Standard Operating Procedure

Title: **Document Management and Version Control**

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Applicability: Human Participant Research

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This document is effective from the date of the last approval signature and will be reviewed in three years.

Document History

Version	Date of Release	Modified by	Description of Change
1.0	17/08/2022	CRDO – Stephanie Firth	New Issue
2.0	12/06/2024	CRDO – Iona Walton	Revised procedure for the management and tracking of documents in a database. This included updates to fields recorded, control of document access and inclusion of eBinder document management.

Contents

1.0 PURPOSE

To provide the procedure for document management and control, including drafting, issue, filing and revision of clinical trial documents at Melbourne Children's.

1.1 Quality Improvement

This SOP ensures:

- All staff within a clinical trial team and contributors are working on the same document versions during document development/updates.
- All staff are using the most recent approved version of a document.
- Efficiency in filing and access to documents throughout the trial life cycle.

2.0 SCOPE

This SOP applies to all Melbourne Children's employees involved in the management of controlled documents associated with clinical trials. This includes:

- Staff conducting trials at MCRI at the Sponsor level (Sponsor-Investigators, and members of the central coordinating trial team)
- Staff supporting externally sponsored trials when either RCH or MCRI is a recruiting site (Site Principal Investigator and their site team).

This SOP does not apply to Clinical Research Development Office (CRDO) staff responsible for the management of Melbourne Children's clinical trial Standard Operating Procedures (SOPs), Guidance, Work Instructions, Fact Sheets and associated template forms/logs/checklists. In this case, there is a separate SOP: MCTC201 METIS Management.

MCRI-Sponsor-Investigators and RCH/MCRI Site PIs are responsible for implementing the procedures set out in this SOP. Controlled documents include (but are not limited to):

- Protocol
- Participant/Parent Guardian Information Statement and Consent Forms
- Standard Operating Procedures (SOPs), Work Instructions, Manual of Procedures (MoPs), and associated template forms/logs/checklists
- Guidance Documents
- Data Management Plan, Data Sharing Plan, Clinical Monitoring Plan

This SOP does not differentiate between electronic and paper files, unless otherwise specified.

This SOP is mandatory for clinical trials of investigational medicinal products /investigational medical devices to facilitate the management of essential documents in accordance with ICH Good Clinical Practice, E6 (R2).

This SOP may be used by staff conducting other types of clinical research at the discretion of the Sponsor-Investigator/Site Principal Investigator, to support best research practices.

3.0 RESPONSIBILITY

It is the responsibility of the Sponsor-Investigator/Site Principal Investigator (PI) to manage controlled documents generated for their trials in accordance with this SOP.

It is the responsibility of all Melbourne Children's employees to ensure they have read, understood and adhere to the currently authorised version of documents applicable to their role. All employees should be vigilant for

procedures and information which require standardisation and take the initiative to address the need for document revisions and/or a new SOP as outlined in MCTC001 Guidance: Creation of New Standard Operating Procedures.

4.0 PROCEDURE

4.1 Document Database

The Sponsor-Investigator/Site PI/delegate will set up and maintain a controlled document database to record the following for all trial-specific controlled documents:

- Document ID (if required)
- Document title
- Document status
- Version number
- Approval date
- Effective date
- Review deadline – with set review period (e.g. 3 years)

You might also include:

- Author's name
- Reviewer's name
- Approver's name

The Sponsor-Investigator/Site PI/delegate will ensure the controlled document database is viewable for their respective central coordinating team/site team and for review by internal/external auditors and regulatory inspectors. This may be uploaded in a read-only format to a central location such as a shared computer drive, team website, Teams/SharePoint, or Florence eBinders.

4.2 Document Version Control

4.2.1 Version numbering

For major amendments such as a change in procedure or additional information provided, the primary version number should increase in sequentially: e.g. version 1.0, version 2.0, version 3.0. For minor amendments such as administrative changes, minor errors etc., the version number should increase in sequential increments of 0.1 e.g. version 3.1, 3.2, 3.3, etc.

4.2.2 Central document control

When using paper files and/or a Shared Drive such as Teams, SharePoint, etc, one individual should be designated **'document controller'** to ensure consistency of the document control process within the project. The document controller should have exclusive access to edit the document database.

To begin a new draft of a document, the author must send a request to the document controller. The document controller will then release a template of the document that has been requested and give the author access to edit. The document controller will update the document with the metadata required.

To review new drafts or documents due for review, the author must contact the document controller to release the document for review to nominated reviewers. The document controller will record reviewer names and version number, and update the status of the document to 'under review' in the document database once released.

Once a document has been reviewed and approved by the reviewers, they must notify the document controller who will remove all edit access for author and reviewers and fix any formatting issues. Once the document is cleaned of edits and comments, the document controller will turn the document into the appropriate format e.g. Word docx, PDF etc. A copy of the final document is to be provided to the author or individual responsible for filing in intended location, e.g. regulatory binder (TMF, ISF), external sites or document repository.

4.3 Document Development

4.3.1 Drafting

All documents in draft form should be clearly marked as such in both the file name and in the document properties.

Ensure drafts are watermarked or otherwise clearly identified as a draft in the document content. Drafts should be created as per standardised templates to ensure clarity and consistency. Before you commence drafting a new document, check with the relevant support group if a template is available. For example, CRDO, CEBU, RCH Research Ethics & Governance Office and LifeCourse.

4.3.2 Review

The document should be reviewed by at least one other party with expertise relevant to the document subject matter close to the document's completion. This review will ensure it is grammatically correct, understandable, relevant, accurate, and compliant with the relevant regulations and guidelines.

The author should also consider:

- Who will be impacted by new document and/or process; and
- Who may have an impact on the new document and/or process

and engage these stakeholders for review.

When document is ready for review, the document controller will 'release' the document as detailed in 4.2.2 Central document control to ensure the most current version is being viewed and/or edited at all times.

4.3.3 Authorisation

The controlled document must be approved by the lead individual/delegate of:

- The publishing group
- The most affected group(s)

Should the authoriser(s) require changes, the document will return to the author for additional changes. It is recommended that consideration is given to the Authoriser in the development process.

The author and reviewer/authoriser must be different people. Formal review and approval must be documented in the document database.

4.3.4 Finalising

When the document is ready to be finalised:

- Remove the 'Draft' watermark
- Update the footer containing the document version number and publication date
- Schedule a date for periodic review (See 4.5 Periodic Review)

- If changes have been tracked or comments made in a word document, save a new version of the document with tracked changes 'approved', tracking turned off, and any comments deleted.
- The final version must be signed off by the author(s) with hard copy or electronic signatures.
- The final version must be reviewed, approved and signed off by the relevant department head(s) or delegate(s) with hard copy or electronic signatures.
- If applicable, signature blocks must be completed with hard copy or electronic signatures in the version tracker.

4.4 Document Issue

Following approval, the finalised document must be distributed by all relevant department, employees and/or research participants with:

- A description of document contents and/or changes e.g. Summary of Changes, as a part of the document (see MCTCC111a Template: SOP / Guidance Documents), or in the body of distribution correspondence. E.g. email communication about the new document issue.
- The name / ID of any of the document(s) being replaced.
- The date of implementation
- The date of scheduled review (See 4.5 Periodic Review)
- If applicable, an outline of who is affected by the issue/changes to documentation
- If applicable, training guidelines for affected staff

Where the document must not be altered it should be published as a .pdf or other non-writable file format. Should the site/department be permitted to customise the document, it should be published as a .pdf with writable form fields, a .docx, or equivalent writable file format with a Creative Commons License Attribution-Noncommercial 4.0 International (CC BY-NC 4.0) . It must be made clear which sections can be altered and which are essential.

The relevant department and/or employees should confirm receipt of the new documentation and the withdrawal of any superseded or obsolete documents.

Employees working with or being guided by the document should be trained prior to the effective date, and MUST be trained prior to commencing duties relevant to the document. Training should be documented in training logs.

4.4.1 Issue via eTMF platforms

Trials using **Florence eBinders** may do this by uploading the new document to Florence and sending an announcement to members of relevant trial teams. This will ensure that shortcuts to the superseding document are automatically updated.

Trials using SiteDocs may do this by uploading the new document to SiteDocs and generating a workflow to ensure all relevant users are notified and trained. If a document is superseded, the workflow will now carry over to the new document. A new workflow will have to be generated.

4.5 Document revisions

Documents should be reviewed and updated as required e.g. responding to changes in regulatory requirements, improvements in study processes.

The author or document controller of the document should initiate the review three months before the review date.

If changes are required, the author should follow the procedures outlined in 4.3 Document Development, followed by procedure outlined in 4.6 Document Withdrawal to retire the superseded version .
If no changes are required, the document controller will reissue the document with the same version number.

If the author/reviewers identify that the document is no longer required, the publishing group will initiate the procedures outlined in 4.7 Obsolete Documents.

The person authorised to approve the changes (refer to 4.3.3 Authorisation for guidance) must sign and date as reviewer and approver on the document. The document controller will then update the document database with the new revision date, and name and title of the author and person approving the revision.

4.5.1 Approval via eTMF platforms

Within Florence eBinders, the authoriser(s) may sign an addendum page and update the expiry date on the document, to indicate their approval for the documents ongoing use.

Within SiteDocs, if a document is signed and time stamped by the authorising staff member (I.e. Quality Officer, Clinical Trials Manager) via a workflow, it is deemed to be approved for the documents ongoing use.

Revisions can be required for a number of reasons, including changes in regulatory requirements, in response to adverse events, to provide additional or clearer information to study participants, or even to reflect a change in branding. All employees should be vigilant for procedures and information which may require amendment, and communicate the need for document revisions where required. Please refer to CRDO's guide on Corrective and Preventative Action Plans for more guidance.

4.6 Document Withdrawal

Where using paper files and/or a shared drive, the document controller must:

Use a marker to put a diagonal line over all pages of the hard copy in the Trial Binder or watermark the electronic file 'Superseded' or 'Obsolete' as applicable

- Update the Electronic file name with the new status
- Update the corresponding document tracker
- Update the document registry

All hard copies outside the TMF/ISF must be destroyed, and the files removed from active use. All relevant departments/sites must confirm with the document controller that all out-of-use documents have been withdrawn/destroyed.

When using an eBinder platform, the withdrawn document will:

- Be filed in the version history superseding document; or
- Be moved to a new folder which can only be accessed by the Binder administrator and/or archivist.

4.7 Obsolete Documents

If a document falls out of use, is replaced by a new document (as opposed to being superseded by an updated version of the same document), or otherwise must be removed from use, a member of the research

team should submit a request for discontinuation in writing, which must be approved by the Principal Investigator or their delegate.

On approval, studies using a shared drive and/or paper filing must withdraw the document. The document controller will update the document status to 'obsolete' and archive the file.

Where using an eBinder platform such as Florence or SiteDocs, the document controller should move the obsolete document to a folder titled 'Obsolete documents', created in the same place the document was previously filed.

5.0 GLOSSARY

Clinical Research Development Office (CRDO)

CRDO provides education and training to facilitate and increase capacity for clinical and public health research across the Melbourne Children's campus. This includes the development and implementation of Standard Operating Procedures and templates to enable researchers to conduct high quality research.

Clinical Trial

A clinical trial as defined by the NHMRC are trials that can involve investigating new or existing medicines, medical devices and other medical or non-medical interventions. For example, a clinical trial could involve new drugs, medical devices, biologicals, vaccines, surgical and other medical treatments and procedures. Psycho-therapeutic and behavioural therapies help service changes, preventative care strategies and educational interventions are also examples of clinical trials. Researchers might also conduct clinical trials to evaluate diagnostic or screening tests and new ways to detect and treat disease.

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.

Investigational Medicinal Product (IMP)

A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

Investigational Medical Device (IMD)

A device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device.

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 (eg, 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.

Melbourne Children's

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.

Participant

A participant is a person that is the subject of the research.

Protocol

A document that describes the objective(s), design, methodology, statistical considerations, and organization 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.

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.

6.0 REFERENCES

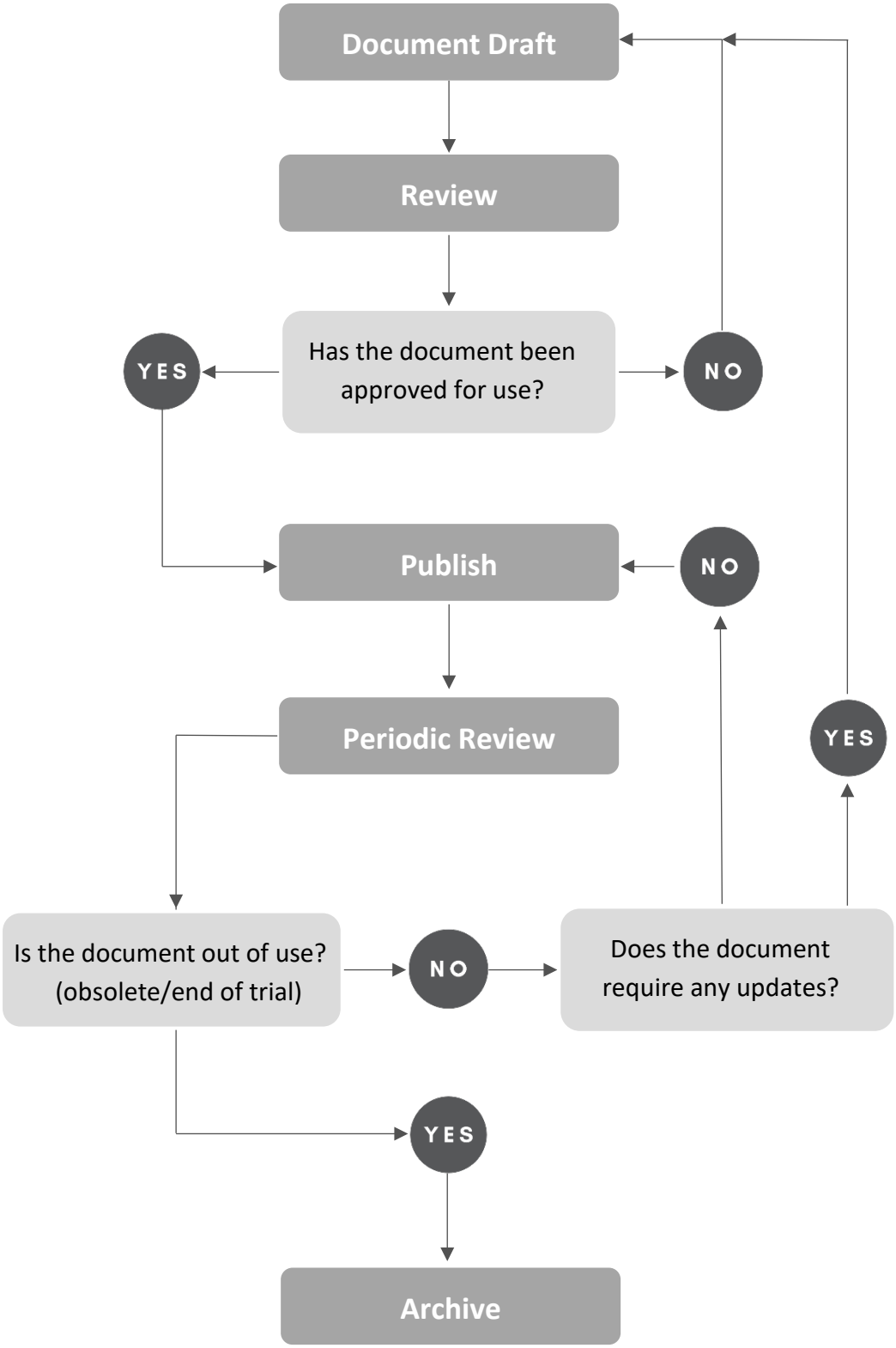
Clinical Trials Project Reference Group: National Standard Operating Procedures for Clinical Trials, including Teletrials in Australia available at https://www.health.gov.au/sites/default/files/2023-07/national-standard-operating-procedures-for-clinical-trials_0.pdf.

7.0 COLLABORATORS

This SOP was reviewed by the Melbourne Children's Clinical Trial SOP Working Group.

8.0 APPENDICES

APPENDIX A: Document Creation and Update Workflow



9.0 RELATED DOCUMENTS

MCTC001 SOP | Creation of New Standard Operating Procedures

MCTC017 Template | Study Staff Training Logs

MCTC076 Guidance | Electronic File Naming Conventions

MCTC111a Template | External SOP

MCTC201 SOP | METIS Management