UNIVERSITY OF MALAYA MEDICAL CENTRE
MEDICAL RESEARCH ETHICS COMMITTEE
SOP II: INITIAL REVIEW PROCEDURE

1.0 OBJECTIVES

This SOP describes the eligibility of applicants and the application platform; the submission of application; the criteria of protocol review; the reviewing process including the expedited review as well as full board review and the workflow of special meetings.

2.0 SCOPE

The UMMC-MREC reviews the protocol of research which are being conducted using the name of the Faculty of Medicine, University of Malaya (FOM-UM) or UMMC. These include studies submitted to the UMMC-MREC by:

- FOM-UM staff and students,
- UMMC staff and students,
- UM staff and students who are not from FOM-UM,
- Non-UM/UMMC principal investigators (PIs).

This SOP applies to the actions by the UMMC-MREC from the submission of new study application to the decision on an application. This SOP also describe the full board meeting which may also involves discussion on post approval matters.

3.0 RESPONSIBILITIES

The UMMC-MREC uses an online application submission system. It is the responsibility of the Secretariat Staff to communicate with the Information Technology personnel to resolve any arising issue in the system. The Secretariat Staff is also responsible in processing and ensuring the documents submitted in a protocol is complete before forwarding it to the Chair or Deputy Chair. The Secretariat Staff also has responsibilities in arranging for MREC meeting and to ensure that the deliberations and discussions in the MREC meeting are adequately documented.

The Chair and Deputy Chair are responsible to review all protocols submitted. They also decide whether a study protocol should be granted expedited approval or tabled for meeting. The committee members are responsible to review, evaluate and propose a decision for the protocols tabled for MREC meeting.

The Principal Investigator (PI) is responsible for submitting a complete set of documents to the MREC in the application.

4.0 APPLICATION ELIGIBILITY AND PLATFORM

4.1 Application eligibility

4.1.1 Only investigators who are from UMMC or FOM, University of Malaya should apply for ethics approval from the UMMC-MREC. Investigators who are not from UMMC/FOM must appoint one PI from UMMC/FOM to apply for the research ethics approval.

4.1.2 Students (post-graduate) from FOM can apply for the research ethics approval but he/she must include his/her supervisor's name (who are from UMMC/FOM) when applying.

4.1.3 Students who are not from FOM or undergraduate students from FOM should appoint one staff from UMMC/FOM to apply for the research ethics approval as the PI.

4.1.4 Research assistant (RA), study coordinator (SC), clinical research officer (CRO) or any personnel from the pharmaceutical company are not allowed to apply for UMMC-MREC research ethics approval; instead the UMMC/FOM investigator who is in the same team should apply for the research ethics approval.

4.2 Application platform

4.2.1 All applications for new study are to be submitted online at:

- *http://my.ummc.edu.my* – for UMMC/FOM staff who have Single Sign On (SSO) account login at (e-Service >iResearch)
- *https://eservices.ummc.edu.my* - for UMMC staff/FOM staff/FOM student who does not have Single Sign On (SSO) login

4.2.2 Figure 1 summarised the eligibility of application as well as the application platform according to the category of applicants.

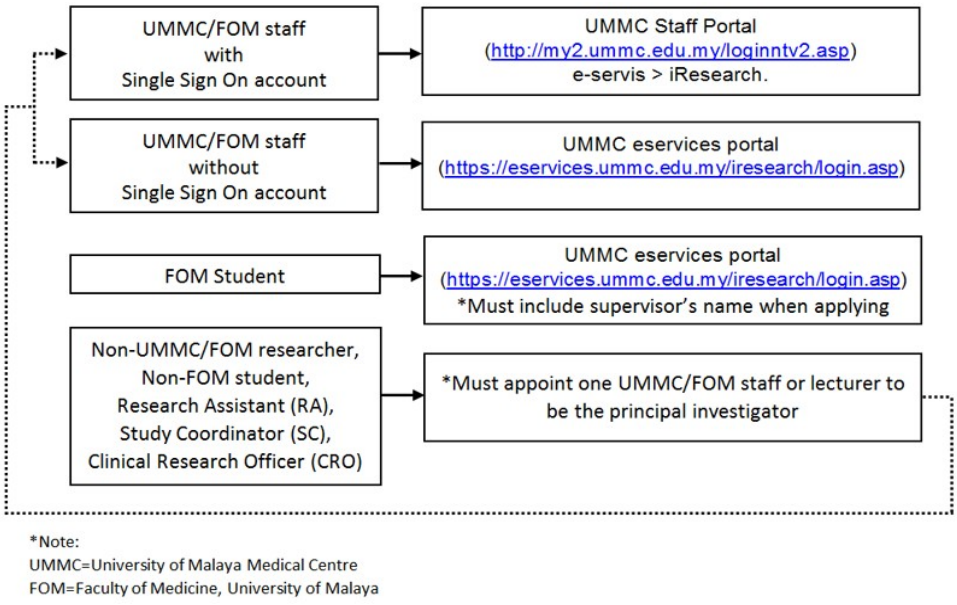


Figure 1. Application Eligibility and Platform

Date of acceptance: 19 July 2017

5.0 APPLICATION SUBMISSION

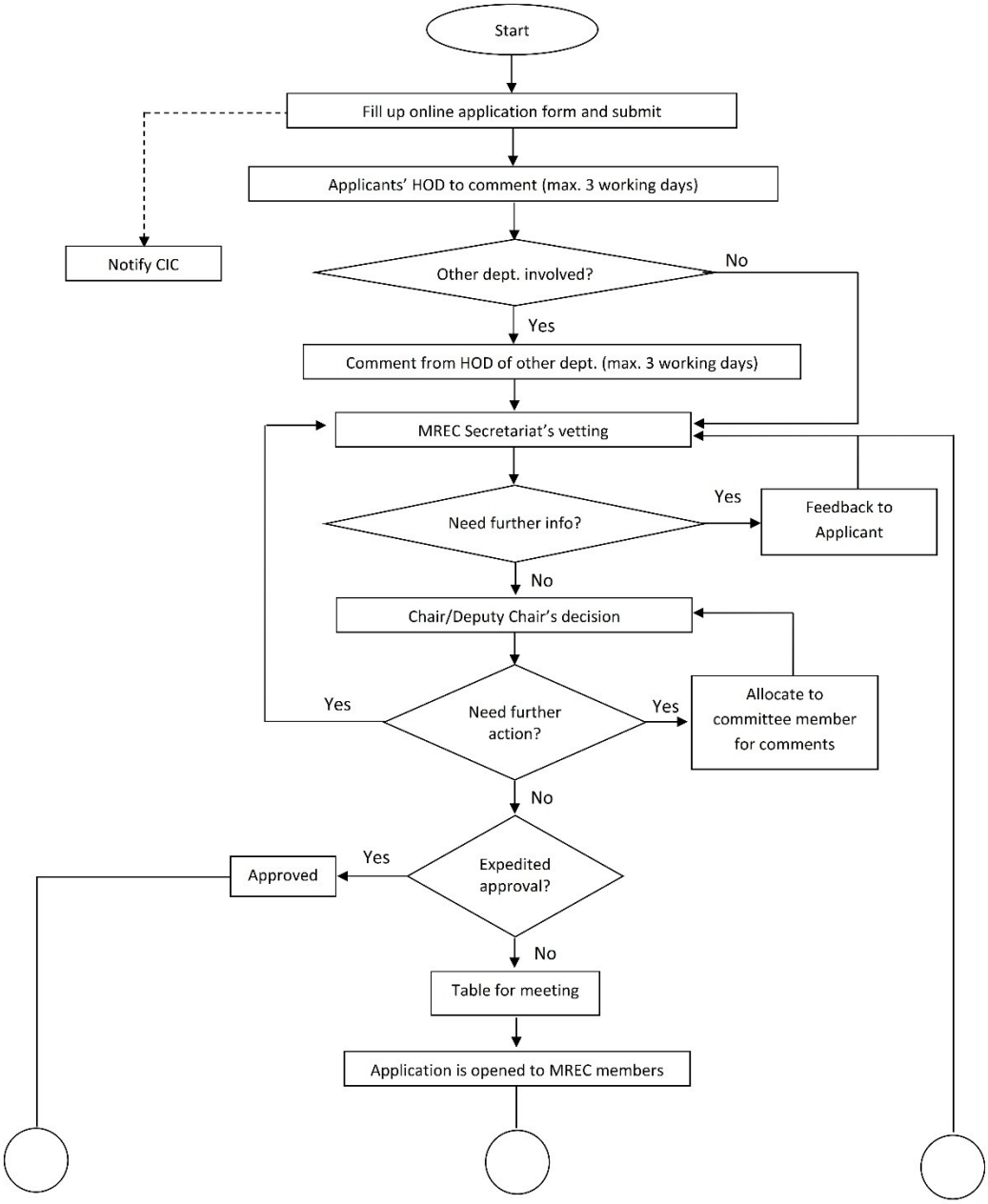
5.1 All applications must be submitted through the online application system as described in section 4.2.1.

5.2 All items in the online application form must be answered and accompanied by the following documents. Wherever applicable, version number and version date must be provided:

- 5.2.1 Full study protocol, including the version no. and version date.
- 5.2.2 Written informed consent form, written in English or Bahasa Malaysia, including the version no. and version date.
- 5.2.3 Subject recruitment procedures / advertisements (if applicable)
- 5.2.4 Written information (participant information sheet) to be provided to subjects (if applicable), including the version no. and version date.
- 5.2.5 Questionnaires, data collection form, interview guide (if applicable)
- 5.2.6 Investigator's Brochure (if applicable).
- 5.2.7 Available safety information (if applicable).
- 5.2.8 Information about payment and compensation available to subjects (if applicable).
- 5.2.9 PI's and all co-investigators' current curriculum vitae in brief.
- 5.2.10 PI's and all co-investigators' with direct patient care GCP certificates (for clinical trials only).

5.3 Figure 2 shows the process of new study application.

MEDICAL RESEARCH ETHICS COMMITTEE - PROCESS FLOWCHART (NEW STUDY)



Date of acceptance: 19 July 2017

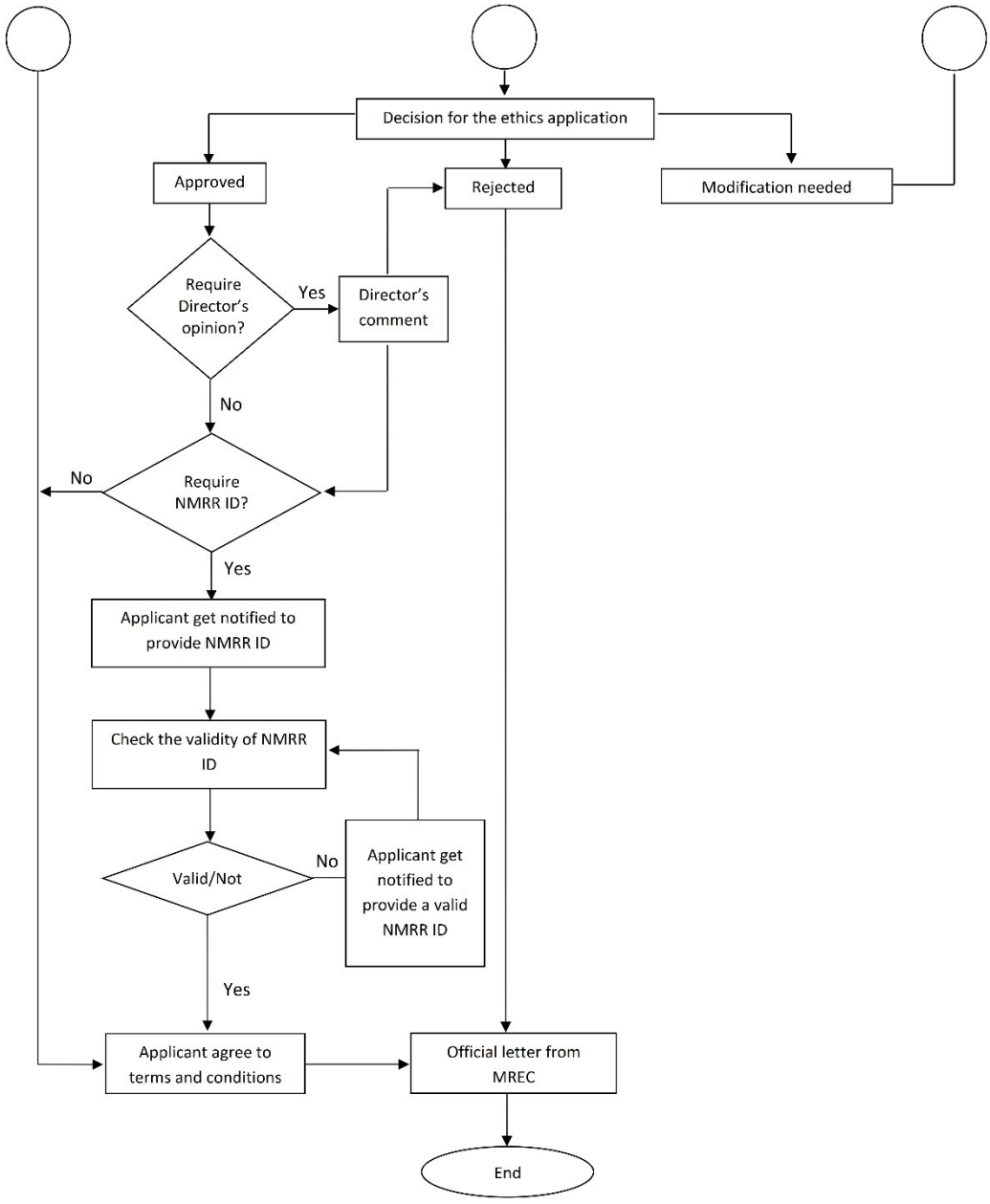


Figure 2.The process of new study application

Date of acceptance: 19 July 2017

6.0 INITIAL REVIEW WORKFLOW

6.1 Preliminary stage

6.1.1 Online application shall be sent to the HOD of which the PI is affiliated to for comments. The application will proceed to next stage if there is no comment received from the HOD after 3 working days.

6.1.2 If the study involves other departments, the application shall be sent to the respective HOD for comments. The application will proceed to next stage if there is no comment received from the respective HOD after 3 working days.

6.1.3 Following that, the application shall be sent to the MREC Secretariat to check for completeness of application according to the submission checklist.

6.1.4 To do this concurrently in the future.

6.2 Classification of review

6.2.1 All new study application will be forwarded to the Chair or Deputy Chairfor review.

6.2.2 The Chair or Deputy Chair will decide whether the proposed application or report should be:

- granted expedited review and approval
- tabled for discussion at the MREC meeting
- referred back to the applicant for clarification or revision (if information is incomplete or unclear)
- referred to relevant committee member, HOD, relevant experts or any other relevant authority for comment before further action is to be taken

6.2.3 Expedited review and approval are considered for studies that pose no more than minimal risks to subjects e.g:

- no intervention or interference to treatment
- no invasive procedures
- involve collection of small volume blood samples
- involve only questionnaire, qualitative interview, case-notes, laboratory studies and retrospective studies

6.2.4 For expedited review and approval, no quorum is required.

6.2.5 Studies that do not achieve the criteria stated in item 6.2.3 will be reviewed at an MREC meeting.

7.0 PROTOCOL REVIEW

7.1 A review checklist is used for all reviews including expedited and full board review.

7.2 Each protocol is evaluated in terms of:

7.2.1 Competency of investigator - to consider the qualifications of the investigator for the proposed study, as documented by current curriculum vitae and / or any other relevant documentation to determine whether the investigators have the necessary experience and skills to conduct the study.

7.2.2 Purpose of study - to determine if the study objectives and outcomes are clear and well explained.

7.2.3 Study justification - to find out if the study answers an important question and whether similar studies have been done before.

7.2.4 Scientific rigour - to evaluate the protocol and find out if the study design to answer the research question is appropriate.

7.2.5 Vulnerable population - to find out the measures taken to ensure vulnerable subjects (if involved) such as pregnant women, children, the indigenous groups, sex workers and prisoners are not being disadvantaged.

7.2.6 Benefits - to assess whether there are benefits to the subjects.

7.2.7 Risks - to identify the risks to the subjects and the actions taken to minimise them, especially studies that involve the use of placebo, untested procedure (investigatory or therapeutic) as well as involving genes or stem cells.

7.2.8 Confidentiality - to make sure that the researchers kept the data confidentially and anonymity participants' information.

7.2.9 Informed consent - to check whether the language and content of the participant information sheet and consent form are appropriate and that these state that the participant is voluntary.

7.2.10 Compensation - to assess whether the subjects are being compensated appropriately, particularly the amount and the method of payment so that compensation does not give undue influence to the subjects to participate in the study.

7.3 The review time of a new study from the receipt of an application by the secretariat to the MREC's first decision is 1 month.

8.0 MREC MEETING WORKFLOW

8.1 Regular Meeting Schedule

8.1.1 The closing date for applications to be considered at an MREC meeting for the month shall normally be the end of the first week of the month.

8.1.2 If there are less than 3 working days in the first week of the month, then the closing date may be moved to the second week of the month.

8.1.3 Applications received after the closing date shall be considered at the next scheduled meeting.

8.1.4 The MREC meeting shall normally be conducted once a month except that there shall be no meeting in December.

8.1.5 The meeting schedule and application deadline is shown on the MREC application website and updated yearly.

8.2 Notification and Distribution of the Meeting Agenda

8.2.1 The secretariat sends reminders to all MREC committee members of the scheduled meeting by 3 working days before the meeting, stating the date, time and the venue of scheduled MREC meeting.

8.2.2 The secretariat also sends minutes of the previous meeting and the meeting agenda of the upcoming meeting including the list of studies tabled for meeting, with the protocol title, protocol numbers, MREC ID No. and the name of PI.

8.2.3 The MREC committee members can view the detailed information of the studies tabled for meeting in the online system and evaluate the studies at any time once the studies are tabled for meeting.

8.2.4 The secretariat will also notify and invite all PIs of studies which are tabled for meeting to attend the MREC meeting by 3 working days before the meeting about the date, venue and the respectively time slot they have to be present in the meeting.

8.3 Preparation of members' meeting folders, study protocols and study protocol-related submissions scheduled for review

8.3.1 The secretariat makes copies of the meeting agenda of the current meeting and the review assessment form, which are distributed to the MREC committee members during the meeting.

8.3.2 The study protocols and study protocol-related documents are available for the members to review via the online system and are also projected during the meeting.

8.3.3 The meeting agenda shall be collected after the meeting and shredded.

8.3.4 The review assessment form shall be collected after the meeting and filed.

8.4 Determination of quorum

8.4.1 Quorum is defined as the presence of at least five of the MREC Committee Members and should consist of:

1.1.1 at least one scientific/medical member
2.1.1 at least one lay member
3.1.1 at least one non-institutional member
4.1.1 both male and female members

8.4.2 In studies that involve children, the opinion of a paediatrician should be available.

8.4.3 On the appointed meeting time, the Secretary determines quorum viability and informs the Chair to indicate readiness to call the meeting to order.

8.5 Calling the meeting to order and completion of required procedures prior to review proper

8.5.1 The Chair or the designated member in the Chair's absence calls the meeting to order upon confirmation of quorum by the Secretary.

8.5.2 The Chair of MREC can allow an observer to be present in the meeting but the observer shall not be entitled to vote. The observers shall sign a confidentiality agreement regarding meeting deliberations, research information and matters related to the meeting.

8.5.3 The Secretary documents the proceedings of the meeting, including theopinions and actions taken with respective reasons, for inclusion in the meeting minutes, and subsequent communication with the principal investigator.

8.5.4 The Chairman calls for declaration of Conflict of Interest (COI) in respect of any study protocol or submission scheduled for review. Members declaring COI are documented by the secretariat staff. The Chair instructs the members who declared COI to recuse themselves from the deliberation of the respective study protocol for which the COI declaration was made.

8.5.5 The Chair then presides over the review of the minutes of the previousmeeting.

8.5.6 The Chair proceeds to facilitate discussion of matters arising from the minutes, the results of which are noted by the secretariat staff for inclusion inthe minutes of the current meeting.

8.5.7 Then, the Chair proceeds to facilitate the review of new study applications which are tabled for MREC meeting.

8.5.8 The Chair instructs the member who had previously declared conflict of interest (COI) to recuse himself/herself from ensuing study protocol deliberation by leaving the room just before the respective study protocol is discussed and deliberated. In some instances, such panel members may be called in by the panel to answer questions to assist in the board in arriving at a board action, but under no circumstances participate in the decision.

8.6 Discussion of New Study Applications and the conduct of PI interview

8.6.1 The Chair or Deputy Chair review all protocols before tabling the high-risk protocols for a full board meeting. The other committee members are also able to access and comment on the protocols before the meeting. The reviews were done using the review checklist as explained in section 7.2.

8.6.2 All PIs or representative (who has to be a Co-I) of studies tabled for a full board meeting have to attend the meeting for an interview session.

8.6.3 During the full board meeting, each PI will be asked to briefly describe the study protocol. The PIs will also be assessed in accordance to the review checklist. The PIs/representative may also be asked to revise any part that is deemed necessary by the committee.

8.6.4 After the interview, the committee will discuss and come to a decision on the study. Approval will only be granted if the majority of members who are present approve the study.

8.6.5 The Secretary is a non-voting member, but he/she is allowed to give comments and opinions.

8.6.6 The MREC may invite independent consultants with expertise in special areas for assistance but the invitee shall not be entitled to vote.

8.7 Notification of MREC's decision

8.7.1 All MREC decisions on new studies shall be documented via the online system.

8.7.2 Types of decisions are as stated below:

1.1.1 Approved

2.1.1 Modifications required prior to approval

3.1.1 Rejected

8.7.3 Once a decision is made on a study, a notification email will be automatically generated by the system and sent to the PI.

8.7.4 For approved/rejected study, the PI has to login into their application account to access the decision letter.

8.7.5 The decision letter includes the following information:

a) Study title
b) Name of PI
c) MRECID Number
d) The documents reviewed
e) The decision of review (approved, expedited approved or rejected)
f) Comments for the decision made
g) Post approval instructions for PI
h) The date of decision
i) The date of the MREC meeting (Not applicable for expedited review)
j) The names and designations of MREC members involved in the decision (Not applicable for expedited review)

8.7.6 For clinical trials, the PIs need to register the study with the National Medical Research Registry (www.nmrr.gov.my) before they will be able to generate the approval letter.

8.7.7 For studies that require modification, the PIs will be notified by email to access the online system for the revision required

to be made. They are required to revise the protocol and submit the necessary documents/information via the online system. The Chair or Deputy Chair then again evaluate the protocol and decide whether to give expedited approval or to table it in next MREC meeting.

8.7.8 For studies that are rejected, the PIs can re-submit to the revised protocol to the MREC, also via online system.

8.7.9 If errors are detected in the letter, the PIs can request the MREC Secretariat to amend and reissue the decision letter. MREC Secretariat shall keep a record of versions of the initial and corrected letters.

8.8 Reports of expedited approval to Modified Pending Protocols

8.8.1 The Chair reports all the study protocols and study protocol-related submissions that were approved that were satisfactorily modified.

8.8.2 The Chair also asks the committee members if there is any objection or comment on the expedited approved studies as listed in the meeting agenda.

8.9 Report of Expedited Review

8.9.1 The Chair reports all the study protocols and study protocol-related submissions that were approved via expedited review.

8.9.2 The Chair also asks the committee members if there is any objection or comment on the expedited approved studies as listed in the meeting agenda.

8.10 Discussion of Study Protocol Amendment application

8.10.1 The Chairman will present the list of protocol amendment applications that have been granted expedited approval.

8.10.2 Protocol amendment applications that are tabled for full board meeting will be discussed among committee member for any of the following actions:

- Approve
- Request information
- Recommend further action
- Pending, if major clarifications are required before a decision can be made

8.10.3 If deemed necessary (when the amendments are felt likely to affect the subjects' safety), the PI will be called for an interview.

8.11 Discussion of Annual Study Report

8.11.1 Annual Study Report

8.11.2 The Chair will present the list of annual study report that have been granted expedited approval.

8.11.3 Annual study reports that are tabled for full board meeting will be discussed among committee member for any of the following actions:
- Approve
- Request information
- Recommend further action
- Pending, if major clarifications are required before a decision can be made

8.11.4 If deemed necessary (eg. poor progress or safety is concerned), the PI will be called for an interview.

8.12 Discussion of Study Closure Report

8.12.1 The Chairman will present the list of study closure report that have been granted expedited approval.

8.12.2 Study closure report that are tabled for full board meeting will be discussed among committee member for any of the following actions:
- Approve
- Request information
- Recommend further action
- Pending, if major clarifications are required before a decision can be made

8.12.3 If deemed necessary, the PI will be called for an interview.

8.13 Discussion of Early Study Termination application

8.13.1 The Chair presents, if any, early study termination of previously approved study protocols.

8.13.2 The Chair calls on the committee members to recommend any of the following actions:
- Approve
- Request information
- Recommend further action
- Pending, if major clarifications are required before a decision can be made

8.13.3 If deemed necessary, the PI will be called for an interview.

8.14 Discussion of Site Visits Report

8.14.1 The Chair of the Site Visit Sub-committee will present the report on site visits that have been conducted (if any).

8.14.2 The MREC Chair calls on the committee members to recommend any of the following actions:
- No further action
- Request information
- Recommend further action
- Pending, if major clarifications are required before a decision can be made

8.15 Discussion of Study Protocol Non-compliance (Deviation or Violation) Report

8.15.1 The Chair present, if any, Study Protocol Non-compliance (Deviation or Violation) Report of previously approved study protocols. Non-compliance may be in the form of non-compliance with post-approval requirements.

8.15.2 The Chair calls on the committee members to recommend any of the following actions:

- No further action
- Request information
- Recommend further action
- Pending, if major clarifications are required before a decision can be made

8.16 Discussion of Queries, Notifications and Complaints

8.16.1 The Chair presents, if any, Queries, Notifications and Complaints received.

8.16.2 The Chair calls on the committee members to recommend any of the following actions:

- No further action
- Request information
- Recommend further action
- Pending, if major clarifications are required before a decision can be made

8.17 Discussion of SAE report

8.17.1 The Chair of the SAE subcommittee presents, if any, reports of the SAE Subcommittee. The Chair calls on the UMMC-MREC members to deliberate on the recommendations of the SAE Subcommittee and decide on action such as:

- No further action
- Request information
- Recommend further action
- Pending, if major clarifications are required before a decision can be made

8.18 Adjournment of the meeting

8.18.1 Before closing the meeting, the Chairman calls for any non-study protocol matters that need attention or action, as the need arises.

8.18.2 With no further matters for discussion, the Chairman formally adjourns the meeting, with the time noted by the Secretariat Staff who is documenting the meeting.

8.19 Collection and storage or disposal of meeting materials

8.19.1 The secretary collects all meeting materials, including the distributed minutes of previous meeting, the current meeting agenda and the documentation collected for the minutes of

the current meeting; mindful that these materials are confidential.

8.19.2 The secretary files all meeting materials that must be stored the files according to protocol and shred the files that are not to be kept.

9.0 SPECIAL MEETING WORKFLOW

9.1 Preparation for Conducts of Special Meeting

9.1.1 A special meeting may be called by the Chair or is proposed by a member of the MREC or the Director of the UMMC.

9.1.2 The decision to call a special meeting is based on the following criteria:

- Urgent issues (if delay will affect or have impact on the public benefit, national economy, etc.)
- Occurrence of unexpected serious adverse events
- A matter of life and death
- Other similar situations

9.1.3 The Secretariat informs the MREC committee members, including the invited persons, about the special meeting.

9.2 Conduct of Special Meeting

9.2.1 Quorum is defined as the presence of at least five MREC committee members described as follows:

- At least one scientific/medical member
- A non-scientific member or lay person
- At least one non-institutional member
- A member/or invited guest with expertise on the item to be discussed

9.2.2 A special meeting may be conducted between the members through tele/video conference.

9.2.3 The meeting is conducted in the same sequence as MREC meeting with similar corresponding actions (if applicable).

9.3 Collection and storage or disposal of meeting materials

9.3.1 The Secretariat Staff collects all meeting materials, including the documentation collected for the Minutes of the meeting; mindful that these materials are confidential.

9.3.2 The secretary files all meeting materials that must be stored according to protocol and shredded the files that are not to be kept.