrange for archiving of files and retrieval of files via the Research Team Leads (or deputy). This process is described in the Archiving Working Instruction.

An external Sponsor can arrange the archiving on behalf of the investigator subject to the following being implemented:

- The archive arrangements are formally agreed and documented between the Sponsor and NuTH FT.
- A formal procedure is in place such that the documents are only released from the external archive with the approval of the investigator and NuTH FT.
- The records go directly between the investigator site and an archive facility independent of the Sponsor, thereby ensuring that the Sponsor does not have uncontrolled access to the investigator files.

4.2. Documents to be archived

Essential documents are defined as documents which individually and collectively permit the evaluation of the data produced and are stored in the TMF so that the clinical trial can be reconstructed for audit and monitoring purposes. Essential documentation is defined in GCP Guidelines (Sections 8.2, 8.3, 8.4), including minutes from all trial related meetings and must be retained until notification from the Sponsor. All archived documentation should be complete, legible and readily available to anyone with a legitimate need to access them.
Particular attention should be paid when records are stored on electronic, magnetic, optical or other non-indelible media. Suitable controls should be implemented to ensure these records cannot be altered without proper authorisation and the creation of an audit trail.

The pharmacy site file may be archived separately as long as its location is clearly referenced in the TMF/ISF and vice-versa. At NuTH FT the pharmacy department is responsible for the archiving of the pharmacy site file.

4.3. How should documents be archived?

The documents to be archived must be prepared to ensure survival over the designated archive period to minimise the possibility of damage to the documents during the archival period.

Source data documents that form part of the medical records should remain with the medical records. Readouts on heat-sensitive paper (e.g. ECG readouts) should be

photocopied and the copy kept with the original within the patient notes as heat-sensitive paper fades over time. Duplicate copies of the source data documents should not be kept with the essential documents.

The archive boxes will be identifiable by completing a spread sheet with the name and reference number of the study, Sponsor, Investigator, the date of archiving and the expected end date of archiving. This will be linked to the barcode placed on the outside of the box A contents sheet should be placed inside each box, detailing the documents contained within that box. The archive boxes should be stored in a secure, environmentally-controlled location, i.e. fire protection without water sprinkler systems, water damage protection procedures.

If not to be stored in the approved archive facility, details of the archiving location should be recorded by the CI and notified to the Sponsor.

Electronic documents / data

Activities such as data management, statistical analysis, and reporting and trial management systems mean that electronic documents and data are likely to need to be retained. This may be on a server or on transportable media (e.g. USB drives, CDs etc.) It is recommended that more than one copy of the data is retained e.g. data archived on a specific server should be subject to back up. The back-up media should be stored in a separate location with consideration given to storing the data in differing formats on different types of media.

Access to archived documents or data must be:

- Suitably restricted; either by:
  - User access levels to the archive area of a server; or,
  - Controls put in place to access the storage area where the media are retained.
- Protected from unauthorised changes to maintain authenticity

Future access should be maintained by:

- Maintaining the system (hardware and software) to access data in its original format
- Use of a new system to emulate the old software
- Migration of the data into a new format to ensure continual access with new software

Consider potential deterioration or obsoleting of media used to store data. Potential solutions may include:

- Transfer of data to an alternative media
- Store media under appropriate conditions
- Consider transfer of data to a new media as technology advances (although any transfer or migration should be validated)
- Undertake periodic test retrieval or restores to confirm ongoing availability of data
- When data is migrated to a new media or format, transfer to be validated and fully documented (i.e. audit worthy) to ensure that authenticity of data is maintained

4.4. How long documents should be archived

- For trials where the clinical trial data is used to support a marketing authorisation the documentation must be retained for at least 15 years after completion or discontinuation of the trial or for at least two years after the granting of the last marketing authorisation in the European Community or for at least two years after formal discontinuation of clinical development of the investigational product, whatever is longest.

- For trials involving medical devices, there are currently no definite guidelines. For NuTH FT sponsored studies it is recommended to store trial data for 5 years. For hosted studies, please confirm with the trial Sponsor.

- Records relating to the full traceability of the IMP for Advanced Therapies must be retained for 30 years after the expiry date of the product or longer if required by the clinical trial authorisation. This includes relevant documentation contained in the Sponsor and investigator files as well as trial subjects' medical records.

- For all other research the essential documentation must be retained for 5 years after the completion or discontinuation of the trial, or for a duration specified by the study Sponsor. (This includes the majority of CTIMPs sponsored by NuTH FT, which will involve IMPs that already hold a marketing authorisation).

Centralised records that may be relevant to a number of trials (e.g. SOPs, staff training records or maintenance and calibration records for equipment used in the trial at a

Phase 1 unit/NHS clinical research unit) should also be considered in the arrangements for archiving and retention (including superseded versions or obsolete records e.g. training records of personnel who have left the organisation) as they may be required to be produced to demonstrate compliance.

Medical records form part of the source data for research and must also be retained and accessible if required.

It is the responsibility of the Sponsor to inform NuTH FT as to when documents no longer need to be retained. The Sponsor should notify investigators in writing when their trial records can be destroyed. If an investigator becomes unable to take responsibility for their essential documents (e.g. relocation, retirement etc.) the Sponsor should be notified in writing of this change and informed as to whom the responsibility has been transferred.

4.5. Multicentre NuTH FT sponsored CTIMPs

It must be ensured that the same regulations are adhered to at all participating sites. Archiving SOPs of participating sites should be reviewed for compliance by the relevant Trial Manager. Confirmation that the archiving facilities meet the regulatory requirements needs to be documented and confirmed with the R&D team in the NJRO. All documentation confirming this should be filed in the TMF and documented in the close out report.

4.6. NuTH FT Archiving Facility

The Trust maintains an archiving facility at:

Datatron Document Image Archiving Ltd.
Unit 6 Mercury, Orion Business Park
North Shields
NE29 7SN

5. References

6.1. Medicines for Human Use (Clinical Trials) Regulations 2004 [SI 2004/1031]
6.2. Medicines for Human Use (Clinical Trials) Amended Regulations 2006 [SI 2006/1928]
6.3. Section 8 of ICH Harmonised Tripartite Guideline for Good Clinical Practice (1996)
6.4. ICH GCP Addendum E6 (R2) (2016)
6.5. European Union Good Clinical Practice Directive 2005/28/EC

6.6. European Commission Detailed Guidance on Good Clinical Practice Specific to Advanced Therapy Medicinal Products (2009)
6.7. Data Protection Act 1998
6.8. NuTH FT Clinical Records Management Policy
6.9. Good Clinical Practice Inspectors Working Group (GCP IWG) Guideline on GCP compliance in relation to trial master file (paper and/or electronic) for content, management, archiving, audit and inspection of clinical trials (31 March 2017) EMA/15975/2016

7. Appendices

N/A