Standard Operating Procedure:

Archiving

# Purpose

This standard operating procedure (SOP) describes the procedures for archiving material relevant to clinical research projects and the activities undertaken by the archivist.

# Scope

This SOP is applicable to all clinical research sponsored by the University of Birmingham (UoB). Where clinical research is sponsored by another institution, this procedure should be followed as far as possible, and in line with the contractual agreement between the UoB and the other institution. This SOP also applies to clinical research approved by a UoB research ethics committee (REC) that is required to follow the UoB Principles of Good Clinical Practice (GCP) for Clinical Research (UoB-GCP-POL-001). This SOP may be used as a guidance document in all other cases.

# Implementation plan

This SOP will be implemented in line with this document’s effective date.

# Stakeholders

Note that where the UoB takes on the sponsor’s responsibility for archiving, the UoB will delegate the majority of these duties to the chief investigator (CI) or to a clinical trials unit (CTU), who may delegate these duties further to their team(s). All delegation of duties will be documented (e.g. using the CI declaration and/or the Clinical Trials Task Delegation Log (UoB-SPO-QCD-001)).

* CI: the CI may delegate activities to members of their team, although evidence of CI oversight and approval is still expected and may not be delegated where ‘no delegation allowed’ is indicated. The SOP will state where delegation is possible. For clinical research approved by a UoB REC, the role of CI may be referred to as the principal investigator (PI), or the supervisor for postgraduate research students.
* Archivist: the person(s) responsible for archiving for clinical trials of investigational medicinal products (CTIMPs). In the CTUs the quality assurance (QA) managers take on the responsibilities of the archivist. For non-CTIMPs and studies, there is no formal archivist.
* Research Ethics, Governance and Integrity Team (REGI).

# Background and rationale

For the purposes of this SOP the terms ‘clinical research’ or ‘project’ will cover CTIMPs, other interventional trials (e.g. surgical trials, device trials and non-CTIMPs, and any other projects deemed to be ‘interventional’ by the sponsor) and clinical studies. ‘Material’ covers the documents within the study/trial master file (S/TMF), as well as electronic data and documents.

Following the completion of a project the essential material that individually and collectively permit evaluation of the conduct of the project and the quality of the data produced, must be stored securely and be readily accessible for inspection or audit. This material serves to demonstrate the compliance of the CI and sponsor with the standards of GCP and with all applicable regulatory requirements and to allow the reconstruction of the project.

The storage of the project material must be appropriate to ensure materials remain complete and legible throughout the required retention period. The type of storage required can be assessed using a risk-based approach, taking into consideration the type of project (i.e. CTIMP, trial, study) and the length of the required retention period. Long-term storage of material in an office filing cabinet for example may provide a suitably secure environment for the retention period, provided risks around security, location, size, environment and pests have been considered. However, as the retention of documents within the TMF is a legal requirement for CTIMPs, these trials require the most robust level of storage, and it is recommended that a specialist archive facility is used. For the purpose of this SOP the term ‘archiving’ will be used to refer to both archiving of material from CTIMPs and long-term storage of material related to all other clinical research, where the criteria described above are met. Where it is intended to relate to CTIMPs only this will be specified.

# Process map

# Process map outlining the steps detailed in the document.

# Procedure

## Retention period

1. The CI (or delegate) will include the costs for archiving in funding plans at the project set-up stage, based on an estimate of the quantity of material, the required retention period and type of storage area required (e.g. is an external archive facility required?).
2. The CI (or delegate) will document details of the retention times for all research project material, or the process used to determine how long particular material will be retained and how this will be documented. See also Guide to Retention Times (UoB-ARC-QCD-003).
* For all projects, the [Concordat on Open Research Data (PDF – 180 KB)](https://www.ukri.org/wp-content/uploads/2020/10/UKRI-020920-ConcordatonOpenResearchData.pdf) and the [UoB Research Data Policy](https://intranet.birmingham.ac.uk/as/libraryservices/library/research/rdm/Policies/Research-Data-Management-Policy.aspx) state that primary research data and research evidence should be preserved and accessible for a minimum of 10 years, unless:
* The project did not open to recruitment. In this case, for clinical trials a 5-year retention period will be applied in accordance with the [Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 (PDF – 71 KB)](https://www.legislation.gov.uk/uksi/2006/1928/pdfs/uksi_20061928_en.pdf).
* The project is of clinical or major social, environmental or heritage importance in which case this is extended to 20 years or longer.
* Specified by the funder as requiring a longer retention period.
* For CTIMPs, the [European Directive 2003/63/EC, Annex 1, Chapter 5.2 (c) (PDF – 366 KB)](https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:159:0046:0094:en:PDF) states that where trial results are planned to be used for registration purposes, essential clinical trial documents (including case report forms (CRFs)) are required to be archived either:
* for at least 15 years after completion or discontinuation of the trial
* for at least 2 years after the granting of the last marketing authorisation and when there are no pending or contemplated marketing applications
* for at least 2 years after formal discontinuation of clinical development of the investigational product
* for as long as the product is authorised for all other documentation pertaining to the trial, i.e. the protocol, SOPs, written opinions on the protocol and procedures, investigators brochure, CRFs, final report and audit certificates (if available)
* for 5 years after the product is no longer authorised for the final report.
* For CTIMPs run in EU countries [Clinical Trial Regulation (EU) No 536/2014 Article 58 (PDF – 757 KB)](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf), implemented 31-Jan-2022, states that the content of the TMF will be archived for at least 25 years after the end of the trial. For international CTIMPs run outside of the EU, trial material will be retained in accordance with national legislation.
* For advanced therapy investigational medicinal products (ATIMPs) trials, the sponsor of the trial and the investigator/institution where the ATMP is used must keep their parts of the traceability records (as per [Annex 1 of EudraLex Volume 10, Chapter 5, ‘Detailed guidelines on good clinical practice specific to advanced therapy medicinal products’ (PDF – 406 KB)](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/atmp_guidelines_en.pdf)) for a minimum of 30 years after the expiry date of the product.
1. The CI (or delegate) will ensure during the set-up stage of the project that the investigator sites are aware of the archiving arrangements for the investigator site file (ISF), including:
* that the retention of the ISF and medical files are the responsibility of the PI at site and that this is captured in a clinical trial agreement/site agreement
* that the ISF is stored separately to the S/TMF as this will contain participant identifiable information such as the participant identification log, which must not be held in the S/TMF. See also Essential Documents Development and Maintenance SOP (UoB-ESD-SOP-001)
* the need to store documents until a signed agreement, confirming that they may be destroyed, has been provided by the CI (or delegate) or the pharmaceutical company if applicable, or by the sponsor where the CI is no longer available
* the need for medical notes to be destroyed according to local policy.
1. The CI (or delegate) will ensure during the set-up stage that laboratories analysing clinical research material are aware of the archiving requirements, including:
* the need to archive the laboratory master file (LMF) alongside all source data and reported data. See Laboratory Set Up and Management SOP (UoB-CRL-SOP-001) for further information
* the need to archive all non-trial/study-specific data, e.g. equipment validation and maintenance records, staff training records, quality assurance reports etc.
* for CTIMPs, the need to detail who will be responsible for the archiving of laboratory documentation and data at trial closure in a sample analysis for clinical trials contract between the laboratory and the sponsor (where the laboratory is not part of the sponsor’s organisation) or an internal memorandum of understanding between the laboratory and the CI (where the laboratory is part of the sponsor’s organisation).
1. Where appropriate, the CI (or delegate) will document, in an agreement, the requirements that the sponsor’s vendors or other agents will meet in relation to document retention. Agreements will cover all eventualities to ensure that material remains available for inspection for the specified retention time.
2. The CI (or delegate) will risk assess the need for performing quality checks of archived material and document the decision, for example in the archive plan (see Archiving Plan (UoB-ARC-QCD-001) for further information).
* Consideration should be made to the type of research (e.g. trial, study), the length of retention period, the type of material archived (e.g. electronic and access to specialist software/files).

### End of retention period

1. The CI (or delegate) will assess whether archived materials may be destroyed, or whether the archive period needs to be extended.
* For CTIMPs:
* this may be in liaison with the archivist and pharmaceutical company, where applicable
* the archivist (or delegate) will arrange for permanent removal of paper material from the archive location, and its subsequent destruction. Alternatively, where an external archive facility is used, the archivist (or delegate) will arrange for the facility to securely and confidentially destroy the material and ensure that evidence of this destruction is obtained
* the archivist (or delegate) will ensure that documentation regarding the destruction of both paper and electronic archived material is retained.
1. The CI (or delegate) will provide sites with a signed authorisation when material is no longer needed to be retained and appropriate destruction can be arranged.

## Archiving plan

1. The CI (or delegate) will document the details of which project material is to be archived, where it is to be archived and the retention period.
* For projects approved by a UoB REC, details relating to data retention will be stipulated in the Application for Ethical Review Form.
* For all HRA-approved projects, development of an archiving plan is advised and as a minimum, details about data retention will be stipulated in the protocol. See also Essential Documents Development and Maintenance SOP (UoB-ESD-SOP-001) for further information.
* For CTIMPs, the CI (or delegate) will develop an archiving plan during the trial’s set-up phase. See Archiving Plan (UoB-ARC-QCD-001) for a template.
1. The CI (or delegate) will ensure the storage location is suitable for the type of clinical research and the duration of the retention period. The risks around security, location, size, environment and pests will be considered when deciding on a storage location.
* For CTIMPs, it is recommended that an external archive facility is used.
1. For CTIMPs, upon trial closure, the CI (or delegate) will send the archiving plan to the REGI, along with confirmation that the ISFs have been archived in line with the archiving plan.

## Archiving of paper documents for all projects

1. The CI (or delegate) will review the S/TMF to ensure that no files are missing. See also Essential Documents Checklist (UoB-ESD-QCD-001) for further information.
* For CTIMPs, the CI (or delegate) will include, as a minimum, all relevant documents as listed in section 8 of the [ICH Harmonised Tripartite Guideline for Good Clinical Practice (PDF – 651 KB)](https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf) for archiving.
1. The CI (or delegate) will prepare the documents for storage in, for example, an archive box.
* Efforts should be made to maximise the contents of each box whilst ensuring they are maintained in good order and not crushed or too tightly packed.
* Documentation for multiple research projects may be stored in a single archive box as long as it is easy to distinguish between them, and for CTIMPs this will be clearly documented in the archive system. In order to maximise space when using boxes, remove bulky storage items such as ring binders or hanging files wherever possible; large envelopes or simple card folders may be used instead to keep grouped items together.
* Remove large metal clips where possible, although it is not necessary to remove paper clips or staples.
* Remove plastic wallets if possible as they stick to the documents over time and the print will transfer to the inside of the plastic wallet.
* Remove rubber bands as they will cut into paper and become sticky over time.
* Remove sticky notes as they will leave residue which will attract dirt and mould.
1. The CI (or delegate) will seal and clearly label the box (see Archive Label (UoB-ARC-QCD-002) for a template). This will include:
* a brief description of the contents on the outside (e.g. project name/acronym, range of participant identification numbers, document types such as CRFs etc.)
* no indication that it contains confidential participant identifiable data.
1. The CI (or delegate) will store the material in the archive location for the duration of the retention period. For CTIMPs this will be the responsibility of the archivist (or delegate).
* Where an external archive facility is used the material will be transferred to the facility by the archivist (or delegate) within 12 months of preparing the material for archiving.
1. Where appropriate, the CI (or delegate) will document the transfer of custody of data or documents in relation to the research project, e.g. transfer of a marketing authorisation to another organisation.

## Electronic archiving for all research projects

### For study/trial systems and electronic data:

1. The CI (or delegate) will deactivate study/trial systems where applicable and restrict user access to the system and other electronic data to only certain individuals upon notification that the research project is concluded. This may involve submitting a request via the [IT Service Desk](https://universityofbirmingham.service-now.com/itportal/).
* For CTIMPs, the archivist (or delegate) will obtain confirmation of deactivation along with a table/record count list for the project’s system and these will be filed in the archive system. See Data Management SOP (UoB -DMA-SOP-001) for further details.
1. The CI (or delegate) will assess any requests for study/trial system reactivation or access to electronic data and if appropriate, will reactivate the system or reinstate access. This may involve submitting a request via the [IT Service Desk](https://universityofbirmingham.service-now.com/itportal/).
* Details of the approval and access request will be documented.
* For CTIMPs, requests for system reactivation or access requests will be assessed by the archivist (or delegate). Evidence of the approval given for such requests and details of the reason for access will be filed in the archiving system.
1. The CI (or delegate) will implement measures to ensure archived electronic data is maintained and accessible for the duration of the retention period.
* Consideration should be given to the possibility that media, software and hardware could become obsolete over time. If data is transferred to a new media or new format, it is recommended that this transfer is documented, and the transfer process validated.

### For project mailboxes:

1. To ensure that documents can be accessed, the CI (or delegate) will print key emails and store them as paper material as described above.
2. The CI (or delegate) will ensure that upon notification the project is concluded:
* All project-essential emails stored in staff mailboxes will be moved into the project mailbox prior to implementing access restrictions.
* A request will be made via the [IT Service Desk](https://universityofbirmingham.service-now.com/itportal/) to restrict access to the project mailbox to designated individuals, e.g. the CI or the trial management team leader for trials run in a CTU.
* For CTIMPs, the size of the mailbox and the number of folders within will be documented. The document will include a wet signature and date, and will be forwarded to the archivist (or delegate) for filing in the archive system.
1. The CI (or delegate) will ensure that when individuals are no longer involved with the project any relevant emails are printed and added to the paper material or transferred to the project mailbox.
2. The CI (or delegate) will assess any request for access to the mailbox after it has been deactivated and if appropriate, submit a request via the [IT Service Desk](https://universityofbirmingham.service-now.com/itportal/).
3. The CI (or delegate) will submit a request via the [IT Service Desk](https://universityofbirmingham.service-now.com/itportal/) for the mailbox to be deleted when the end of the retention period has been reached unless there is a legitimate purpose requiring longer mailbox retention.

## Archivist responsibilities for CTIMPs\*

\*In addition to those mentioned above.

1. The REGI will ensure that a named individual(s) (i.e. an archivist) is appointed to be responsible for archiving documents and data for CTIMPs.
* The individual(s) will be appropriately trained, and training will be documented and reviewed on a regular basis. See Training SOP (UoB-TRN-SOP-003) for further details.
* The individual(s) will have a clear legal link to the sponsor and clear documentation will be retained to support the appointment.
1. The archivist (or delegate) will set up and maintain an archive system for the oversight and logging of archived material; both paper and electronic.

### Data quality checking

1. The archivist (or delegate) will use a risk-based approach (e.g. considering the type of material archived, the retention period, type of project and type of archive location used) to determine the frequency at which quality checks of archived data will be performed, and will document the frequency e.g. in the archiving plan. See Archiving Plan (UoB-ARC-QCD-001) for further details.
2. The archivist (or delegate) will identify data to be retrieved for a quality check. The following will be considered when deciding which data is to be retrieved:
* Findings from previous data-retrieval quality checks or previous visits to the archive facility (where applicable) that might instigate a reason for document-specific box retrieval; therefore, refer to all relevant reports completed since the last data-retrieval quality check.
* The impact of time on the integrity of the archived material; for example, consider retrieving a selection of archived boxes that have been stored for varying lengths of time.
1. The archivist (or delegate) will perform the quality check and ensure each quality check is documented. Checks may include:
* For archive boxes, perform a visual inspection to confirm that:
* the correct box has been returned
* the box was returned in a timely fashion
* the box and its contents are maintained in good condition.
* For trial mailboxes:
* reconcile the mailbox size and folder list from the archive system
* ensure emails are not corrupted by checking a sample.
* For trial systems:
* reconcile the trial system’s table/record count list from the archive system
* ensure records are not corrupted by checking a sample.

### Post-data-checking process

1. For archive boxes, the archivist (or delegate) will return the box to the archive. Where an external archive facility is used, this will be performed in line with their instructions.
2. For mailboxes, the archivist (or delegate) will ensure access to the mailbox is removed by submitting a request via the [IT Service Desk](https://universityofbirmingham.service-now.com/itportal/).
3. For trial systems, the archivist (or delegate) will ensure that the trial system is deactivated and access is revoked. See Data Management SOP (UoB-DMA-SOP-001) for further information.

### Data retrieval

1. The archivist (or delegate) will assess and manage any requests for the retrieval of materials, including the tracking of material, the expected duration of retrieval, and the reconciliation of material post-retrieval. The archivist (or delegate) will ensure that the request and approval for the retrieval of archived material is documented in the archive system.
2. The archivist (or delegate) will arrange for materials to be retrieved.
* For paper material, retrieve the material from the archive or, where an external archive facility is used, request the retrieval of boxes from the facility as per the archive facility’s instruction.
* For electronic material, request that access to electronic material be granted.

### External archive facilities

1. Where an external archive facility is used, the archivist (or delegate) will arrange for paper materials to be transferred there.
2. The archivist (or delegate) will maintain oversight of external archive facilities by:
* performing a pre-contract vendor assessment in accordance with Compliance Review SOP (UoB-CPR-SOP-001)
* working with the [UoB Contracts Team](https://intranet.birmingham.ac.uk/finance/rss/contracts/index.aspx) to ensure appropriate contracts are in place for the use of the external archive, to ensure that the documents are stored appropriately and are, for example, not moved to locations that have not been approved by the archivist
* performing periodic quality checks to ensure the ongoing integrity of the documents (see ‘Data quality checking’ section above).

# List of expected outputs

* Documented evidence of the retention period for project material, and an archiving plan (where applicable).
* Where third party vendors are used, evidence that the requirements for retaining records is documented in an agreement.
* Restricted access to electronic documents, study/trial systems and project mailboxes.
* Details of any requests to access paper or electronic data documented, along with evidence of the approval for such access.
* Where investigator sites are used, requirements for archiving at site documented in a clinical trial agreement/site agreement and signed authorisation from the CI to destroy archived material.
* Where laboratories are used to analyse or process clinical-trial samples, the details about who is responsible for the archiving of laboratory documentation are documented in a sample analysis for clinical trials contract/memorandum of understanding.
* Documented assessment of the need to perform quality checks of archived material.

### For CTIMPs

* Named individuals responsible for archiving, i.e. archivists appointed by the sponsor, and documented evidence that these individuals are appropriately trained and have appropriate links to the sponsor.
* Evidence of an archiving system being in place for oversight and logging of archived material.
* Evidence of pre-contract assessments and contracts in place for the use of external archive facilities, where applicable.
* Evidence of the deactivation of trial systems.
* Evidence of the request and approval for the retrieval of, or access to, archived material.
* Evidence of quality checks being performed on archived material.
* Evidence of the destruction of archived material at the end of the retention period.

# Related documents

* UoB-ARC-QCD-001 Archiving Plan
* UoB-ARC-QCD-002 Archive Label
* UoB-ARC-QCD-003 Guide to Retention Times
* UoB-CPR-SOP-001 Compliance Review
* UoB-CRL-SOP-001 Laboratory Set-up and Management
* UoB-DMA-SOP-001 Data Management
* UoB-ESD-QCD-001 Essential Documents Checklist
* UoB-ESD-SOP-001 Essential Documents Development and Maintenance
* UoB-GCP-POL-001 UoB Principles of GCP for Clinical Research
* UoB-SOP-QCD-001 Clinical Trials Task Delegation Log
* UoB-TRN-SOP-001 Training

Access to the full UoB QMS for clinical research is available via the [CRCT website](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/index.aspx).

# References and frameworks

* Clinical Trial Regulation (EU) No536/2014 Article 58: <https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf>
* Concordat on Open Research Data:
<https://www.ukri.org/wp-content/uploads/2020/10/UKRI-020920-ConcordatonOpenResearchData.pdf>
* EudraLex Volume 10, Chapter 5, ‘Recommendation on the content of the trial master file and archiving’: <https://health.ec.europa.eu/system/files/2016-11/v10_chap5_en_0.pdf>
* EudraLex Volume 10, Chapter 5, Annex 1, ‘Detailed guidelines on good clinical practice specific to advanced therapy medicinal products’:
<https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/atmp_guidelines_en.pdf>
* European Directive 2003/63/EC: <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:159:0046:0094:en:PDF>
* ICH Harmonised Tripartite Guideline for Good Clinical Practice:
<https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf>
* Medicines for Human Use (Clinical Trials) Amendment Regulations 2006: <https://www.legislation.gov.uk/uksi/2006/1928/pdfs/uksi_20061928_en.pdf>
* Scientific Archivists Group, ‘A Guide to Archiving Electronic Records’: <https://the-hsraa.org/wp-content/uploads/2017/12/AGuidetoArchivingElectronicRecordsv1.pdf>
* Scientific Archivists Group, ‘Guidance on the Archiving of Good Clinical Practice Material’:
<https://the-hsraa.org/resources/publications/good-clinical-practice-guide-archiving>
* UoB Research Data Management Policy:
<https://intranet.birmingham.ac.uk/as/libraryservices/library/research/rdm/Policies/Research-Data-Management-Policy.aspx>
* UoB Services:
* Contracts Team: <https://intranet.birmingham.ac.uk/rssd/research-support/contracts.aspx>
* IT Service Desk: <https://universityofbirmingham.service-now.com/itportal/>
* REGI: researchgovernance@contact.bham.ac.uk

# Abbreviations and definitions

| Term | Description |
| --- | --- |
| Archive system | A collection of documents detailing the content, location, transfer details and review outcomes of archived documents pertaining to a clinical trial. |
| Archiving | Long-term storage of (study/trial) materials, where those materials are not required to be kept in an active format. The storage environment must be deemed a suitably secure environment for the required retention period, with risks around security, location, size, environment and pests having been considered. For CTIMPs, the long-term storage of the materials is under the control of an archivist and in an archive fit for the purpose of the specific trial.  |
| Archivist | The person who defines and maintains an archive index recording all essential documents that have been entered into the archive, and who approves, tracks and retrieves documents on loan from the archive. |
| ATIMP | Advanced therapy investigational medicinal products |
| CI | Chief investigator |
| Conclusion of a project | The point in time where all project closure procedures have been completed, including final analysis. |
| CRF | Case report forms |
| CTIMP | Clinical trials of investigational medicinal products |
| CTU | Clinical trials unit |
| External archive facility | An off-site archive facility that is used to archive materials that are expected to be no longer used, e.g. the TMF after a trial is closed and the final report is generated. |
| Final analysis | An analysis of project data performed on the final cohort of participants with follow-up as defined by the protocol and statistical analysis plan. |
| GCP | Good Clinical Practice |
| ISF | Investigator site file. See ‘Site file’. |
| Laboratory master file (LMF) | A file containing evidence of a documented approach to GCP compliance in the laboratory. |
| PI | Principal investigator |
| Project mailbox | Central mailbox stored on the University of Birmingham’s email system. Used as a central email address and storage facility for all emails relating to the project. Access to the mailbox is allocated to specified staff members as required. |
| REC | Research ethics committee |
| REGI | Research Ethics, Governance and Integrity Team |
| Site file  | The site file contains all essential documents held by principal investigator(s) conducting a trial which individually and collectively permit the evaluation of the conduct of a trial and the quality of the data produced. Also known as the investigator site file (ISF).  |
| SOP | Standard operating procedure |
| Study/trial master file (S/TMF) | The study/trial master file consists of essential documents kept at the sponsor (or delegate) site, which enables both the conduct of a clinical study/trial and the quality of the data produced to be evaluated. The filing system can be in the form of a single file or a number of files as deemed most appropriate. |
| Study/trial system  | The study/trial system describes the software and database used to store and manage clinical research data used for the analysis of outcome measures as defined in the protocol. This may include databases containing data, contact databases and data-tracking systems. |
| UoB | University of Birmingham |

See also the [Glossary of Terms](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/Glossary-of-Terms.aspx).