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The Department of Research and Innovation, in collaboration with the Cancer Centre Clinical Trials Unit, has developed a series of standard operating procedures (SOPs) designed to facilitate good clinical trials practice and compliance with applicable regulatory requirements for clinical trial research at Bendigo Health. These SOPs are based on those developed by the Parkville Cancer Clinical Trials Unit (PCCTU) who have kindly granted permission for adaptation and use at Bendigo Health.

SOP 10: Essential Document Management for Clinical Trial Research

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	Final revisions by:	Approved on behalf of the Interdisciplinary Research Steering Committee by Chair:
Name	Dr. Rani Watts	Dr. Angela Crombie
Position Title	Clinical Trials Research Manager	Director of Research and Innovation
Signature		
Date	20-Dec-2021	20-Dec-2021

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1. Introduction and Background

International Council for Harmonisation (ICH) of Good Clinical Practice (GCP) guidelines defines essential documents as "*documents which individually and collectively permit evaluation of the conduct of the trial 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 and with all applicable regulatory requirements.*" (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. ICH Harmonised Guideline. Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2) (2016) sec. 8.1)

Site ICH GCP and local regulatory compliance is demonstrated through the accurate collection and maintenance of essential documents. Filing essential documents in an orderly and timely manner is important in the management and oversight of clinical trials.

Essential documents are kept in a study specific investigator site file (ISF) and maintained by delegated members of the study team as documented on the *Site Signature and Delegation of Duties Log*.

The SiteDocs portal is a collaborative online portal used by Bendigo Health to store essential documents electronically. Electronic documents are accessed centrally by secure login and managed in collaboration with the study team, and applicable sponsor/contract research organisation (CRO).

2. Objective

To describe the procedures relevant for the collection and maintenance of essential documents for clinical trials coordinated by Bendigo Health.

3. Scope

This standard operating procedure (SOP) applies to all clinical trials coordinated by Bendigo Health.

4. Ownership and Responsibility

The Principal Investigator (PI) and relevant department study team will be responsible for the collection and maintenance of all essential documents throughout the duration of the clinical trial.

5. Glossary of Terms

Please refer to *Bendigo Health's Clinical Trial Research Standard Operating Procedures Glossary of Terms* (see Related Documents) for a full supporting glossary.

6. Procedure

6.1 Collection of Essential Documents

It is the responsibility of the PI / delegate to ensure all essential documents are collected prior to clinical trial initiation and maintained throughout the clinical trial.

All essential documents may be subject to inspection or audit (as outlined in *SOP 7: Hosting a Regulatory Inspection, Sponsor or HREC-Initiated Audit for Clinical Trial Research*, see Related Documents).

6.1.1 Investigator Site File

Documents are filed according to the *Investigator Site File Table of Contents* template (see Related Documents) to maintain consistency across Bendigo Health.

6.1.2 Electronic Investigator Site File

An electronic Investigator Site File (eISF) for each trial is located in the Collaboration Module of the SiteDocs portal.

These electronic folders contain trial specific documents only. A standard table of contents is used in each trial folder to maintain consistency.

General site documents including site personnel documents, equipment records and supporting department documentation are located in the Core Documents module of the SiteDocs portal. These documents are imported to the e-ISF at the conclusion of the trial.

SiteDocs portal access is managed by the responsible department and provided by secure login. SiteDocs portal accounts must be set up with personal email accounts for audit trail purposes. Sponsor and CRO representatives will be provided access to Core Documents and the trial specific eISF as applicable.

Essential documents that are available in the SiteDocs portal will not be uploaded into sponsor/CRO portals. They can be retrieved directly from the SiteDocs portal by sponsor/CRO representatives.

6.1.3 Hardcopy Binder for Wet-Ink Documents

Departments may request clinical trial sponsors/CROs to provide one hard copy site file at the

beginning of a trial to hold wet ink essential documents. All other study related documents will be uploaded to SiteDocs.

Wet ink signature documents are scanned and electronically certified in the SiteDocs portal as an accurate and complete representation of the original paper document. The original documents will be kept in a hardcopy ISF binder. This binder will use a condensed version of the *ISF Table of Contents* (see Related Documents) so that documents may be easily located.

The following information should be displayed prominently on the cover and spine of the hardcopy ISF:

- HREC and SSA reference numbers
- Protocol number and short name
- Site number
- Name of PI
- Specific folder number and total number folders

All documents contained in the hardcopy ISF should be retained in a secure area accessible only to the PI and study team.

6.2 Curriculum Vitaes (CVs)

All study team members are required to provide an abbreviated CV. The CV should detail clinical experience and relevant training. CV's are required to be updated every two years or when a change in position has occurred.

Each department will maintain a central file containing the wet ink signed original CV. Copies of CV's will be filed into clinical trial specific ISF for viewing and collection by the clinical research associate (CRA) at next monitoring visit. Alternatively, the signed CVs will be available for CRAs to download from the Core Documents module of SiteDocs.

6.3 ICH GCP Certification

All study team members are required to complete an approved ICH GCP training, with refresher training as required within three years. If study team members hold an approved ICH GCP certificate they will not be required to complete any further GCP training requested by individual sponsors.

Copies of the certificates will be filed into the relevant clinical trial ISF. Alternatively, copies of the certificates can be viewed and downloaded from the SiteDocs portal.

6.4 Medical Licences

Each investigator will list on their completed CV their professional registration number. Up to date and current information about their registration status is available to sponsors via the APRHA website and may not be collected or maintained in the ISF by the study team.

6.5 Statement of Investigator (1572 Form)

If required, the sponsor is required to provide the PI with a complete and accurate 1572 form to sign. Any external laboratories utilised by clinical trial participants for routine blood draws will not be considered as part of the services engaged for the clinical trial.

This is not required as outlined in Frequently Asked Questions – Statement of Investigator (Form FDA 1572) (U.S. Department of Health and Human Services et al, 2010, sec. 29). The original wet ink 1572 will be available for collection by the CRA at their monitoring visit with a certified copy uploaded to the SiteDocs portal.

6.6 Financial Disclosure Form (FDF)

If required, FDFs will be collected from investigators.

The original wet ink FDF will be available for collection by the CRA at their monitoring visit with a certified copy uploaded to the SiteDocs portal.

6.7 Delegation of Duties Log

As outlined in *SOP 4: Clinical Trial Research Delegation of Duties* (see Related Documents).

6.8 Training Records

As outlined in *SOP 3: Clinical Trial Research Training* (see Related Documents).

6.9 Patient Logs

A pre-screening/screening log will be used for clinical trials where a pre-screening participant informed consent form (PICF) is approved. For all clinical trials, the following two logs will be maintained:

- Participant identification log: a confidential list of names of all clinical trial participants and their allocated clinical trial identification numbers.
- Enrolment log: chronological enrolment list of clinical trial participants by clinical trial identification number.

To ensure confidentiality, participant logs will not be provided to the sponsor electronically but may be viewed at monitoring visits.

6.10 Source Documents

Where the clinical trial protocol requires data to be generated based on calculations (i.e. creatinine clearance, RR intervals or QTcF, etc) the source data used in these calculations will be made available; however there is no requirement to include evidence of the calculation itself.

6.11 Clinical Trial Correspondence

Essential correspondence reconstructs key clinical trial activities, decisions or significant information. Such correspondence is limited and only accounts for a few documents as most correspondence information is available in other formats (i.e. eCRF audit trail, newsletters, ethical approval monitoring letters). The essential correspondence listed below (but not limited to) will be filed in the electronic ISF:

- Correspondence with ethics and governance committees
- Correspondence with data safety management boards
- Correspondence with regulatory authorities
- Sponsor confirmation or approval of processes, documents, and decisions (i.e. newsletters, safety cohort/recruitment updates, monitoring letters, protocol change summaries, meeting minutes, treatment beyond progression)
- Communication regarding clinical trial misconduct and how issues are resolved

Important correspondence informs and directs clinical trial management. Such correspondence is only relevant for the duration of the clinical trial and may require further documentation in an additional source (i.e. electronic medical record notes). Important correspondence will be filed in email storage.

Non-essential correspondence makes up the majority of all clinical trial correspondence. Any communication that has been resolved, relevant for a short period of time or available in other format (i.e. database audit trail, newsletter or approval letter) is considered non-essential and will be deleted once redundant.

7. Dissemination and Implementation

The Department of Research and Innovation at Bendigo Health is responsible for the dissemination and implementation of the Bendigo Health SOPs related to clinical research. Any content updates will be tabled at the Clinical Trials Sub-Group and the Interdisciplinary Steering Committee meetings. Content updates will be accompanied by relevant promotions and training.

Approved SOPs will be published on the Bendigo Health intranet and available through the SiteDocs portal. SOPs will be made available in hard copy format upon request to: clinicaltriasresearchsupport@bendigohealth.org.au.

Any updates to the existing approved SOPs will be disseminated internally, and will be effective immediately.

8. Monitoring Compliance and Effectiveness

SOP compliance will be monitored as part of the Bendigo Health SOP monitoring and audit process, initiated by the Clinical Trials Sub-group.

Any queries concerning the effectiveness of the SOP identified during the Bendigo Health monitoring and audit process or through use will be escalated to the Interdisciplinary Research Steering Committee to advise.

9. Review and Updating

This SOP will be reviewed every two years, or when changes to legislation or working practices impact upon the content of this document. This SOP may be merged with another SOP if appropriate or removed entirely if it becomes redundant.

10. Reference(s)

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. ICH Harmonised Guideline. Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2) (2016).

U.S. Department of Health and Human Services, Food and Drug Administration et al. (2010). Frequently Asked Questions – Statement of Investigator

11. Related Document(s)

SOP Glossary of Terms
SOP 7: Hosting a Regulatory Inspection, Sponsor or HREC Initiated Audit for Clinical Trial Research
SOP 10: Essential Document Management for Clinical Trial Research
SOP 4: Clinical Trial Research Delegation of Duties
SOP 3: Clinical Trial Research Training
Template: Investigator Site File Table of Contents
Template: Site Signature and Delegation Duties Log
Template: ISF Folder Label
Template: Participant Screening & Enrolment Log
Template: Clinical Trials Investigator Curriculum Vitae

12. Amendment History

Version	Date	Amended By	Details of Amendment
2	20-Nov-2021	Jasmine Gillingham Dr. Rani Watts	• Revisions made in line with amendments to those made by the Parkville Precinct Clinical Trial Unit; Minor administrative amendments