

Guidance 4

Monitoring Guidelines for Sites

1. Background

The monitoring process is an on-going and intensive programme initiated by the IMPACCT Trial Coordination Centre (ITCC) and involves all sites. Monitoring is an important internal mechanism for ensuring compliance with Good Clinical Practice (GCP) and ITCC's own internal procedures, maintaining the quality of participant data for each of the studies undertaken by ITCC, and provides an excellent way ensuring quality across the Collaborative.

While there is a Standard Operating Procedure for monitoring (*refer* SOP 5.18 Monitoring), these guidelines have been collated to assist all sites in a more practical sense.

2. Preparation

Adequate preparation enables the monitoring visit to proceed in a smooth manner with fewer disruptions to the daily work of the site team.

The ITCC monitoring team attempt to give sites at least two (2) weeks' notice of an on-site or telephone (remote) monitoring visit (14 calendar days), and in many cases the negotiation of a suitable visit date means that there is often four (4) weeks or more notice of the date listing the ID numbers of the participants (PID) to be monitored.

Sites are asked to set some time aside in the days prior to the scheduled visit to undertake the following activities:

For On-Site Monitoring Visits:

- Prepare the **Investigator Site File (ISF)**:
 - Ensure the folder or files are up to date, contain all necessary supporting documentation and are in order. The monitor will check the entire folder or file contents at the first on-site visit. On subsequent visits there are selected sections that will be reviewed. The following sections should have particular attention given prior to each visit:
 - Ethics or RGO correspondence, in order and complete, including approvals, amendments, reports and adverse event reports.
 - Staff Signatures and Delegation Log (SSDL) up to date and tagged for easy reference.
 - The CV, either full or abridged for each person on the SSDL.

- Site staff training records are complete and on file including the current GCP training certificates for each person on the SSDL.
 - Patient Master Index printed off and containing the ID numbers to be monitored so that the PID and the medical record number can be matched.
 - Signed consent forms for participants (if not stored in the study files).
 - Monitoring Log should be up to date showing previous visits and tagged for easy reference. This log will be signed by the monitor(s) at the completion of the visit and will need to be signed by the members of the site team who assisted with the visit.
- Prepare the **participant files**
 - Ensure all the relevant data collection worksheets are within the participant's file and filed in order of their use. Ensure that all the required source documents are also within the file such as:
 - Patient completed scores
 - Questionnaires and assessment tools
 - Concomitant medications log
 - Pathology reports,
 - Print off online conversions
 - Adverse event log and Serious Adverse Event reports.
- Locate the **clinical records**
 - Paper files.
 - These must be requested from the Medical Record (MR) Department with the appropriate approvals well in advance. They should be requested to be provided to the team office if possible, rather than held within the medical record department. Care should be taken to ensure that the volume provided by MR includes the appropriate clinical record for the time the participant was in the study and follow-up.
 - Check the file for the informed consent form and tag its location.
 - Tag the pages that refer to the informed consent discussion(s).
 - Tag the pages that indicate study commencement.
 - Electronic medical records.
 - Ensure that the appropriate login for the ITCC monitor has been obtained. If login has not been obtained, the site team need to be prepared to login to the system and remain with the monitors during the clinical file reviews. An alternative to this is to print off electronic records that relate to the study,

however access to the other parts of the record should be available on request.

- The print-out of the electronic medical record must be certified by the person who generated the document (by a dated signature) to confirm that it is an accurate and exact copy of the original.
- Print-outs can be certified by either a signed and dated written statement on the front page of the paper copy (e.g. “I, [name], certify that this document (X pages in total) is an accurate and exact copy of the original”) or through the use of a validated process (e.g. a stamp). All pages of the certified copy must be paginated and secured.
- The e-record (or print-out if applicable) needs to enable the monitor to review all of the content in order to ascertain eligibility, such as prior medical history, pathology, and prescription records.
- Ensure familiarity with the content and structure of the e-record. If necessary, make notes of where the study documentation can be located, specifically:
 - informed consent form and documentation of the process.
 - The progress notes relevant to the patient participation, either inpatient, outpatient or community outreach notes.
 - Medication charts, infusion records relevant to the study.
- Ensure the monitors have **adequate facilities**:
 - Monitoring requires the review of numerous records and reports simultaneously and making notes and completing checklists. This takes up a reasonable area of desk space. The monitors also discuss each participant as the records are being reviewed.
 - If possible, the monitors should be provided with:
 - A separate room in order to discuss the findings for each participant confidentially and to spread the records in order to adequately review them
 - A desk or table large enough to accommodate two people sitting side by side with room to open records and files at the same time
 - Room space to accommodate any suitcases and other files that are part of the review.

For Telephone (Remote) Monitoring Visits:

- Review your **Investigator Site File (ISF)** and ensure these are up to date, contain all necessary supporting documentation and are in order. The same ISF sections that apply to on-site visits should have particular attention given prior to each remote monitoring visit.

- A copy of the most current SSDL will be requested by the monitor and should be provided by email prior to the scheduled telephone visit:
 - Check the log is up to date, all site staff working on the study have signed the log and have been delegated duties by the Principal Investigator (PI) after completing all required study training.
 - Check all site staff no longer working on the study have a 'stop date' entered on the log and that the PI has signed this off.
- A copy of the current Training log/records and Monitoring Visit Log will be requested by the monitor and should be provided by email prior to the scheduled telephone visit.
- Prepare the **participant files** for the participants that will be reviewed.
 - Ensure all the relevant data collection worksheets are within the participant file and copies have been uploaded to the electronic Case Report Form (eCRF) database prior to the telephone visit.
 - Ensure that all the required source documents are also within the file such as:
 - Patient completed scores
 - Questionnaires and assessment tools
 - Concomitant medications log
 - Pathology reports,
 - Print out of the online conversions
 - Adverse event log is up to date and all Serious Adverse Event reports are complete and on-file and copies have been sent to ITCC prior to the telephone visit.
- Locate the **clinical records**
 - Paper files.
 - These must be requested from the Medical Record (MR) Department with the appropriate approvals well in advance and available on the day of the telephone visit.
 - Check the file for the informed consent form and tag its location.
 - Tag the pages that refer to the informed consent discussion(s).
 - Tag the pages that indicate study commencement.
 - Electronic medical records.
 - Ensure you are familiar with the electronic medical record system and where to locate each of the specific data elements that will be reviewed such as informed consent discussion, admission details, medication chart, documentation of study commencement etc.
- Check **eCRF data entry** is up to date and complete for all participants that will be monitored.

3. During the visit

On-Site Monitoring Visits:

The monitors attempt to disrupt the working day of the study staff as little as possible but some situations arise during the course of the review that require assistance from the team in order to progress the review. For example:

- Documents cannot be located, without which the review of that participant cannot progress.
- Documentation is not consistent with other documents and requires clarification in order to continue the review without unnecessary file notes or corrective actions.

In addition, the monitors require a short period of time towards the end of the visit to summarise the findings, with both the site coordinator/study nurse and the PI, so that the report that follows the visit is as expected. It gives the opportunity to discuss any study wide issues of problems and well as specific participant problems.

The monitors will attempt to complete the data corrections and file notes during the visit if time permits and any photocopying. A copy of the corrective action sheet will be left at the end of the visit to enable actions to be taken quickly.

The Monitoring Log will be signed at the end of the visit and will be left out so that site staff can also sign it.

Telephone (Remote) Monitoring Visits:

Adequate facilities should be utilised during a telephone monitoring visit including access to a telephone, computer/internet, and desk large enough to accommodate numerous files. The call should be taken in a private room or office to maintain participant privacy and confidentiality.

The focus of the telephone visits will be to review and obtain verbal confirmation that the following data elements are documented in the participant's medical records/clinical notes:

- Informed consent process and documentation
- Eligibility including confirmation of admission details, confirmation that all assessments/measures required to confirm eligibility criteria were completed, review of concomitant medications for potentially exclusionary treatments, review of medical assessment for potentially exclusionary co-morbidities/health conditions
- Primary endpoints including completion of all required measures and assessments at each visit, checking accuracy of calculated scores for clinician assessments
- Consistency of dates and compliance with visit schedule
- Compliance with administration of study drug
- Safety and adverse events including review of medical assessments such as vital signs/ physical examination and concomitant medications that may indicate unreported adverse events

- Study termination: reviewing reason for cessation/withdrawal/completion and verification of the daily assessments in the days prior to that event

In addition, the following other items may also be reviewed during the call to assess overall site health and compliance:

- Protocol deviations and violations
- Recruitment activities, eCRF data entry and completion of participant data collection worksheets
- Discussion of issues identified during data verification activities
- Site staff changes and resources at the site
- Assessment of requirement for additional site staff training
- Unresolved corrective action items or site issues
- Recurring issues such as those related to consent, documentation, delegation of duties, and issues related to organisation, access to information or source data
- Availability of important regulatory and essential documents in the ISF such as CVs, training records, HREC/RGO documentation, Serious Adverse Event Reports etc.

During the telephone visit, the relevant participant files and medical records must be readily accessible so that the above data points can be located and checked when responding to the monitor's questions.

If time permits, it may be possible to complete data corrections during the telephone visit as each participant is reviewed.

For each participant reviewed, the monitor will complete a corrective action sheet detailing the findings of the visit. This will be emailed along with the visit report within 14 days of the telephone monitoring visit.

The Monitoring Log will be signed at the end of the visit and a copy will be returned by email so the site staff can counter sign. This log should then be filed in the ISF.

4. Follow-up to the visit

After an on-site or telephone monitoring visit, the monitor will send an email report summarising the findings of the visit within 14 calendar days following the visit. This email will include:

- a summary of the visit outlining:
 - Date(s) of monitoring visit
 - Name of site and site personnel in attendance
 - Name of monitor(s)
 - A summary of the review process
 - A summary of the findings, for the site and the organisation
- an electronic copy of the corrective action sheet(s) (PDF or excel)

The Principal Investigator is required to confirm by reply email to acknowledge receipt and review of the monitoring report and the findings summarised therein.

In the event that notable recurring issues or serious breaches are identified at a monitoring visit, a follow-up telephone call will be scheduled with the Principal Investigator to discuss an appropriate corrective and preventative action plan.

The email report is to be filed within the monitoring section of the ISF.

The corrective action sheet should have the following activities performed:

- The column headed 'Required action' will specify the outcome required in order to rectify the 'Findings'. Look at this column and relate this to the relevant participant file or issue.
- The column headed 'RedCap query raised' will specify if a corresponding data query related to the finding has been raised in the eCRF database.
- Complete the 'Required action' as specified.
- Complete the column 'Actual outcomes' detailing the action taken, this might be:
 - a file note
 - confirmation of training or a discussion/meeting
 - a correction to the specific data item within a worksheet or eCRF
 - location and confirmation of a document
- If a query has been raised, access the eCRF database to make the necessary updates as appropriate and respond to the query.
- Complete the 'REDCap query resolved' column
- Complete the 'Date completed' column.
- Send the completed corrective action sheet back to the ITCC. Any relevant file notes, corrected data collection worksheets, medication pages, etc., should be uploaded to the eCRF database or emailed to the ITCC to confirm that the action was completed. Do not provide documents that contain identifiable information. Examples of corrective actions are provided below.
- The ITCC will review the returned corrective action sheet and the monitor will enter their initials and a date in the column headed 'ITCC resolution confirmation' to confirm that the finding is resolved and closed.

5. Second and subsequent visits

After initial monitoring, subsequent monitoring visits will review only those sections of the ISF that required updating since the previous visit, such as:

- Ongoing HREC/RGO communications, submissions, and approvals
- Protocol amendments
- Staff Signatures and Delegation Log
- Monitoring log
- The next list of participants

- Any corrective actions that are outstanding from the previous visit

Examples: Corrective actions

Findings	Lists the problem or issue. Can be related to site documents, organisation, or participant review. Anything related to the visit that is not as it could or should be.
Required action	Suggestion for how the finding can be rectified. Can be a single suggestion or a number of suggestions in order to rectify, correct or resolve the issue listed as a finding.
REDCap query raised	Indicates if a data query linked to the finding has been raised in the eCRF database which needs to be reviewed, actioned and responded to.
REDCap query resolved	Respond with Yes, No or N/A to confirm that the data query has been resolved. If no, provide a reason.
Actual outcomes	The action taken by the site to rectify the finding. May be one or all of the suggestions made by the monitor/s or may be another outcome as a result of the site reviewing the circumstances.
Date	The date recorded by the site when the outcome was completed, and the finding has now been resolved.

Additional examples: Corrective actions

Finding	Required action	Actual outcome
General documents		
Missing documents	Regulatory documents, consent forms, worksheets, source documents, eligibility documents	Locate document and confirm
		Reconstruct document from other sources and file note that source was used
		Cannot locate and file note to confirm document did exist and can be verified by person
		Cannot locate and cannot be confirmed, file note. This may be a protocol violation
HREC documents missing, approval for amendment 1.3 cannot be located	Locate approval and confirm File note lost document, obtain copy from HREC	Approval found in other folder, attached
Doctor is not listed on the SSS, but has performed medical assessments	File note by PI: explained protocol, qualifications have been checked, appropriate delegated activities were assigned, delegated tasks were performed as per delegation	File note attached to the relevant worksheet and copy attached to the SSS
Consent forms		
Consent form has not been dated by patient	File note that patient missed placing the date and was incorrectly inserted by study staff	File note attached (written by staff member who obtained or witnessed consent)
	Staff training that patient must sign and date the consent form	Discussed at team meeting on (date) and noted in meeting minutes.
		Written procedures provided to nurses
Consent form not signed by patient	File note by person who obtained consent	Person no longer employed at site; file note attached. (if the file note cannot be written by person who obtained consent, this is a protocol violation)
		Refer to comprehensive clinical progress notes
Incorrect consent form in use	File note to explain difference in version of consent form	File note attached
		HREC informed that incorrect version has been approved, or not listed on approval letter, attached
Data Collection Worksheets		
Worksheet missing	Locate and confirm to ITCC, provide copy, and enter data	Worksheet found, data entered, and copy attached OR Not completed, worksheet constructed from clinical record, withdrawal worksheet, file note written, worksheet and file note attached, data entered in eCRF.

Finding	Required action	Actual outcome
Document is incorrect or conflicts with other documents	Worksheet against source, Eligibility against clinical record, Prescription not followed or incorrect, consent form problem	Correct the document if it can be confirmed by other documents, initial and date the correction
		File note the correction such as medical assessment, dosing can be confirmed as correct, file note that date on consent form was correct (signed by person who took consent)
		File note to explain discrepancy, may be a protocol violation
Medical assessment indicated no previous adverse reaction to opioids, medical record records allergy to morphine	Review clinical record, amend medical assessment, file note eligibility, amend worksheet (initial and date correction)	Medical record records allergy, but actually the reaction was dose related, assessed by investigator as no problem, medical assessment form has note added
Documents are incomplete	Consent form not fully filled in, signatures missing, missing data points, PID missing from pages, dates of review for confirmation for study	Complete if possible, initial and date
		File note to confirm that incomplete was correct at the time and can be confirmed
		File note that data is missing and cannot be traced as person has left, may be a protocol violation
[PID] 24 hours. NuDesc for 8am blank	Complete worksheet (initial and date correction) File note that score not done Protocol violation	8am score located on source document in clinical record (archived in different place). Worksheet amended; copy attached
Response assessment (or primary outcome) is inconsistent with other data or is incorrect (according to monitor calculations)	Reassess, correct worksheet, file note. Protocol violation	File note attached. Worksheet corrected and copy attached
PID, date, study nurse initials missing from the top of each page	The information is required on each page for identification purposes	All of the header information should be completed but does not need to be sent to ITCC. <i>Note:</i> This is the only exception whereby ITCC do not need to be provided with evidence the action has been completed
PI has not signed the eligibility (or cessation/withdrawal) worksheet	PI to sign and date worksheet, with appropriate notation of actual date of signature	Worksheet signed and dated by PI, dated xx/xx/xx
PI has not circled appropriateness to continue study	PI to circle worksheet with initial and date of change	Worksheet amended; copy attached