SOP number	**51.024**	Version	**2.0**
Title	**Archiving Essential Documents from Clinical Research – Process for a GGC Sponsored/Co –Sponsored Clinical Trial of an Investigational Medicinal Product (CTIMP) and/or Clinical Investigation of a Medical Device (CIMD)**		

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SOP category	NHS GG&C Sponsor R&I
Staff category	

Staff Category	R	A	C	I
Research Governance Manager		X		
Research & Innovation Systems Manager	X			
Sponsor Research Co-ordinators	X			
Innovation Contracts Manager	X			
Research Information Officer (IO)	X			
R&I Sponsor Pharmacy	X			
Project Management	X			
Research Governance	X			
Chief Investigators	X			
University of Glasgow Head of Research Regulation and Compliance	X			
Data Management Team			X	
Laboratories (Involved in Primary, Secondary End Points and exploratory)				X

1. Scope

This procedure applies to staff with responsibility for components of the TMF and will apply to staff out with NHS Greater Glasgow and Clyde, with the Archivist ensuring communication, documentation and procedures are followed.

2. Purpose

The purpose of this SOP is to describe procedures that will be used by R&I NHSGGC to meet requirements of the Medicines for Human Use (Clinical Trial) Act 2004 and the Data Protection Act of 2018, as amended, when archiving the clinical trial investigation documentation for trials sponsored by NHSGGC or Co-sponsored with University of Glasgow (UoG).

3. Procedures

3.1. Abbreviations/Definitions

ATIMP	Advanced Therapy Investigational Medicinal Product
CTIMP	Clinical Trial of an Investigational Medicinal Product
CIMD	Clinical Investigation of a Medical Device
GCP	Good Clinical Practice
CI	Chief Investigator
PI	Principal Investigator
PIS	Participant Information Sheet
PM	Project Manager
QC	Quality Checks
R&I	Research & Innovation department
RC	Sponsor Research Co-ordinators
RCB	Robertson Centre for Biostatistics
IO	Research Information Officer
mNCA	Model Agreement for Non-Commercial Research between the Sponsor/Co-sponsors and a Participating Site
MHRA	Medicines and Healthcare products Regulatory Agency
NHSGGC	Greater Glasgow Health Board
TMF	Trial Master File - contains all trial essential documentation which should be sufficient to adequately reconstruct the trial activities undertaken, along with key decisions made concerning the trial
ISF	Investigator Site File
SIV	Site Initiation Visit
UoG	University of Glasgow
Essential documents	individually or collectively permit evaluation of the conduct of a trial and the quality of the data produced

3.2. Background

The process of archiving provides long term secure storage for essential study trial records (paper and electronic) usually comprising:
a) The Trial Master File (TMF) (SOP 51.016),
b) The Investigator Site Files (ISFs) and
c) The medical records of trial participants.

These records are retained following the end of a Clinical Trial of an Investigational Medicinal Product CTIMP and/or Clinical Investigation of a Medical Device (CIMD) in order to allow reconstruction of a trial, potential further analysis of project data and to enable Medicines and Healthcare products Regulatory Agency (MHRA) inspection and monitoring in accordance with Good Clinical Practice (GCP).

3.2.1. Trial Master File (TMF)

At the close of a trial, the Sponsor/Co-Sponsors will ensure essential documents are archived in accordance with the terms within the protocol. As details of the archiving arrangements may be present in several locations, for example the IRAS application form, contracts with Vendors, Co-Sponsorship agreements, it is the responsibility of the Sponsor R&I Co-Ordinator to ensure they are all in alignment with each other. Ultimately the details outlined within the protocol are those which must be followed. The complete Sponsor/Co-sponsors TMF will cover the entire TMF index (Form 51.016A) and the owners of each section will be responsible for archiving their sections of the TMF as outlined in SOP 51.016. The section owner will review their completed TMF sections to ensure the required QC activity has taken

place prior to archiving, this will be evidenced in Form 51.024A before being sent to the IO who will record in Form 51.024E, both forms will then be held indefinitely.

3.2.2. Investigator Site File (ISF)

NHSGGC and UoG as Sponsor/Co-sponsors are responsible for ensuring that archiving takes place for participating sites' essential documents, oversight of this activity will be carried out by the IO. It is the responsibility of the sites to carry out the archiving activity for their documentation.

As part of the Site Initiation Visit (SIV) and as well as part of the trial closure, the Project Manager (PM) and Monitor will discuss and document archiving arrangements with each participating site. Each participating site will be responsible for archiving their ISF (Form 51.016C) and should follow the archiving requirements documented within the protocol in conjunction with direction from the PM and/or Clinical Trial Monitor. The delegation of trial archiving activity to participating sites will be stated in the Model Agreement for Non-Commercial Research between the Sponsor/Co-sponsors and a Participating Site (mNCA) and reflect the retention period as stated within the trial protocol, the protocol is seen as the source of truth for archiving requirements and other documents must be made to reflect its contents. The mNCA, as prepared by the Sponsor R&I Co-Ordinator, should include the following clause to delegate the archiving and destruction activities to the participating site:

"NHS Greater Glasgow and Clyde as Sponsor/Co-sponsor will notify the Participating Site when archiving activities can begin. The Participating Site will archive the site study documentation for the period of time outline in the trial protocol in line with regulatory requirements. Once this period has elapsed NHS Greater Glasgow and Clyde will contact the Participating Site to confirm whether destruction of these documents is required. The site is responsible for ensuring that the medical records of participants involved in research are retained for the appropriate periods.

The Participating Site should only archive their trial documentation once they have received notification from the trial PM (or delegate) that they can do so and similarly only organise for the destruction of archived documentation when the approval to do so is given by the trial Sponsor/Co-sponsors."

3.2.3. Medical Records of Trial Participants

Medical notes will be archived in accordance with the principles outlined in NHS standard care guidance, as the medical notes are related to Research there will be a requirement to retain them for a period of 25 years which will be outlined in trial Protocols going forward, any existing periods outlined within Protocols will be adhered to.

At SIV, the PM will discuss the plan that the notes of subjects who have been involved in clinical trials should be clearly identified to prevent premature destruction (i.e. to include stickers to the notes with a "do not destroy" or "retain until" with a date clearly marked).

On completion of a research study it is the responsibility of the Principal Investigator (PI), or delegated individual to ensure that the medical notes of all research participants are labelled appropriately to ensure adequate retention.

3.3. Archivist

It is a requirement of the Medicines for Human Use (Clinical Trials) Regulations for the Sponsor to have named individuals responsible for archiving trial material, these individuals are referred to as the archivists. The ownership of the TMF is shared across multiple sections, the owner of each section is the archivist for their own section with the activity overseen by the Information Officer (IO). Each archivist will complete Form 51.024A to ensure the content is complete, accurate and representative of trial activity before sending to the IO to record on a trial by trial basis using Form 51.024E. This relationship is illustrated in Figure 1.

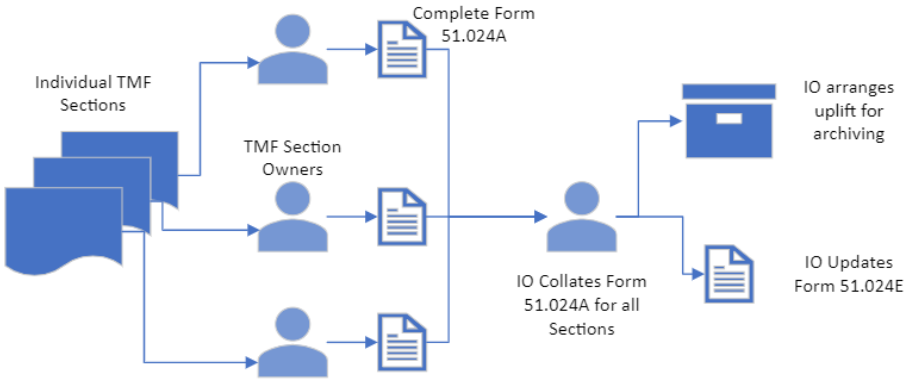

Figure 1 – Relationship between Section Owners and IO

3.4. Retention period

The study retention period will commence from the date of receipt of MHRA notification of the end of trial declaration unless stated otherwise in the protocol. The retention period is the legal requirement which must be met as outlined in the Medicines for Human Use (Clinical Trials) Regulations, it does not necessarily mean the time period documents will actually spend in archive. Figure 2 outlines the difference between the retention period and time in archive.

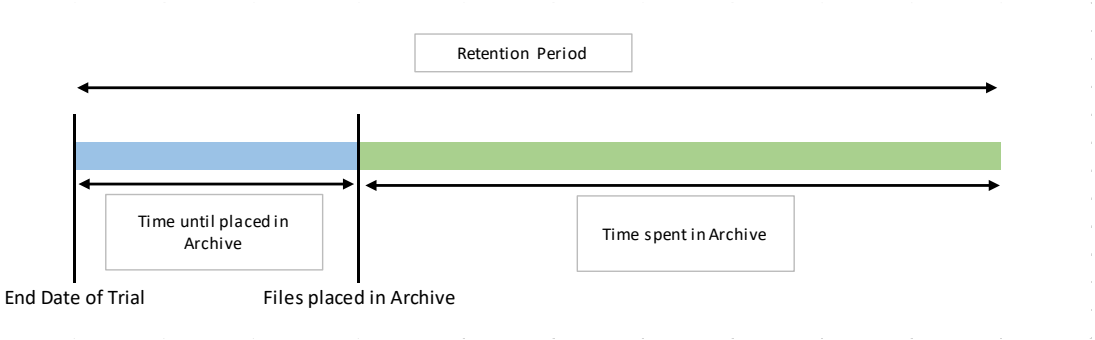

Figure 2 – Retention Period

The end of trial should be clearly defined in the trial protocol and IRAS application (i.e. database lock). For trials that require long term follow-up, this should be included in the trial protocol, participant information sheet and consent form. The follow-up should be part of a subsequent R&I study application and linked with the CTIMP/CIMD deemed as complete.

For trials which have been discontinued, retention period will commence after MHRA acknowledges the trial early termination notification sent by the Sponsor/Co-sponsors.

Retention of the documents within the TMF (including the ISF) is a legal requirement, and these should be archived for at least five years or as amended after the conclusion of the trial, or if longer, as documented within the study contract and protocol.

A number of scenarios where the legal minimum requirement is longer than the 5 year minimum and this must be considered when determining the retention period.

- Trials where the data is used to support a marketing authorisation the documentation should be retained for at least 15 years or as amended after completion or early termination of the trial or for at least two years after the granting of the last marketing authorisation.
- Advanced Therapy IMP trials documentations should be retained for 30 years.
- Paediatric studies: 3 years after the youngest participant turns 18 or 5 years after conclusion of trial (whichever is longest).

3.5. Costing

The provisional arrangements and costings for archiving the TMF will be agreed between the CI and the Sponsor/Co-sponsor Research Co-ordinator (RC) during the initial Sponsor review process. Costs for archiving are the responsibility of the CI and must be included in the application for funding. As archiving period for CTIMPs/CIMDs is expected to be increased in the near future it is recommended to secure archiving costs for 25 years.

3.6. Archiving process overview for Sponsor/Co-sponsor TMF

All relevant teams are responsible for preparing their documents for archiving as per SOP 51.016 and this SOP, these individuals will be the named archivist as per section 3.3.

Once MHRA acknowledges the End of Trial declaration the retention period for the trial will begin, however, other factors may then impact when documents may be placed into archive (see Figure 2). Factors such as Monitoring Close-out status, upload to public database, publications, follow up activity, etc., once all requirements to begin placing documents in archive have been met, the PM (or designee) initiates the archival process for the trial by informing all relevant parties that the archiving process can begin. The date at which documents are placed into archive does not impact on the retention period for the trial, this is governed solely by the End of Trial declaration. The PM (or designee) records the archiving starting date and all point of contacts on Form 51.024E, along with completed Form 51.024A by each owner and sends the form to the IO. Form 51.024E will also be saved in the trial "Archiving" eFolder and on Q-Pulse, the completed record on Q-Pulse will be retained indefinitely.

Project Managers (or their designees) working across Cancer Research UK Clinical Trials Unit (CRUK CTU, Glasgow) coordinating CTIMPs and CIMDs use archiving processes as per this SOP and CRUK CTU SOPs.

Archiving should be completed within as expedient of a time frame from the End of Trial notification as possible, however this can be impacted by several factors as discussed previously. Therefore, archiving should begin when agreement is given by the PM and the CI. Each team must inform the IO when their corresponding files are ready to be archived and the IO will follow up with all teams responsible for archiving and all participating sites that did not get in contact after three months of approval to archive from the PM. The reasons for delays and a new agreed timeline for archiving will be captured on Form 51.024E; furthermore the IO will set up a new reminder to contact the relevant parties at the agreed date.

When files are ready for archiving each party will contact the IO to arrange documentation and Iron Mountain pick-up (as per section 3.8). Once all sections of Form 51.024E are filled in and the trial archiving process is complete the IO will:

- Update SReDA with the 'Archiving Date' (date when the all section of the study have been sent to archiving) and records each archiving box number in the 'Archive Reference field'.
- Update SReDA 'Archiving Destruction Date' with the proposed date of destruction from form 51.024E.
- Run yearly reports to identify studies nearing end of archival retention period to confirm that they can be destroyed at the end of the retention period.
- Save in the trial "Archiving" eFolder all Iron Mountain and any other party additional archiving documentation.
- Maintain a permanent record of Form 51.024E for each trial on Q-Pulse.

3.7. Vendors (i.e. data management/processors, external laboratories, etc.)

For NHSGGC sponsored and Co-sponsored studies the responsibility for archiving trial documentation also applies to all third party contractors (i.e. Laboratories for sample processing and analysis and data management and processing vendors). The archiving costs should be agreed in advance at the grant application stage.

Each responsible party will archive as per their local requirements and/or in conjunction with advice from the Sponsor/Co-sponsors (via the PM) as agreed in the vendor TMF plan that should be attached in the contract with the vendor and/or Co-sponsorship agreement. The TMF plan (such as Form 51.016L) will capture the process of indexing and filing documentation in the vendor TMF and the archiving arrangements for when the trial is complete. If the agreement is for vendor to archive independently, the vendor will provide to the Sponsor/Co-sponsors with documentation to verify they have all required documentation that's forms the section of the TMF they have responsibility, it has been sufficiently QC checked and is ready for archive, this will then be retained and recorded in Form 51.024E which is retained indefinitely.

3.8. Archiving Process for Hard Copy Files of Sponsor/Co-sponsors TMF

Once TMF folders are stored in the archiving boxes, the IO will arrange Iron Mountain collection. An Iron Mountain barcode is attached to each box prior to being sent to the storage facility in order to identify the box if and when it is required to be returned from the storage facility. The barcodes will be provided by the IO once the boxes are ready for archiving. IO will also ensure that the Iron Mountain Paperwork has been completed online at www.ironmountainconnect.com and arrange for the physical pick up and transport of boxes for archiving. The archiving boxes will be collected by Iron Mountain and transported to their secure archiving facility. The IO will capture all relevant archiving information on Section A of Form 51.024E and save all relevant archiving documentation in the trial "Archiving" eFolder.

3.9. Archiving Process for Electronic Files

Electronic filing ('e-filing') is permissible, provided that issues relating to e-filing have been fully addressed. These include, but are not limited to:

- access to software which allows the data to be read for the duration of the period of retention
- controlled access to e-filing
- a Disaster Recovery Plan in the event of loss of data
- sponsor/co-sponsor permission for use of e-filing or conversion of paper filing into e-files
- acceptability of e-consent signatures
- use of an Electronic Data Management System (EDMS) for storing the source data (e.g. medical notes).

All trial electronic files that cannot be printed will be copied on a USB drive or external hard disk and archived along with the trial paper files using Iron Mountain boxes as stated at section 7.3.

Whilst paper/electronic TMF files are archived and destroyed, pseudo anonymised data (for follow-up purposes) and/or anonymised data within study databases are generally kept as these potentially can be subject to requests for data sharing indefinitely after a study has concluded.

3.10. Retrievals

The retrieval of documents from external storage should be kept to an absolute minimum.
Any trial documents retrieval requests by the research team should be emailed to ggc.researchandinnovationsponsor@ggc.scot.nhs.uk detailing reasons for retrieval and associated costs. If the retrieval has been requested by the research team, the costs of retrieval should be met by the CI.

The request for retrieval and any other relevant communication including retrieval documentation should be saved electronically in a subfolder named "Retrieval" of the trial Archiving eFolder.
Once approved by the Sponsor/Co-sponsors, the IO will contact Iron Mountain and/or any other relevant party and begin the retrieval process and record all information in the Section B of Form 51.024E (Trial documentation retrieval process). If documentation to be retrieved is part of the ISF, the IO will liaise with the relevant Participating Site to process the retrieving request.

3.11. Destruction of Archived Files

The IO will run annually reports titled "Date of Destruction Report" from SReDA (which will be available for all users) on studies nearing or passed their proposed destruction date.

At the end of archiving period the IO will liaise with the Sponsor Research Co-Ordinator who must confirm with the CI that the destruction of archived files can take place. The IO will inform the participating site(s) when destruction of TMF is approaching and of approval to destroy.

Unless the research team and/or sponsor teams advises that the retention period for the trial should be extended, all trials that have been confirmed as passed their destruction date will be securely destroyed by Iron Mountain at the archiving representatives' request.

Whilst archiving can take place in parts, the destruction of trial documentation should all be done around the same time where possible. Destruction of TMF should not take place if the final report has not been submitted. Form 51.024E captures the date when the trial final report is provided to Sponsor/Co-sponsors and regulatory bodies.

The IO will follow up and confirm with all parties (Iron Mountain and all participating sites) when destruction is complete and record all information on Section C of Form 51.024E (Destruction of TMF process). Any relevant destruction documentation and correspondence (i.e. Iron Mountain certificate of destruction) will be saved in the trial "Archiving" eFolder. Before destruction of each CTIMP and/or CIMD trial, the "Archiving" eFolder and a copy of complete Form 51.024E on Q-Pulse will be saved indefinitely for Regulatory and audit purposes. These archiving efolders will be moved in the corresponding yearly subfolders of a generic eFolder named "ARCHIVE (CTIMP_CIMD)" found in the R&I department common drive and server.

If a trial has passed the required archiving period and has never been archived each team responsible for the TMF should destroy their corresponding section. The IO will confirm the destruction dates with all relevant parties and complete Section C of Form 51.024E as audit trail.

Any requests for permission to destroy TMF documentation should be directed to the RC. If the retention period has passed it is assumed that it is acceptable to destroy the archived file, the RC will make efforts to engage, where possible, with the relevant stakeholders from the trial team. They will present that the retention period has passed and that the plan is to destroy the archived files within 3 months. The RC will request positive confirmation of their consent to continue or if there are any objections, in the absence of objections the process of destruction may continue. In the event of no responses from key stakeholders following the 3 month window, the RC will bring this to the CTIMP Oversight Committee for permission to continue.

3.11.1. Destruction of Files not held at Iron Mountain

In the event a trial has passed its required retention period and the destruction of the files has been agreed as per the above, yet the files are located on site and not within Iron Mountain, they may still be destroyed as normal. To destroy of files locally, the standard confidential waste process may be utilised. If however the number of files is too large for this to be feasibly achieved, an approved vendor for this purpose may be utilised, such as Iron Mountain or the organisation responsible for destruction of confidential waste used within the site. A record of this destruction must still be made as normal within Form 51.024E.

4. Referenced Documents/resources

- SOP 51.016 - Preparation and maintenance of a Trial Master File
- Form 51.016A - Sponsor TMF Index
- Form 51.016C - PI File Index
- Form 51.016J - TMF Cover Sheet
- Form 51.016K - TMF Index Pages
- Form 51016L - Vendor TMF Plan (Data Management)
- Guideline 51.016A - Quality Control of Trial Master File
- Form 51.024A - Essential Documents for Archiving – Archiving Checklist (for CTIMPs)
- Form 51.024E - Trial Archiving Oversight
- SOP 53.012 - Monitoring Clinical Research – Site Close Out Monitoring Visit
- Medicines for Human Use (Clinical Trial) Act 2004
- Data Protection Act of 2018

5. Related documents

- None

6. Document History

Version	Date	Description
1.0	12/04/18	Release of First Version
1.1	24/05/18	Minor changes to section 5.2.1
2.0	20/12/2023	Admin updates, changes to TMF and destruction process, change of R&D to R&I, new author Forms 51.024 A, B, C and D made obsolete as Sponsor archiving process has been updated and these forms do not reflect SOP 51.024 changes. The Sponsor TMF QC processes will be performed using Form 51.016K and Guideline 51.016A, therefore replacing the two archiving checklists (Form 51.024 A and D). Agreement on Delegation of Responsibility for Archiving is captured at the start of the trial during SIV and in the mNCA between the sponsor and the participating site, therefore not needed as a separate Form 51.024B to be used at the end of trial. Archiving certificate (Form 51.024C) not required as email confirmation from relevant parties will be saved in the trial Archiving eFolder and the information will also be captured as part of a new Form 51.024E – Trial Archiving Oversight Form 51.024E – Trial Archiving Oversight – New form to capture all archiving and retrieval steps of a trial