STANDARD OPERATING PROCEDURE (SOP)

Title: **Archiving of Clinical Trial Investigator Site Files, including Case Report Forms**

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1. PURPOSE

The purpose of this document is to describe the procedure for MCRI/RCH Site Principal Investigators (PIs) to archive the Investigator Site File (ISF) and to facilitate compliance with Good Clinical Practice (GCP), the Therapeutic Goods Administration (TGA), the Health Records Act 2001 (Vic), the National Standard Operating Procedures for Clinical Trials, including Teletrials, in Australia, the Australian Code for the Responsible Conduct of Research, and any other applicable regulatory requirements.

All Essential Documents relating to a clinical trial ISF must be archived in accordance with this Standard Operating Procedure (SOP).

1.1. Quality Improvement

Compliance with this SOP ensures the documents and the data they contain are preserved and remain legible for the duration of the retention period.

1.2. Participant Safety

Compliance with this SOP ensures the participants confidential information is protected.

2. SCOPE

This SOP applies to the archiving of both paper and electronic Essential Documents filed in the ISF. Note the ISF may be a mixture of paper and electronic essential documents, fully paper-based or fully electronic.

This SOP provides the procedure for managing archiving of both paper and electronic Essential Documents for all clinical trials conducted at the Melbourne Children's Campus. It includes archiving the site copy of the Case Report Form (CRF)/electronic data capture (EDC).

This SOP does not cover the procedure for archiving the following:

- Trial Master File (TMF) and Site Information Files (SIFs) for MCRI-sponsored trials. This procedure is currently under development. Please contact the Clinical Research Development Office (CRDO) for further information.
- Teletrials conducted by the RCH Children's Cancer Centre (CCC) Clinical Trial Unit (CTU).
- Clinical trial participant medical records. This is the responsibility of RCH Health Information Services. Note that the RCH electronic medical record will be maintained indefinitely.

3. RESPONSIBILITY

This SOP applies to all members of the Melbourne Children's Campus who are responsible for the archival of the ISF, including the site copy of the CRF.

The PI is responsible for managing the archiving of the ISF in accordance with this SOP. The PI may delegate the tasks of managing the archiving/retrieval from archive of ISF essential documents to a member of the research team ('Delegated Staff'). This delegation must be documented in the Study Delegation of Duties Log.

For externally sponsored trials where RCH/MCRI is a site:

> The PI is responsible for ensuring archiving responsibilities between the RCH/MCRI site and external Sponsor are documented in contracts.

For MCRI-sponsored trials where RCH/MCRI is a site:

> The Sponsor-Investigator should ensure that the archiving responsibilities for both the ISF (and TMF) are clearly outlined in the MCRI Certificate of Sponsorship delegation of responsibilities.

4. PROCEDURE

4.1. Equipment and Supplies

For archiving paper essential documents, archiving materials include:

- standard archiving boxes and barcode labels provided by the archiving facility
- archiving labels (see Appendix 2) for the box lid
- electronic archive document log (see Appendix 1).

For archiving electronic essential documents and the eCRF, use either Florence eBinders or a dedicated archive folder on the MCRI share drive set up with restricted user access and permissions. If archiving essential documents on the MCRI share drive, please contact CRDO for further advice and guidance.

For CCC CTU only: For archiving SiteDocs electronic essential documents, follow the SiteDocs user guide for further instructions.

4.2. Preparing Documents for Storage

The PI may delegate the responsibility of preparing essential documents for archiving to a member of the study team ('Delegated Staff').

4.2.1. Paper documents

- Remove any staples, plastic pockets, adhesive tape, paperclips, bulldog clips, sticky notes and adhesive tabs. If bulldog clips were being used to hold large bundles of paper together, you may separate out into smaller bundles and place in manilla folders to reduce risk of losing pages.

- If plastic page dividers are used, a blank sheet of A4 paper should be placed between the plastic and any documents. Ink should not be touching plastic to prevent degradation of the ink.

- To ensure documents are enduring, trace paper (e.g., ECGs), carbon paper, fax thermal paper, and pages repaired with adhesive tape must be photocopied using a process that is certified and stamped as certified copy. Archive the certified copy together with the original.

  Note: Certified paper copies of documents may be obtained according to MCTC002 SOP Copying and Certifying Essential Documents.

4.2.2. Electronic Documents

- If digitising paper records for electronic filing, use a procedure for generating certified copies.

  Note: When digitising paper records, the system of transfer should be verified (e.g., by a dated signature) or be generated through a validated process to produce an exact copy. MCRI's Guideline for Digitisation of Paper Records at MCRI meets this requirement. Additional information can be found here.

- Check that the file names facilitate easy search and retrieval of documents once archived and rename any files that do not meet this requirement.

  Note: It is recommended clinical trial teams adopt a file naming convention to facilitate search and retrieval of documents. For example, MCTC076 Guidance Electronic File Naming Conventions

4.3. Archival Procedure

4.3.1. Paper Documents

- Trial documentation will be stored off-site using approved off-site storage vendor for medical records. The archival company details can be given to sponsors upon request. Note it is acceptable for the Sponsor to provide financial assistance if using an off-site storage vendor.

  - Archiving Facility Details:

- Grace
    - Address: 9 Ashley Street, West Footscray, VIC 3012, Australia
    - Telephone: +61 3 9680 0300
    - Email: recordsvic@grace.com.au
- ZircoDATA (previously known as Iron Mountain)
    - Address: Level 4 973 Nepean Highway, Bentleigh, VIC 3204, Australia
    - Telephone: 13 ZIRCO (13 94 72)
    - Email: services@zircodata.com.au

- Requests for archiving materials (i.e. boxes and barcodes) with Grace can be made using the MCRI Intranet Archiving Service Desk. Choose option "I wish to order materials (e.g., bar codes, boxes)", enter cost centre code, enter the quantity of materials to be requested and save. Be aware that each box requires it's own unique barcode.

- Documents for different trials must be archived in separate boxes. The exception to this rule is Children's Oncology Group (COG) trials run through the CCC CTU, in which case more than one trial may be archived in the same box if practical.

- Additional precautionary measures must be taken to protect participant data. For any boxes that contain personal and health information (see Glossary), the boxes must be labelled as such.

- Place contents of the ISF into the boxes, keeping the sections in sequence in accordance with the trial-specific ISF contents index.

- Complete the Template Archiving Label (see Appendix 2), print and affix to the lid of the box. If Sponsor has also provided archiving labels complete and affix these to the lid of the box. Place an additional copy of the completed labels inside the box. This serves as a back-up should the external box label get destroyed or the print fades over time.

- Attach the barcode sticker supplied by the archival facility to the box.

- Secure box with lid and store box in a secure facility until courier collects box for delivery to archival facility (i.e., within locked tambour or locked storage area with minimal risk to hazards and damage).

- Complete the relevant RCH department/MCRI Group/MCTC archive document log. If you are setting up a new archive document log, consider Archiving

Document Log Template (Appendix 1). Each RCH department/MCRI Group/MCTC is responsible for maintaining an archive document log for their trials. The log should be saved in an appropriate location.

- Requests for archiving with Grace can be made via the MCRI Intranet Archiving Service Desk. Select "I have a box packed ready to be archived", enter the collection date and time and click "save".
    - Complete the 'MCRI Archiving Template' provided by the MCRI receptionist organising the box collection.
    - Once completed, provide the 'MCRI Archiving Template' to the MCRI receptionist. This log is sent to the archival facility when booking a collection of completed boxes. The information will be transferred to the archival facilities record database for storage and box recall purposes. **Note consider entering a general contact number and/or email address should queries arise from the archiving facility.*

- Requests for archiving with ZircoDATA can be made via the ZircoDATA online portal. CCC CTU has a general login for this online portal. Please contact CRDO for further advice and guidance.

- Any change in the ownership and location of the archived materials should be tracked in the RCH department/MCRI Group/MCTC archive document log. The PI/study team should make the Sponsor aware of the storage arrangements for the ISF and if at any stage these arrangements can no longer be maintained, the Sponsor should be notified in writing so that alternative storage arrangements can be agreed.

4.3.2. Electronic Records

- Trials managed by SiteDocs Portal eISF are to be archived according to the SiteDocs Portal 4.0 User Guide. Please contact CRDO for further advice and guidance.

- Trials managed by Florence eBinders are to be archived according to Florence Archiving Instructions.

- For trials managed in Share Drive/Teams the eISF should be archived to a dedicated folder on the MCRI share drive set up with restricted user access and permissions. Please contact CRDO for further advice and guidance.

- All electronic documents must be appropriately protected from unauthorised changes, e.g., by converting all documents to PDF-A format.

Emails and eCRF

Email correspondence and the eCRF must be archived on the MCRI network share/group drives which is backed up in two locations on two mediums indefinitely. Access must be restricted by user access levels to the archive area of the server and protected from unauthorised changes.

Note: It is not recommended to archive emails or the eCRF on portable storage devices as these are prone to deteriorate and would require periodic retrieval or restores to be undertaken to confirm that ongoing availability of the data is maintained.

4.4. Record Retention

- Clinical trial records must be kept for a minimum period of 15 years, or until the youngest participant recruited from the site turns 25 years of age, whichever is longer. List the destruction date as 25 years from the archival date if unsure.
- Clinical trial records may be stored for longer than the minimum retention period if required by the applicable regulations, or at the request and prior agreement of the PI, or Sponsor.
- Note the Management of Data and Information in Research: A guide supporting the Australian Code for the Responsible Conduct of Research requires indefinite retention periods for any human participant research, including clinical trials, that involves the following:
    - Gene therapy
    - Data and information with cultural, historical, or other significance, or cultural significance or value to Indigenous governance decision-making.

Note: The RCH Electronic Medical Records are retained indefinitely.

4.5. Retrieval Procedure

- Access to archives must be restricted to delegated staff and authorised personnel (see Glossary). Delegated staff or authorised personnel are responsible for controlling who has access to the archived ISF. Access to the archived ISF should be restricted by role and permission determined by the Principal Investigator. Delegated staff or authorised personnel are responsible for maintaining the documents and checking that no unauthorised changes are made.

4.5.1. Paper Documents

- Track when the ISF is retrieved, accessed, and returned in the Archiving Document Log (Appendix 1).

- Requests for the retrieval of paper records by the sponsor, the local RGO or regulatory bodies must be made in writing to the PI and/or study team.
- Requests for retrieving archived materials with Grace can be made using the MCRI Intranet Archiving Service Desk. Select option "I wish to recall a box archived at Grace" and click "Save". You will be requested to provide the barcode/s corresponding to the box/es (saved in archive document log) you would like to recall and an appropriate cost centre.
- Any documents which are added to the ISF should be tracked in Archiving Document Log (Appendix 1). Any documents which are removed from the ISF should be reconciled prior to re-archiving. This should be tracked in the Archiving Document Log (Appendix 1).
- The delegated staff or authorised personnel are responsible for requesting records be returned to the archiving facility once they are ready to be re-archived.
- The Archiving Document Log (Appendix 1) should be updated with the date records were returned to the archiving facility.

4.5.2. Electronic records

- Tracking of ISF retrieval and access can be done by the audit trail.
- Requests for the retrieval of electronic records by the sponsor, the local RGO or regulatory bodies must be made in writing to the PI and/or study team.
- Delegated staff or authorised personnel are responsible for maintaining the documents and checking that no unauthorised changes are made.
- The person responsible should grant read-only access to those accessing the documents with an audit trail to verify this activity. The audit trail must be maintained with the archived ISF.

4.6. Destruction Procedure

- It is the responsibility of the authorised personnel to maintain the delegation of duties log to ensure a currently employed PI is delegated at the time of record destruction.
- Records must only be destroyed after the minimum period of retention has lapsed and the written approval of the sponsor or delegate has been obtained.
- It is the responsibility of the Sponsor to advise the PI and/or authorised personnel when destruction of the records may occur. The PI and/or authorised personnel may also initiate contact with the sponsor or delegate for confirmation of destruction date(s).
- Confirmation of destruction is to be retained in the Archiving Document Log (Appendix 1).

5. GLOSSARY

Authorised Personnel

A study may be archived for some years and 'delegated staff' may no longer be present. Authorised personnel within the relevant department should receive a hand over and would have responsibility in maintaining archived records (e.g., retrieval of records if required and re-archival). The authorised personnel should be role-based (e.g., Clinical Trial Assistant) to ensure that responsibility rolls over when staff members leave.

Case Report Form (CRF)

Data collection tool used to record all the protocol required information to be reported to the sponsor on each research/trial participant. The CRF may be paper or electronic.

Certified Copy

A copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, content, and structure, as the original.

Clinical Trial

The World Health Organization (WHO) definition for a clinical trial is: 'any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes'.

Children's Cancer Centre Clinical Trial Unit (CCC CTU)

CCC CTU is embedded within the Children's Cancer Centre of the Royal Children's Hospital. The unit focuses on clinical trials that investigate interventions in the diagnosis, treatment and management of cancer in children.

Children's Oncology Group (COG)

The Children's Oncology Group, a National Cancer Institute supported clinical trials group, is the world's largest organisation devoted exclusively to childhood and adolescent cancer research. The COG unites more than 10,000 experts in childhood cancer at more than 200 leading children's hospitals, universities, and cancer centres across North America, Australia, New Zealand, and Europe in the fight against childhood cancer.

Delegated Staff

Delegated staff are those involved in the initial archiving of the study and assigned by the PI at time of archiving. Delegated staff have primary archiving responsibilities.

Essential Documents

Documents which individually and collectively permit evaluation of the conduct of a study 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 (GCP) and with all

applicable regulatory requirements. Filing essential documents at the Sponsor site and participating trial sites also assists with the successful management of the trial.

Good Clinical Practice (GCP)

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Health Information

Health Records Act 2001: Protects the privacy of individuals' health information. Health Privacy Principles (HPP) apply to (1) all personal information collected in providing a health, mental health, disability, aged care or palliative care service; and (2) all health information held by other organisations.

International Conference on Harmonisation (ICH)

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is unique in bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration.

Investigator

A person responsible for the conduct of the clinical trial at a trial site. There are four types of Investigator roles used to describe Investigators with different levels of responsibility for the conduct of clinical trials. These are described below.

Associate Investigator

Any individual member of the clinical trial team designated and supervised by the Principal investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows). May also be referred to as sub-investigator.

Coordinating Principal Investigator (CPI)

If a study is conducted at more than one study site, the Principal Investigator taking the additional responsibility for coordination of the study across all sites in a region is known as the Coordinating Principal Investigator (CPI). This role applies to externally sponsored studies where the Sponsor may be a collaborative research group, commercial Sponsor or an institution. The Principal Investigator at each site will retain responsibility for the conduct of the study at their site.

Principal Investigator

The PI is the person responsible, individually or as a leader of the clinical trial team at a site, for the conduct of a clinical trial at that site. As such, the PI supports a culture of responsible clinical trial conduct in their health service organisation in their field of practice and, is responsible for adequately supervising his or her clinical trial team.

The PI must conduct the clinical trial in accordance with the approved clinical trial protocol and ensure adequate clinical cover is provided for the trial and ensure compliance with the trial protocol.

Sponsor-Investigator

An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a participant. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

Investigator Site File (ISF)

Filing repository controlled by the site Principal Investigator. It is held at the trial site and contains all the essential documents necessary for the site trial team to conduct the trial as well as the essential documents that individually and collectively permit evaluation of the conduct of the trial at the site and the quality of the data produced.

The ISF includes the following: trial documentation, supporting department documentation related to the trial, laboratory documentation, CVs for key trial staff, staff training records, and documents containing personal data that enable the participants to be directly identified, e.g. signed participant consent forms, patient files, participant identification code list, participant-related source documents.

Melbourne Children's Campus

The campus encompassing all staff from The Royal Children's Hospital, Murdoch Children's Research Institute and Department of Paediatrics University of Melbourne who initiate or carry out research under one or more of these institutional affiliations.

Melbourne Children's Trials Centre (MCTC)

Melbourne Children's Trials Centre (MCTC) is a collaboration between the Royal Children's Hospital, The Murdoch Children's Research Institute, The Royal Children's Hospital Foundation and The University of Melbourne. This Centre brings together expertise in research, clinical practice, and education and incorporates anyone who initiates or carries out research under one or more of these institutional affiliations.

Murdoch Children's Research Institute (MCRI)

An Australian paediatric medical research institute located in Melbourne, Victoria, affiliated with the Royal Children's Hospital and the University of Melbourne. The institute has six research themes: cellular biology, clinical sciences, genetics, infection and immunity, population health, and data science.

Participant

A participant is a person that is the subject of the research and from whom data is collected.

Personal Information

Privacy and Data Protection Act 2014: Means information or an opinion (including information or an opinion forming part of a database), that is recorded in any form and whether true or not, about an individual whose identity is apparent, or can reasonably be ascertained, from the information or opinion, but does not include information of a kind to which the *Health Records Act 2001* applies.

Protocol

A document that describes the objective(s), design, methodology, statistical considerations, and organisation of a trial.

Royal Children's Hospital (RCH)

The Royal Children's Hospital is major specialist paediatric hospital in Victoria, the Royal Children's Hospital provides a full range of clinical services, tertiary care, as well as health promotion and prevention programs for children and young people. Its campus partners are the Murdoch Children's Research Institute and The University of Melbourne Department of Paediatrics, which are based on site at the hospital.

Sponsor

An individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study. For investigator-initiated trials, MCRI or RCH will act as the Sponsor but delegate many sponsor responsibilities to the Coordinating Principal Investigator. In this case the CPI has the role of both Sponsor and Investigator and hence the MCTC has adopted the term **Sponsor-Investigator** to reflect the dual role of the CPI in investigator-initiated trials.

Standard Operating Procedure (SOP)

Detailed, written instructions to achieve uniformity of the performance of a specific function.

Study Team

Refers to the extended group of people involved in a research study. This includes the investigator team and any additional members of staff who are involved in the set-up or conduct of the study e.g. research nurse, research assistants.

Trial Master File (TMF)

Filing repository controlled by the Sponsor/Sponsor-Investigator. It is the collection of essential documents that allows the Sponsor responsibilities for the conduct of the clinical trial, the integrity of the trial data and the compliance of the trial with Good Clinical Practice (GCP) to be evaluated.

6. REFERENCES

ARC, NHMRC and Universities Australia: Australian Code for the Responsible Conduct of Research. (2018). Available from: https://www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018

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7. COLLABORATORS

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Kate Scarff / CRDO Lead	Clinical Research Development Office	MCRI
Yasemin Mehmed / Clinical Trials Assistant	Melbourne Children's Trials Centre	MCRI
Iona Walton / Clinical Research Development Officer	Melbourne Children's Trials Centre	MCRI
Jade Sheppard / Clinical Trials Manager	Melbourne Children's Trials Centre	MCRI
Carmel Delzoppo / Data Research Team Leader	Paediatric ICU	RCH

Jennifer Luplow / Research Ethics Manager	Research Ethics and Governance Office	RCH
Kahlia Fox / Clinical Trial Manager	Children's Cancer Centre Clinical Trial Unit	RCH

8. APPENDICES

8.1. Appendix 1: Grace Archiving Log Template

8.2. Appendix 2: Archiving Box Label Template

Archiving Box Label

Box Barcode Number	
Sponsor	
HREC Number	
Box Contents	
DO NOT DESTROY BEFORE DATE (this is a regulatory requirement):	

☐ THIS BOX CONTAINS PERSONAL AND HEALTH INFORMATION.

DO NOT OPEN UNLESS YOU ARE AUTHORISED PERSONNEL.

9. RELATED DOCUMENTS

MCTC001 | SOP: Creation of new Standard Operating Procedures
MCTC002 | SOP Copying and Certifying Essential Documents
MCTC076 | Guidance: Electronic File Naming Conventions
MCTC121 | SOP: Document Management and Version Control

MCTC071 | Guidance: Electronic Investigator Site filing Guidance for MCRI sponsored clinical trials
MCTC176 | Form Electronic Site Investigator File e(ISF) Filing Index for MCRI sponsored clinical trials
MCTC202 | Template: Archiving Box Label
MCTC203 | Template: GRACE Archiving Log

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