Standard Operating Procedure CCTU/SOP011

Monitoring Cambridge Sponsored CTIMPs

1. Scope

It is the Sponsor's responsibility to ensure the trials are adequately monitored as defined by GCP.

2. Purpose

This SOP outlines the Monitoring activities for Cambridge-Sponsored CTIMPs in order that the Sponsor's responsibilities are fulfilled.

The purpose of monitoring of CTIMPs, as defined in ICH-GCP E6 (R2) and the MHRA Good Clinical Practice Guide is to verify that:

- The safety, rights and well-being of trial participants are protected
- Investigators are appropriately selected, trained and supported to complete the proposed clinical trial
- Processes are consistently followed and activities are consistently documented to ensure high quality trial conduct and protocol compliance
- The reported trial data is accurate, complete and verifiable against the source documents
- The conduct of the trial is in compliance with the currently approved protocol / amendment(s), with GCP and with the applicable regulatory requirement(s)
- This SOP can be used to guide the trial team when they carry out site monitoring

3. Definitions and Abbreviations

The headings below contain the definitions of terms and meaning of abbreviations used within the document.

3.1. Definitions

Term	Definition
Cambridge Sponsored	Sponsored by Cambridge University Hospitals NHS Foundation Trust (CUH); or the University of Cambridge (UoC); or jointly by CUH and UoC OR Sponsored by: Cambridge University Hospitals NHS Foundation Trust (CUH) or CUH jointly with the University of Cambridge or Cambridgeshire & Peterborough NHS Foundation Trust (CPFT) or CPFT jointly with the University of Cambridge
Quality Assurance	Planned and systemic actions that are established to ensure that the trial is performed and the data generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement.

Quality Control	Operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.
Monitoring	The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol and any amendments, SOPs, GCP
Departmental / External Monitor	Departmental / External Monitors are monitors contracted to carry out monitoring activities for a specific trial or department.
EPIC	Electronic Patient Record system used at CUH

3.2. Abbreviations

Abbreviation	Meaning
CCTU	Cambridge Clinical Trials Unit
CTIMPs	Clinical Trials of Investigational Medicinal Products
CTM	Clinical Trials Monitor
ICH-GCP	International Conference on Harmonisation – Good Clinical Practice
IMP(s)	Investigational Medicinal Product(s)
SOP	Standard Operating Procedure

4. Undertaken by

This SOP applies to CCTU CTMs, Departmental Monitors and External Monitors (funded through trial budget for monitoring of specific trials).

5. Items Required

- This list of items required is not exhaustive:
- R&D/SOP012 Facilitating Monitoring Visits for Clinical Trials at CUH
- CCTU/TPL030 Monitoring Plan
- CCTU/GD008 Monitoring Activities Guidance Document
- CCTU/FRM010 Monitoring Log
- CCTU/TPL068 Monitoring Report
- CCTU/TPL061 Remote Monitoring Report
- CCTU/SOP040 Risk Assessment Process for CTIMPs
- CCTU/FRM021 CTIMP Risk Assessment Form
- CCTU/INF009 CCTU Risk Assessment Tool
- CCTU/TPL069 Close out Monitoring Report
- CCTU/SOP002 Pharmacovigilance Process for Investigator Teams
- CCTU/SOP015 Trial Master File / Site Files - Essential Document Management
- CCTU/SOP018 Handling of Protocol and Regulatory Non-Compliance in Clinical Trials
- R&D/SOP003 Serious Breach of Protocol or GCP in CTIMPs
- CCTU/SOP007 CCTU Escalation Cascade
- R&D/POL002 Research Misconduct Policy

6. Summary of Significant Changes

Remove review step by fellow monitor

Added guidance on forming a monitoring plan for multi-centre trials

The monitoring report form has been replaced with monitoring report template

7. Method

The following sections provide a description of the processes to be followed when implementing this document's procedures.

This SOP should be used in conjunction with CCTU/GD008 Monitoring Activities.

7.1. Scope of Monitoring

- CCTU CTMs monitor Cambridge-sponsored trials at the Sponsor's site only
- Monitoring at participating sites for multi-centre trials is delegated to the coordination team, unless a departmental or external monitor is contracted to carry out monitoring activities on behalf of the Trust
- A CCTU CTM will review the monitoring report completed for monitoring visits by Departmental or External Monitor in order to maintain oversight of activities at participating sites
- "For cause" monitoring may be carried out if there is cause for concern on a
- trial being carried out at a particular site
- The extent of monitoring and the frequency of visits at the Sponsor's site is determined by the risk level of the trial based on risk assessment carried out according to CCTU/SOP040
- Remote monitoring may be employed to supplement monitoring

7.2. Selection and Qualifications of Monitors

- Monitors are appointed by the Sponsor
- The Monitors will assist communication between the Sponsor and the Investigator
- Monitors should be appropriately trained, and possess adequate scientific and/or clinical knowledge to monitor the trial
- Monitors will be expected to acquire adequate knowledge in order to perform monitoring activities
- Monitors must thoroughly familiarise themselves with the trial IMP(s), trial protocol, written informed consent documents and other trial documents, CCTU SOPs, GCP and other applicable regulatory requirements

7.3. Monitors' Responsibilities

7.3.1. Verify that the Investigator has:

- Submitted and filed all the required reports, notifications, applications and submissions

- Generated documents that are accurate, complete, timely, legible, dated, and identify the trial
- All the documentation and trial supplies needed to for the conduct of the trial comply with applicable regulatory requirement(s)
- Adequate qualifications, resources and facilities, including laboratories, equipment and staff, to safely and properly conduct the trial throughout the trial period
- Conducted the trial in accordance to the approved protocol and all approved amendment(s)
- Ensured that informed consent was correctly taken and documented in the patients records before each participant's participation in the trial
- Only enrolled eligible participants onto the trial
- Adequate knowledge of the trial
- Ensured their trial staff are adequately informed and are appropriately trained in the trial procedures
- Ensured that their trial staff are performing the specified trial functions in accordance with the protocol and any other written agreement between the Sponsor and the Investigator/Institution, that they have not delegated these functions to unauthorised/untrained individuals
- Copies of current Investigator's Brochure or Summary of Product
- Characteristics for marketed products for the duration of trial

7.3.2. Verify that the IMPs:

- Are sufficient in quantity
- Are stored in accordance with manufacturers recommendations and/or the approved protocol
- Are supplied only to eligible participants in accordance with the approved protocol
- If dispensed to participants, are dispensed with necessary instructions on proper usage, handling, storage and return of IMP
- Have a documented audit trail for receipt, use and return (if applicable) at the trial sites
- When un-used and with agreement with the IMP supplier if necessary, are disposed at the trial sites in compliance with the applicable regulatory requirement(s) and is in accordance with the local requirements

7.3.3. Monitors must also:

- Sign the Monitoring log CCTU/FRM010 to document the monitoring visit
- Verify that source documents and other trial records are present, accurate, complete, kept up-to-date and maintained
- Verify accuracy and completeness of the Case Report Form (CRF) entries, source documents and other trial related records against each other. Confirm that:
    - CRFs are completed in a timely manner
    - Data required by the protocol is reported accurately on the CRFs and is consistent with the source documents

  - Any dose and/or therapy modifications are well documented for each of the trial participants
  - Adverse events, concomitant medications and inter-current illnesses are reported in accordance with the protocol on the CRF
  - Unattended visits, tests that are not conducted, and examinations that are not performed are clearly reported on the CRFs
  - All withdrawals and dropouts of enrolled participants from the trial are reported and explained on the CRFs
  - Verify code break incidences are correctly handled and documented in accordance to the protocol and/or relevant SOPs
- Inform the investigator of any CRF entry error, omission, or illegibility
- Ensure appropriate corrections, additions, or deletions are made, dated and initialled with an explanation if necessary by Investigator's trial staff who have been appropriately delegated
- Determine whether adverse events are appropriately reported within the timeframe required by GCP, the protocol, the REC, the CCTU Pharmacovigilance Process for Investigator Teams CCTU/SOP002 and the applicable regulatory requirement(s)
- Ensure that the investigator is maintaining the essential documents as detailed in CCTU/SOP015
- Communicate deviations from the protocol, SOPs, GCP and the applicable regulatory requirements to the Investigator and take appropriate action designed to prevent recurrence of the detected deviations

7.4. Form a Monitoring Plan

- Each trial will have a Monitoring Plan CCTU/TPL030 based on the level of risk involved in the trial
- The level of risk is determined by a risk assessment as described in
- CCTU/SOP040
- The risk assessment is carried out by the Monitor, the Clinical Trials Officer and anyone else that has been assigned to the trial using CCTU/FRM021 and CCTU /INF009 CCTU Risk Assessment Tool
- The monitoring plan must be completed before trial initiation
- For multi-centre trials, monitoring activities at participating sites must be included in the monitoring plan with input from the trial team, including but not limited to:
  - Type of monitoring activities
  - Frequency of monitoring

7.5. Schedule a Monitoring Visit

- The Monitor assigned to the trial will:
- Contact the trial team and/or other relevant departments in advance to schedule a monitoring visit. Follow R&D/SOP012 Facilitating Monitoring Visits for Clinical Trials at CUH

- Identify and notify the trial team and/or other relevant departments which documents are required on the day(s) of visit
- Inform the trial team of the selected participants medical notes required for the visit

7.6. Findings

- In the event of non-compliance with the protocol or regulations refer to CCTU/SOP018 Handling of Protocol and Regulatory Non Compliance
- In the event of any suspicion of breach of protocol or GCP, Monitors must report findings in accordance with R&D/SOP003 Serious Breach of Protocol or GCP in CTIMPs
- In the event of any suspicion of fraud of misconduct, Monitors must report findings in accordance with R&D/POL002
- In the event of any EPIC functionality or EPIC process findings the Monitors will collate and report findings in accordance with CCTU/SOP007 CCTU Escalation Cascade
- All other issues that require escalation refer to CCTU/SOP007 CCTU Escalation Cascade

7.7. Monitoring Report

- Monitoring can span a number of days depending on the complexity of the trial, upon completion of a monitoring visit, The Monitor will:
- Complete a Monitoring Report
    - Routine/ triggered monitoring use CCTU/TPL068
    - Close Out Monitoring use CCTU/TPL069
- Document findings in follow up correspondence for trial team
- Submit both documents to the Regulatory and Quality Manager or designee for review
- Finalise the Monitoring Report and follow up correspondence upon review
- Sign the finalised Monitoring Report with the reviewer
- Provide the trial team in writing with follow up correspondence
- File original signed report and copies of correspondence in the Sponsor File

7.8. Pharmacy Monitoring – unblinded

For a randomised trial where pharmacy is involved with treatment allocation, i.e. treatment allocation information will be recorded in the pharmacy file; a second CTM will be assigned as the unblinded monitor in addition to the main monitor for the trial.

7.9. Remote Monitoring

CCTU/TPL061 can be used for remote monitoring activities. All related documents must be filed in the Sponsor file. Remote monitoring performed by the trial team should be reviewed by the sponsor monitoring team; further details will be documented in the trial monitoring plan.

7.10. Monitoring of Clinical Studies (non-CTIMPs) or externally sponsored CTIMPs

This SOP is specifically for CTIMPs. However, the same principles and activities apply when monitoring clinical studies or externally sponsored CTIMPs in the absence of other procedures.

8. Monitoring Compliance with and the Effectiveness of this Document

a. Process for Monitoring Compliance and Effectiveness

As part of routine monitoring visits, audit and inspection

b. Standards/Key Performance Indicators

This process forms part of a quality management system and is reviewed according to CCTU procedures. Standard Operating Procedures are reviewed every two years.

9. References

The Institute of Clinical Research, Abbreviations used in Clinical Trials.

MHRA, Good Clinical Practice "Grey Guide"

10. Associated Documents

NA

11. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

12. Disclaimer

It is the user's responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

Review date	2 years (or earlier in light of new evidence) from approval date
Owning department:	CCTU QA
Supersedes:	CCTU/SOP011 version 7
Local reference:	CCTU/SOP011 version 8