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Monitoring Visits

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	Written by	Approved by	Approved by
Name	Erfan Jaberiyanfar	Sally Beresford-Harvey	Les Bokey
Job Title	SWSLHD Clinical Trials Manager	Head of Clinical Trials Operations Ingham Institute & SWSLHD	Director of Research, Ingham Institute & SWSLHD
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Signature	On file	On file	On file

1.0 Introduction / Background

In accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guideline, the Sponsor should determine the appropriate extent and nature of monitoring. The determination of the extent and nature of monitoring should be based on considerations such as the objective, purpose, design, complexity, blinding, size and endpoints of the trial.

The Sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials. This flexible approach is intended to permit varied approaches that improve the effectiveness and efficiency of monitoring. The Sponsor may choose on-site monitoring, a combination of on-site and centralized monitoring, or, where justified, centralized monitoring. The Sponsor should document the rationale for the chosen monitoring strategy (e.g. in the monitoring plan). On-site monitoring is performed at the sites at which the clinical trial is being conducted. Centralised monitoring is a remote evaluation of accumulating data, performed in a timely manner, supported by appropriately qualified and trained persons (e.g., data managers, biostatisticians). Centralised monitoring processes provide additional monitoring capabilities that can complement and reduce the extent and/or frequency of on-site monitoring and help distinguish between reliable data and potentially unreliable data.

The Principal Investigator (PI) should ensure that the clinical trial site conducted the clinical trial in accordance with the protocol/amendments, ICH GCP, South Western Sydney Local Health District (SWSLHD) and Ingham Institute standard operating procedures (SOPs) and the applicable regulatory requirements, to ensure that the rights and well-being of human subjects are protected. And that any findings from monitoring visits are followed and the necessary risk mitigations or corrective actions are put in place.

Where the Sponsor is a non-commercial organization there may be minimal monitoring put in place and in this instance it is the responsibility of the PI and clinical trial team members to ensure high standards of data collection, Source Data Verification (SDV) and participant safety are maintained at all times. Data Safety Monitoring Boards (DSMB) are to be established during the design stage of studies.
A DSMB is one of a range of mechanisms available to commercial and non-commercial sponsors to mitigate the risks associated with clinical trials such as participant safety, the risk to data validity and where real or perceived conflicts of interest exists, the risk to trial credibility. Appropriate monitoring plans will need to be developed to be in line with requirements of ICH GCP. The plan should describe the monitoring strategy, the monitoring responsibilities of all the parties involved, the various monitoring methods to be used, and the rationale for their use. Please refer to ICH GCP guidelines and the NHMRC guidelines on DSMB.

2.0 Objective

This SOP provides guidance for clinical trial sites in relation to the preparation required for a

monitoring visit. The document will also provide guidance on follow up processes that adhere to ICH GCP requirements.

3.0 Scope

This SOP applies to all staff involved in clinical trials at SWSLHD and the Ingham Institute.

4.0 Ownership and Responsibility

This SOP applies to those members of the clinical trials team involved in the overall project management of a clinical trial at the approved site. This includes but is not limited to participant recruitment, source documentation and document management of a clinical trial.

5.0 Associate Documents

SOP_CTSU_02 Investigator Responsibilities

SOP_CTSU_03 Communication with Human Research Ethics Committee, Trial Sponsor and Insurer

SOP_CTSU_09 Investigator Site File and Essential Documents

SOP_CTSU_17 Data Recording – source data, case report forms, record keeping and archiving

SOP_CTSU_20 Non-Compliance

FM_012_Essential Document Storage Location

FM_037_Site Monitoring Checklist_Essential Documents

FM_038_Site Monitoring Checklist_Source

6.0 Procedure

6.1 Conduct of monitoring visits

Normally monitoring visits are conducted by the Sponsors representative Clinical Research Associate (CRA) also referred to as the Monitor with the PI and clinical trial team members as per the Clinical Trial Monitoring Plan. The CRA will discuss the monitoring plan with the PI at the Site Initiation Visit (SIV) and ongoing throughout the clinical trial.

Monitoring visits will occur on-site and remotely depending on the monitoring plan. The Sponsor will discuss the frequency of the monitoring visits at site selection and throughout the clinical trial. Commercially sponsored monitoring visits will take place according the Clinical Monitoring Plan that is provided by the Sponsor. The PI and clinical trials team need to consider the implications on the workload, resources and budget accordingly.

6.2 Preparation for the monitoring visit

The PI or delegate will ensure that the paper and or the electronic Investigator Site File (ISF) has all updated essential documentation required for the clinical trial, including but not limited to all documents relating to any Human Research Ethics Committee (HREC) and/or Research Governance Office (RGO) approvals.

If the Sponsor requires documentation of the location of essential documents and source FM_012_Essential Document Storage Location form should be used. All source documents are required to be available for review by the Sponsor for the monitoring visit and this includes the participant's electronic medical records.

The PI and clinical trials team should follow the guidance checklists:

- FM_037_Site Monitoring Checklist_Essential Documents
- FM_038_ Site Monitoring Checklist_Source

All required source documentation relating to recruited participants is required to be up to date. This includes ensuring that all data points have been captured and entered into the appropriate Case Report Form (CRF). All data queries are required to be resolved prior to the monitoring visit if applicable.

Access to source notes will require specific electronic access and needs to be organised more than 2 weeks prior to the visits. Refer to SOP_CTSU_17 Data Recording- source data, case report forms, record keeping and archiving for more information.

If a large number of subjects have been entered into a particular clinical trial the PI and clinical trials team should agree with the Sponsor, prior to each visit, on which subjects they wish to perform SDV.

Appropriate space will need to be allocated for the CRA to utilise during the visit. Also ensure that all supporting departments such as Pharmacy are notified of the visit and a time is arranged for the Sponsor to visit that department.

6.3 During the visit

On the day of the monitoring visit the PI or delegate must be available to show the CRA to their allocated meeting room, and to ensure they have all the required documents for review. It is a requirement that the PI is available for at least a proportion of each monitoring visit to

meet with the CRA to discuss any queries. If the PI can't meet the CRA in person or it is a remote monitoring visit then a phone call or e-meeting should be scheduled.

While monitoring the CRA will require time to go through allocated CRF and associated source documents. A meeting with the appropriate clinical trial team member/s afterwards to discuss any problems or outstanding business is essential. The clinical trials team member/s should make reasonable efforts to meet with the CRA when requested.

The CRA will also be required to visit supporting departments such as the pharmacy and/or pathology to check items as per protocol such as storage conditions and investigational product/ drug accountability. Ensure appropriate arrangements are made in advance with the required supporting departments. It is the responsibility of the CRA to request this in advance of the monitoring visit.

If the visit is due to a serious adverse event, non-compliance or some other specific cause, the CRA should inform the PI of any special requirements beforehand. CRA should provide an agenda prior to every monitoring visit, providing adequate notice to site to prepare based on the agenda requirements.

6.5 Following the monitoring visit

Following each visit it is the CRA's responsibility to provide a written communication to the PI. The PI or delegate must ensure any highlighted issues including data queries following the visit are dealt with promptly.

If the CRA identifies issues related to protocol non-compliance, it is their responsibility to contact the PI as soon as possible by phone or email. Following this, it is the responsibility of the PI to ensure that any issues relating to protocol non-compliance are dealt with in accordance with regulatory requirements. Refer to SOP_CTSU_20 Non-Compliance for further information.

All correspondence of the monitoring visit must be filed in the ISF/eISF. Please see SOP_CTSU_09 Investigator Site File and Essential Documents for more information.

7.0 References

ICH GCP (E6 R2): Good Clinical Practice Guidelines - Annotated by TGA National Statement on Ethical Conduct in Human Research (2023)
Australian Code for the Responsible Conduct of Research (2018)
NHMRC Guideline - Data Safety Monitoring Boards - DSMBs (2018)

8.0 Amendment History

Version	Date	Amended by	Details of Amendment
2.0	22-Feb-2024	Erfan Jaberiyanfar	• Updated list of associated documents. • 1.0 – Update to include reference to DSMB and ICH GCP requirements. • 6.3 – Updated to indicate notice requirements. • Grammatical changes. • Update of reference links.

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