UTS IMPACCT Trials Coordination Centre

Standard Operating Procedure

5.17.1 Medical Monitors

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Introduction / Background

The International Conference on Harmonisation of Good Clinical Practice (ICH GCP) guidelines require organisations that conduct clinical research studies to have a system for the appropriate oversight of the conduct of clinical trials to ensure the safety of study participants.

As the sponsor, UTS is responsible for monitoring study participant safety via the IMPACCT Trials Coordination Centre (ITCC). For most trials this monitoring will be through the establishment of an independent Data and Safety Monitoring Committee, but in some instances the trial can be judged to be adequately monitored through the oversight of a Medical Monitor (MM).

An MM will be appointed by the PaCCSC/CST Scientific Committee under the following criteria.

Where the trial:

- is judged to be low risk
- is recruiting for pilot data
- includes fewer than five sites, and/or two states
- is approved by the Scientific Committee for monitoring by a MM

IMPACCT Trials Coordination Centre collaborates with the MM on safety oversight. This collaboration helps to meet human participants' safety standards as defined by applicable regulations, ICH GCP, and PaCCSC/CST Standard Operating Procedures.

Objective

This SOP describes the PaCCSC/CST procedure for the role of a MM in providing safety oversight to clinical research studies.

This procedure applies to PaCCSC/CST studies where risk/resource assessment indicates the need for medically qualified individuals to be involved in safety oversight of the clinical research study.

Scope

The role of Medical Monitors can be very broad to include safety and other considerations in the development of the protocol, and to advise on inclusion and exclusion criteria through the conduct of the study. The role of the MM within this SOP is restricted to oversight and review of safety reports for clinical trials where a risk assessment has determined that a Data Safety Monitoring Committee is not required.

Ownership and Responsibility

Responsibilities of the PaCCSC/CST Scientific Committee

- To determine if a MM is appropriate for any specific trial
- To recommend an appropriate MM
- To assist MM with pharmacovigilance activities
- To interact with the MM on safety oversight

Responsibilities of the protocol investigators

- To review the six monthly reports from the MM
- To evaluate the consolidated adverse events/Serious Adverse Events (SAEs) and review safety reports
- To consider findings or recommendations from the MM

Responsibilities of the PaCCSC/CST National Manager / National Project Officer

- To contact the MM as determined by the Scientific Committee
- To provide the study protocol and appropriate training in the protocol and safety reporting requirements
- To ensure that MM receives the adverse event reports from sites in a timely manner during the recruitment period
- To provide any follow-up information requested by the MM
- To review findings from MM activities as applicable

Responsibilities of the Medical Monitor

- To review protocol halting rules
- To advise protocol team on safety oversight
- To evaluate adverse events/Serious Adverse Events (SAEs) and review safety reports
- To provide findings or recommendations from the review of adverse events
- To participate in the quarterly protocol investigator meetings
- To advise sponsor of patterns or trends in safety reports
- To review a sample of the reported deaths for safety implications
- To prepare a summary of events for reporting every six months or otherwise agreed period

Procedure

1. Medical Monitor procedures

The PaCCSC/CST Scientific Committee will approve the appointment of an MM to review and evaluate information relevant to the safety of all PaCCSC/CST-supported clinical trials and selected studies approved by the Committee.

The Medical Monitor will:

- be appropriately qualified to provide medical oversight of the trial;
- be independent of the trial, not listed as an investigator and not involved as a Principal Investigator in the recruitment of the trial;
- have a good understanding of safety monitoring in clinical trials and of GCP;
- agree to undertake the role of MM;
- ensure, where required, that reporting to the TGA is undertaken.

The MM will be responsible for providing safety oversight and reviewing the protocol (e.g. study halting rules) and information about the study as it becomes available, such as the Investigational Brochure (IB) and reported safety events.

The PaCCSC/CST MM, in consultation with the protocol investigator team and safety oversight committees, will provide safety review during the execution of the clinical trial. This oversight includes reviewing safety information and providing applicable recommendations.

The PaCCSC/CST MM provides recommendations, as appropriate, to members of the protocol investigator team, which may include, but is not limited to: PaCCSC/CST, the funding body, manufacturer, and participating recruiting sites via the protocol investigator team. This data and safety review facilitates early detection of safety signals and maximises the chances for continued appropriateness of the research and protection of human subjects.

Based on a synthesis of this information, the PaCCSC/CST MM will provide appropriate recommendations to the study protocol investigator team and PaCCSC/CST Scientific Committee (where necessary). When PaCCSC/CST is the study sponsor, the MM is the person who is responsible for reviewing and evaluating safety information.

2. Before the trial

- The protocol investigator team will determine the level of risk of the study and decide the overall safety oversight requirements of the study.
- If the role of MM is considered sufficient to provide the required level of safety oversight for the study, the protocol investigator team then discuss an appropriate MM and subsequently appoint the MM.
- The MM accepts the role in writing.
- The MM for the study is provided with the study protocol.
- The MM discusses, either in meeting or via email, the potential safety implications of the study and reviews the safety reporting procedures.

3. During the trial

- Safety reports are provided by sites in either an unblinded or blinded manner, using the Adverse Event or Serious Adverse Event Report Form. All reports are forwarded to the PaCCSC/CST National Manager and National Project Officer, who review the event for completeness of data and assess if the event is to be reported to HREC and/or MM (*refer* SOP 5.17 Adverse Event Reporting).
- If the event is a grade of 3 or more, or is a Serious Adverse Event and is assessed as not being exempt from reporting (as defined within the study protocol), the email report is then forwarded to the MM for review.
- The MM will review the report to determine if the event report is complete and if there is agreement with the assessment of causality, relationship, and reporting assessment.
- If the report is incomplete, or if further information is required in order to make a full assessment of the adverse event report, the MM emails a request for further information via the IMPACCT Trials Coordination Centre. Further information will be provided back to the MM when available from the reporting site.
- The MM will make an assessment of the adverse event report, based on the information within the initial report and any subsequent follow-up information. This assessment will be:
    - Relationship to study drug
    - Confirmation that the event was a Serious Adverse Event
    - If trial discontinuation is recommended.
- The assessment can be as individual assessment, or aggregated into a table, if numerous reports are received.
- The MM will be asked to provide aggregated assessments to the study protocol investigator team six monthly. This report will contain an overall assessment of the balance of risks and benefits within the trial, such as:
    - No action needed, trial continues as planned
    - Early stopping due to, amongst other things, safety concerns, futility, slow recruitment, or external evidence (refer SOP 4.7.2 Unbinding)
    - Stopping recruitment within a subgroup
    - Extension of recruitment or follow-up, or
    - Advising on or proposing protocol changes.
- Figure 1 details the MM procedure during the trial.

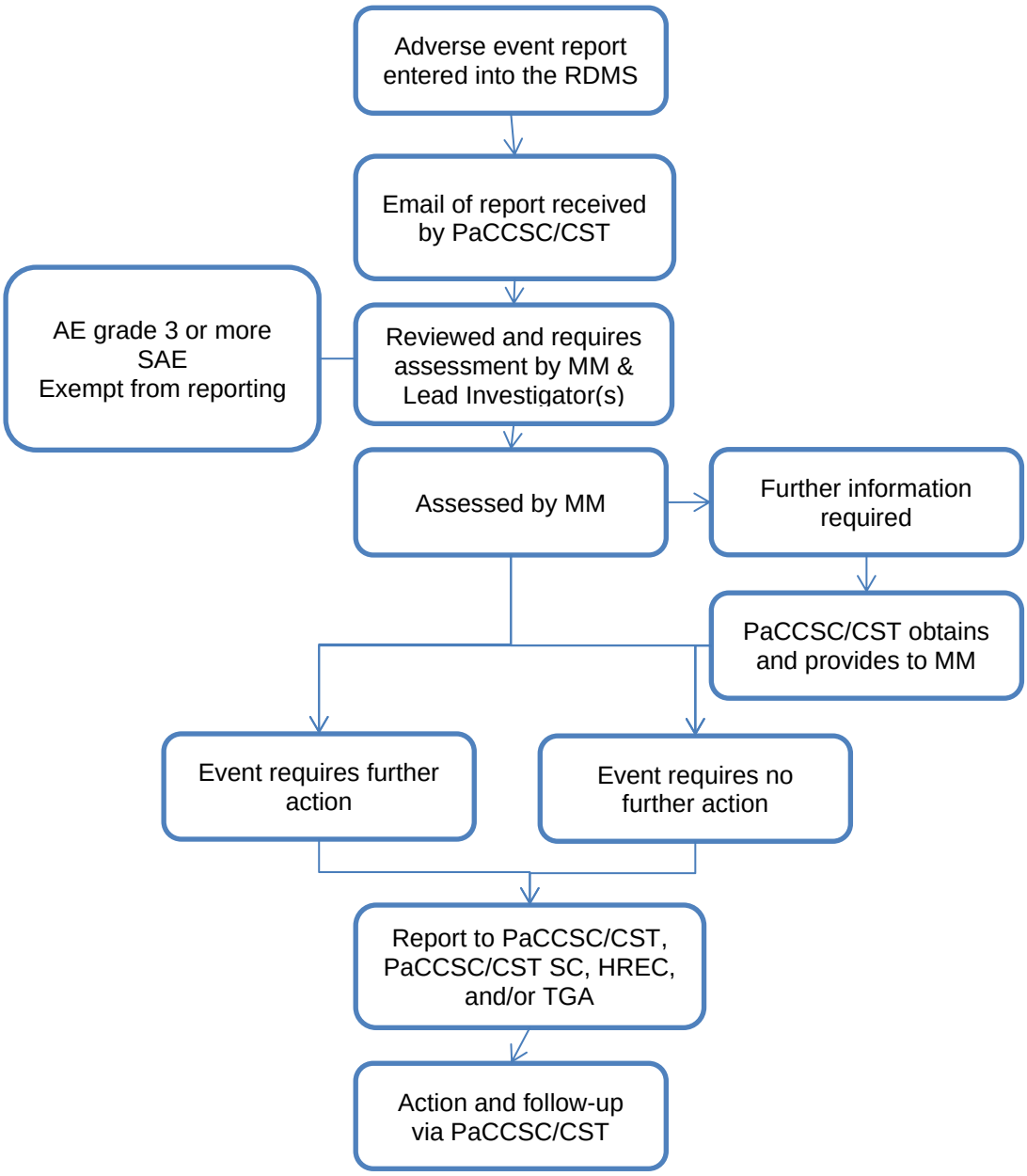


Figure 1 Medical Monitor procedure during the trial

4. After the trial

- The MM may be asked to review the summary tables and reports, or recommendations developed for the clinical study report or safety reporting table in the results manuscript.

Related SOPs

4.7.2 Unbinding
5.17 Adverse Event Reporting

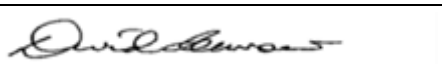
Related documents

N/A

References

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2). November 2016 (accessed 11/02/2020)
https://www.ich.org/page/efficacy-guidelines

History			
Version	Date	Author	Reason
1.0	10/12/2015	B Fazekas, L Devilee	New SOP
1.1	28/02/2018	B Fazekas, S Kochovska	Periodic review Publication of the ICH GCP E6 (R2)
1.2	06/12/2018	L Brown	Update to include CST and ©
1.3	11/02/2020	J Lourdesamy	Periodic Review
1.4	1/12/2021	J Hao	Periodic Review

Approval		
Version	Approval Name	Approval Signature
1.3	David Currow	
1.4	Meera Agar