PK – 7.1 – QSU – 011 – E02

PROSEDUR KUALITI PERMOHONAN KELULUSAN ETIKA PERUBATAN

1.0 PURPOSE

1.1 This procedure describes the process of review, approval, and continuing review of all clinical trials/studies involving humans, before the trial/study been conducted, so as to ensure the protection of the rights, safety and well-being of human subjects involved in research protocols under the aegis of the University of Malaya Medical Centre or Faculty of Medicine, University of Malaya.

1.2 The process includes the review and approval of the study protocol to be used, and where applicable, the means of obtaining and documenting informed consent from study subjects.

2.0 SCOPE

2.1 This procedure is applicable to all research involving:

2.1.1 human participants,

2.1.2 patients' medical records, and

2.1.3 human tissues (only if the personal identity of the subject is required).

2.2 In essence, these include:

2.2.1 clinical trials,

2.2.2 studies requiring extra procedures to be carried out on subjects i.e. any procedure which would not have been normally carried out in the course of the subject's stay / visit to the medical centre and which is proposed to be carried out because of the study,

2.2.3 studies, whether retrospective or prospective, using patient data outside of the researcher's Department, and

2.2.4 questionnaires / surveys involving patients and / or their relatives.

2.3 Special attention will be given to projects involving:

2.3.1 research with children, prisoners and adults not competent to give consent

2.3.2 research involving the use of genetic material, and

2.3.3 research that may impose an undue disadvantage upon participants.

2.4 Studies excluded from the scope of this procedure, i.e. research that may not require ethical review by the Medical Ethics Committee (MEC), include:

2.4.1 research solely involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures and data collection in the public domain, and

2.4.2 diagnostic and therapeutic procedures that are an accepted part of treatment and are recognized as current practice by the appropriate professional body.

3.0 RESPONSIBILITY

3.1 It is the responsibility of the Chairman of the Medical Ethics Committee of the University of Malaya Medical Centre to ensure that the procedures outlined in this document are adhered to.

3.2 This document is applicable to all members of the Medical Ethics Committee of the University of Malaya Medical Centre and all researchers conducting studies on human subjects using the name of the Faculty of Medicine, University of Malaya or the University of Malaya Medical Centre.

3.3 It is the responsibility of the Principal Investigator to obtain approval from MEC before starting the clinical trial/study.

3.4 Principal Investigator must ensure that no subject is admitted to a trial before the MEC issues its written approval/favourable opinion of the trial.

3.5 Principal Investigator should not deviate from the approved protocol. Any amendments to the protocol should not be initiated without prior written MEC approval/favourable opinion of the relevant amendment, except when necessary to eliminate immediate hazards to the subjects or when the changes are only logistical or administrative (e.g. change of monitors, telephone number, etc).

4.0 REFERENCE DOCUMENTS

	Document	Document Number
4.1	Malaysian Guidelines for Good Clinical Practice, 3rd Edition 2011: Section 3, Institutional Review Board / Independent Ethics Committee (IRB/IEC)	Not applicable
4.2	FDA, CPR Part 56 – Institutional Review Board	Not applicable
4.3	International Committee on Harmonization of Good Clinical Practice (ICH-GCP) guidelines	Not applicable
4.4	Terms of Reference and Responsibilities of Medical Ethics Committee, UMMC, 9 October 2012	Not applicable

5.0 TERMINOLOGY

5.1 Definition

(a) Adverse Drug Reaction (ADR): In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase responses to a medicinal product means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.

Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for modification of physiological function (see the ICH Guidelines for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

(b) Adverse Event (AE): Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. Adverse events (AE) can therefore be any favourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product (see the ICH Guidelines for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

(c) Clinical Trial / Study: Any investigation in human subjects intended to discover or verify the clinical, pharmacological and / or other pharmacodynamic effects of an investigation product(s) and / or to study absorption, distribution, metabolism, and excretion of an investigation product(s) with the object of ascertaining its safety and / or efficacy. The terms clinical trial and clinical study are synonymous. It also includes procedures and any other methods performed on human subjects.

(d) Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

(e) Informed Consent: A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial/study, after having been informed of all aspects of the trial/study that are relevant to the subject's decision to participate.

(i) Informed consent obtained can be written or verbal. Written informed consent is a document by means of a written and dated informed consent form, signed by the study subject.

(ii) Verbal informed consent, although not signed by the study subject, should be documented in study records.

(f) Investigator: A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal investigator.

(g) Protocol: A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial/study.

(i) The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents.

(ii) Throughout this document the term protocol also refers to protocol amendments.

(h) Protocol Amendment: A written description of change(s) to a protocol.

(i) Serious Adverse Events (SAE) or Serious Adverse Drug Reaction (Serious ADR): Any untoward medical occurrence that at any dose that:

i) results in death,

ii) is life-threatening,

iii) requires inpatient hospitalization or prolongation of existing hospitalization.

iv) results in persistent or significant disability / incapacity, or

v) is a congenital anomaly / birth defect

(Refer to the Malaysian ICH GCP Guideline for Clinical Safety Data Management : Definitions and Standards for Expedited Reporting).

(j) Subject / Trial Subject: An individual who participates in a clinical trial, either as a recipient of the investigation product(s) or as a control.

(k) Vulnerable Subjects: Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate.

(i) Examples are members of a group with hierarchical structure, such as medical, pharmacy, dental and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention.

(ii) Other vulnerable subjects include patients with incurable diseases, persons in nursing home, unemployed or impoverished persons, and patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

5.2 Abreviation

ADR	Adverse Drug Reaction
AE	Adverse Event
CIC	Clinical Investigation Centre
CMEC	Chairman of Medical Ethics Committee
DCMEC	Deputy Chairman of Medical Ethics Committee
GCP	Good Clinical Practice
MAC	Medical Advisory Committee
MCRC	Medical Centre Research Committee
MEC	Medical Ethics Committee
PI	Principal Investigator
SADR	Serious Adverse Drug Reaction
SAE	Serious Adverse Event
SMEC	Secretary of the Medical Ethics Committee
UMMC	University Malaya Medical Centre

6.0 TERMS OF REFERENCE

(a) The MEC answers to the Board of Management, who appoints all the members, but is independent in its decision-making.

i) The membership of the MEC is as shown in Appendix 11.1.

ii) The Board of Management shall not approve any study that has been disapproved by MEC.

iii) The decision of the MEC are also informed to the Medical Advisory Committee (MAC).

(b) MEC can only convene or make a decision if at least 5 voting members (including 1 member from outside UMMC/Faculty of Medicine, University Malaya and 1 clinical specialist) are physically present. Any member who is involved in a study being decided on shall not be entitled to vote.

(c) Only Ethics Committee members who are independent of the investigation and the sponsor of the study may vote on a study related matter.

(d) Approval will only be granted if the majority of members who are present approve the study.

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

(f) MEC may invite non-members with expertise in special areas for assistance but the invitee shall not be entitled to vote.

(g) Chairman of MEC can allow an observer to be present in the meeting but the observer shall not be entitled to vote.

(h) All members, invitees and observers shall sign a confidentiality agreement regarding meeting deliberations, research information and matters related to the meeting.

7.0 WORK PROCESS AND PERSONS RESPONSIBLE

Procedure	Responsibility
Application	
7.1 7.1.1 Register and apply through online URL as below: i. http:// my.ummc.edu.my – for UMMC/Faculty of Medicine staffs who have Single Sign On (SSO) login (e-Service ⟶ i Research) ii. https:// eservices.ummc.edu.my - for UMMC/Faculty of Medicine staffs who does not have Single Sign On (SSO) login 7.1.2 For protocol amendment, reporting of Serious Adverse Events (SAE), reporting annual study or study termination from UMMC official website, download forms using the following the steps: (http://www.ummc.edu.my ⟶ Explore UMMC⟶ Patient Care, Research and Education ⟶ Researcher⟶ Research ethics)	PI
7.2 Ensure that online application forms for approval of a trial / study are complete with the uploaded file of the following: a) Trial protocol. b) Written informed consent form, written in English or Bahasa Malaysia. c) Subject recruitment procedures / advertisements (if applicable) d) Written information to be provided to subjects (if applicable). e) Investigator's Brochure (if applicable). f) Available safety information (if applicable). g) Information about payments and compensation available to subjects (if applicable).	

Procedure	Responsibility
h) Principal Investigator's and all co-investigators' current curriculum vitae in brief. i) Principal Investigator's GCP certification (for clinical trials only). 7.3 a) Online application shall be send to the HOD to which the PI is affiliated for comments. b) If the study involves other relevant departments other than applicant's department, the application shall be send to the respective HOD for comment. c) After that, the application automatically forwarded to the Manager of CIC for verification of budget and Clinical Trial Agreement (CTA). CIC shall refer to UMMC Director if opinion is necessary. d) Following that, the application shall be send to the MEC Secretariat for vetting of completeness of application/compliance to checklist. 7.4 The following may be submitted in hardcopy, directly to the Secretary of MEC: a) Applications for protocol amendment. b) Any other report.	
Preliminary and Expedited Review 7.5 Submit the application of new study via online system to the Chairman and Deputy Chairman. Protocol amendment application, Serious Adverse Events (SAE), annual study or study termination report or any other report shall be submit to the Chairman/Deputy Chairman of MEC upon receipt of the documents. 7.6 Decide whether the proposed application or report should be: a) granted expedited review and approval, b) tabled for discussion by the MEC, c) referred back to the applicant for clarification or revision (if information is incomplete or unclear), or d) referred to relevant experts or Head of Department, relevant committee member or any other relevant authority for comment before further action is to be taken.	SMEC CMEC/DCMEC

Procedure	Responsibility
7.7 Expedited review and approval are considered for studies that: a) pose no more than minimal risks to subjects e.g: i. no intervention or interference to treatment. ii. no invasive procedures. iii. involve collection of small volume blood samples. iv. involve only questionnaire, case-notes, data collection, retrospective studies. b) are minor changes to approved protocols posing no additional risk to subjects. c) are follow-up report such as annual study reports, closure reports or SUSAR reports. For expedited review and approval, no quorum is required. d) Submission as below shall be acknowledged by the MEC Secretariat and will be tabled for endorsement at the subsequent MEC meeting: i. Annual report ii. Study closure report iii. SAE report iv. Study progress report v. Protocol deviation vi. SUSAR reports vii. Clinical Line Listing report viii. Clinical synopsis report	
Preparation for MEC Meeting 7.8 The closing date for applications or reports to be considered at a MEC meeting for the month shall normally be the end of the first week of the month. a) 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. b) Applications received after the closing date shall normally be considered at the next scheduled meeting. c) The MEC meeting shall normally be conducted on the third week of each month. 7.9 Notify all Committee members of the scheduled meeting by 3 working days before the meeting.	SMEC

Procedure	Responsibility
7.10 Notify and invite to appear for the MEC meeting, the Principal Investigator of a study tabled for discussion / evaluation by 3 working days before the meeting, stating the: a) date. b) time. c) place of the relevant scheduled MEC meeting. 7.11 Committee members can view the list of all studies for discussion/evaluation in the online system at any time. 7.12 Secretariat shall prepare a list of all studies for discussion / evaluation, showing their protocol title, protocol numbers, MEC ID No. and name of Principal Investigator (for documentation).	

Procedure	Responsibility
Medical Ethics Committee Meeting	
7.13 Conduct MEC meetings at least once in two months.	CMEC
7.14 Inform MEC members of all items granted expedited review and approval by the CMEC / DCMEC since the last meeting of MEC.	
7.15 Evaluate each proposal tabled for the meeting.	MEC
a) Consider the qualifications of the investigator for the proposed study, as documented by current curriculum vitae and / or any other relevant documentation the MEC requests.	
b) Determine that the risks to subjects are minimized and reasonable in relation to anticipated benefits.	
c) Require that information given to subjects on part of the informed consent is in accordance with ICH-GCP guidelines.	
- Request for translations if the study population would require that particular language.	
7.16 Review both the amount and method of payment to subjects to assure that neither presents problems of coercion or undue influence on the trial subjects.	
7.17 All MEC decisions on new studies shall be documented via online system. Types of decisions are stated below:	CMEC
a) Approval.	
b) Modifications required prior to approval.	
c) Disapproval/Rejection.	
d) Termination / suspension of any prior approval.	
For **a)**, if it is an interventional study, PI needs to register the study into www.nmrr.gov.my	
For **b)**, PI are required to submit the necessary documents/information via online system to the Secretariat of MEC. Chairman/Deputy Chairman can give expedited approval for this submission or decide whether to tabled it in next MEC meeting.	PI
For **c)**, PI can resubmit to the MEC, also via online system.	

Procedure	Responsibility
Notification of MEC Decision	
7.18 Table the minutes of the MEC meeting with decisions at the next scheduled MAC and UMMC Board of Management meeting for information.	SMEC
7.19 Decision of MEC on new studies shall be generated online once the decision has been made. Decision on protocol amendments, SAE and any other reports received in hardcopy or not included in the online system, will be informed by hardcopy via e-mail to the applicant in 14 working days after the date of the relevant MEC meeting. The information shall include: a) The decision of MEC, including reasons for decisions and procedures for appeal. b) The date of the MEC meeting. c) The names and designations of MEC members involved in the decision. d) The materials reviewed.	SMEC SMEC
7.20 Archive a copy of the minutes of MEC meetings and correspondence with investigators.	

Procedure	Responsibility
7.21 Archive the application and accompanying documents for at least 3 years after the termination of a study. 7.22 Make accessible all archived documents for inspection and audit by authorized persons.	SMEC
Changes to Approved Studies	
7.23 Promptly report to MEC, any: a) Deviations from or changes to the protocol to eliminate immediately hazards to the trial subjects. b) Changes or observations (including SAE) that increase the risk to subjects and / or affect significantly the conduct of the trial. c) New information that may affect adversely the safety of the subjects or the conduct of the trial. d) Any trial which is prematurely suspended or terminated.	PI of approved clinical trial/study

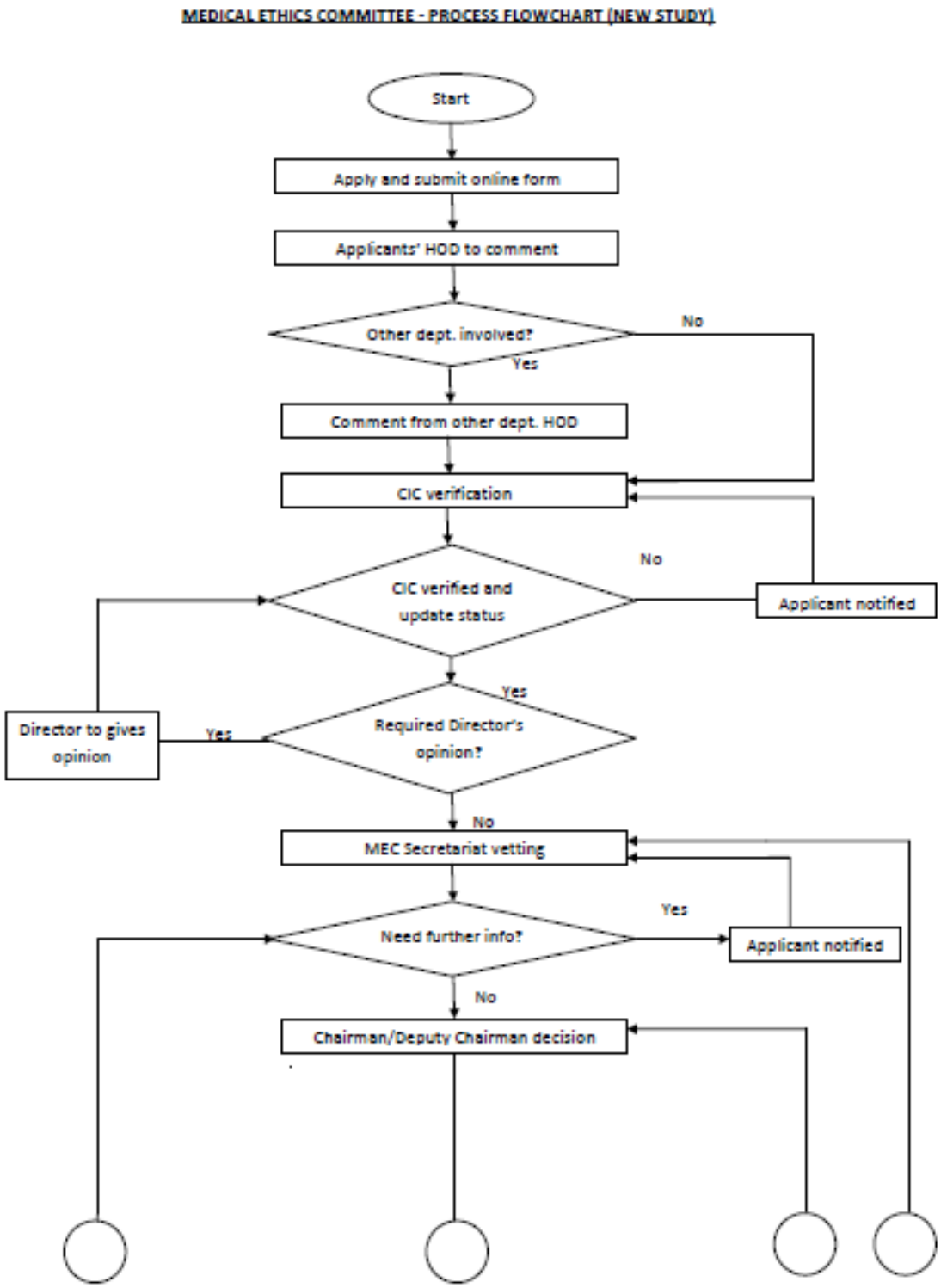
Procedure	Responsibility
Monitoring of Clinical Trials 7.24 Provide the MEC with the following information: (a) The commencement of the clinical trial. (b) Status of the study annually, including patient enrolment status and AE listing. (c) All Serious Adverse Events (SAEs) have to be reported by the investigator to MEC immediately and not more than 48 hours of notification. A written report on the MEC SAEs form (BK-MIS-1118) is to be submitted promptly and not more than 7 days to MEC. CIC shall assist MEC in the monitoring of SAEs. During extended public holidays, SAE are to be reported to the Director of UMMC.	PI of approved clinical trial/study

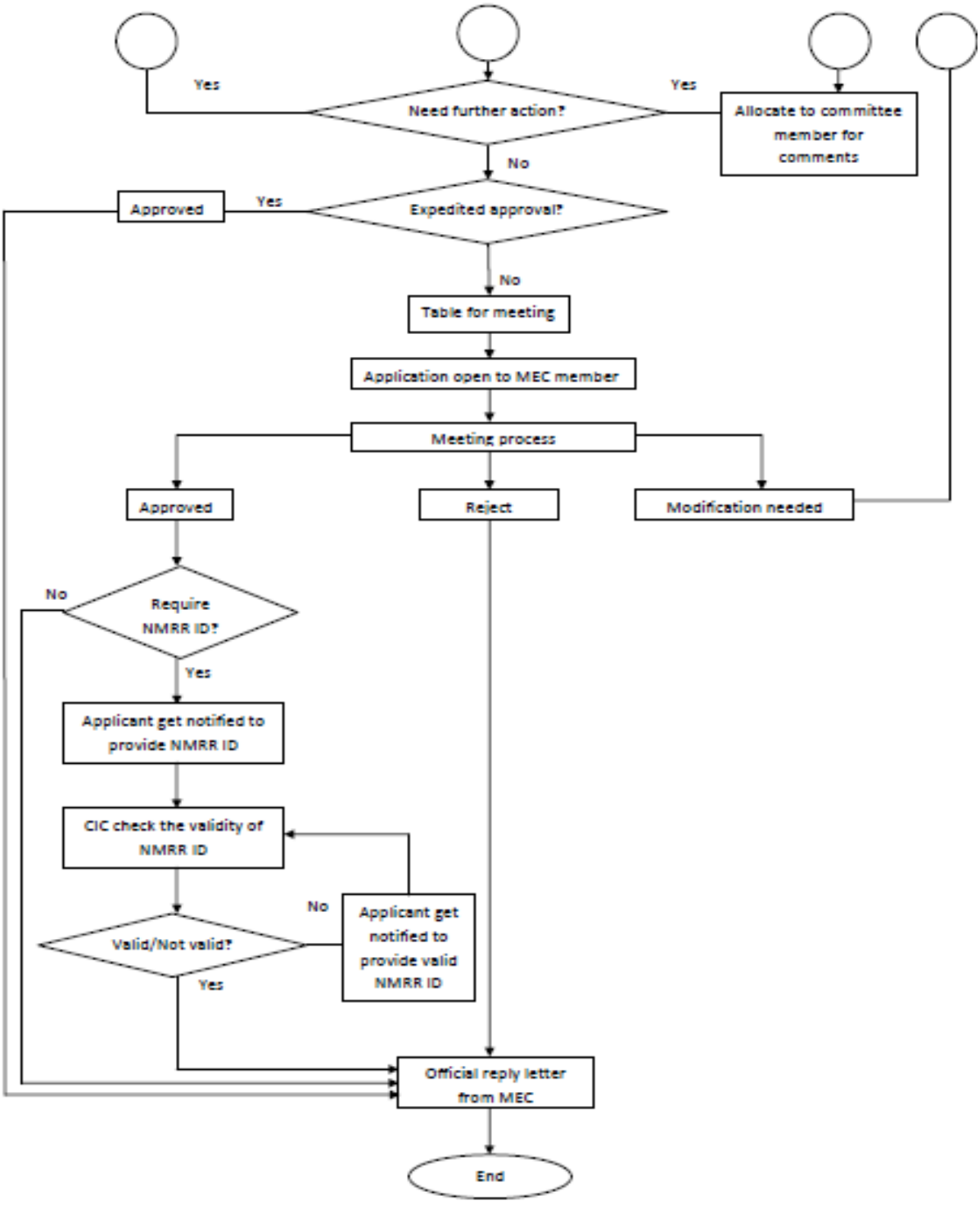
Procedure	Responsibility
(d) UMMC MEC is adopting the same safety reporting requirement as the National Pharmaceutical Control Bureau (NPCB) for **FOREIGN SUSAR**. The reporting timeframe for the investigator to the MEC, UMMC and type of report to submit is illustrated as below: i) Suspected Unexpected Serious Adverse Reaction (SUSARs) that is Fatal/Life Threatening: As soon as possible as but not later than 7 calendar days from awareness of event by investigator, followed by a complete report within 8 additional calendar days. ii) All other than SUSARs: As soon as possible as but no later than 15 calendar days from awareness of event by investigator. Follow up information should be actively sought and submitted as it becomes available. Foreign SUSAR from the following do not require reporting: i) Clinical Trial not conducted in UMMC. ii) Suspected drug is known to be other than trial drug (e.g. Other treatments, placebo or comparator drug). iii) SAE and not drug related. iv) Suspected Expected Serious Adverse Reaction. (e) Closure report within one month after the study closure or termination.	PI of approved clinical trial/study
7.25 Ensure that all documentation on the conduct of the trial meet the Malaysian ICH-GCP requirements.	PI of approved clinical trial/study
7.26 The MEC may conduct audits of ongoing trials/studies as part of its monitoring activities.	MEC
8.0 Amendments to MEC letters	
8.1 If errors are detected in any letters (e.g. approvals of studies, approvals of amended protocols, acknowledgement of follow-up reports), the investigator can request the MEC Secretariat for the issue of a corrected letter.	SMEC
8.2 MEC Secretariat shall keep a record of versions of the initial and corrected letters.	

9.0 QUALITY RECORDS

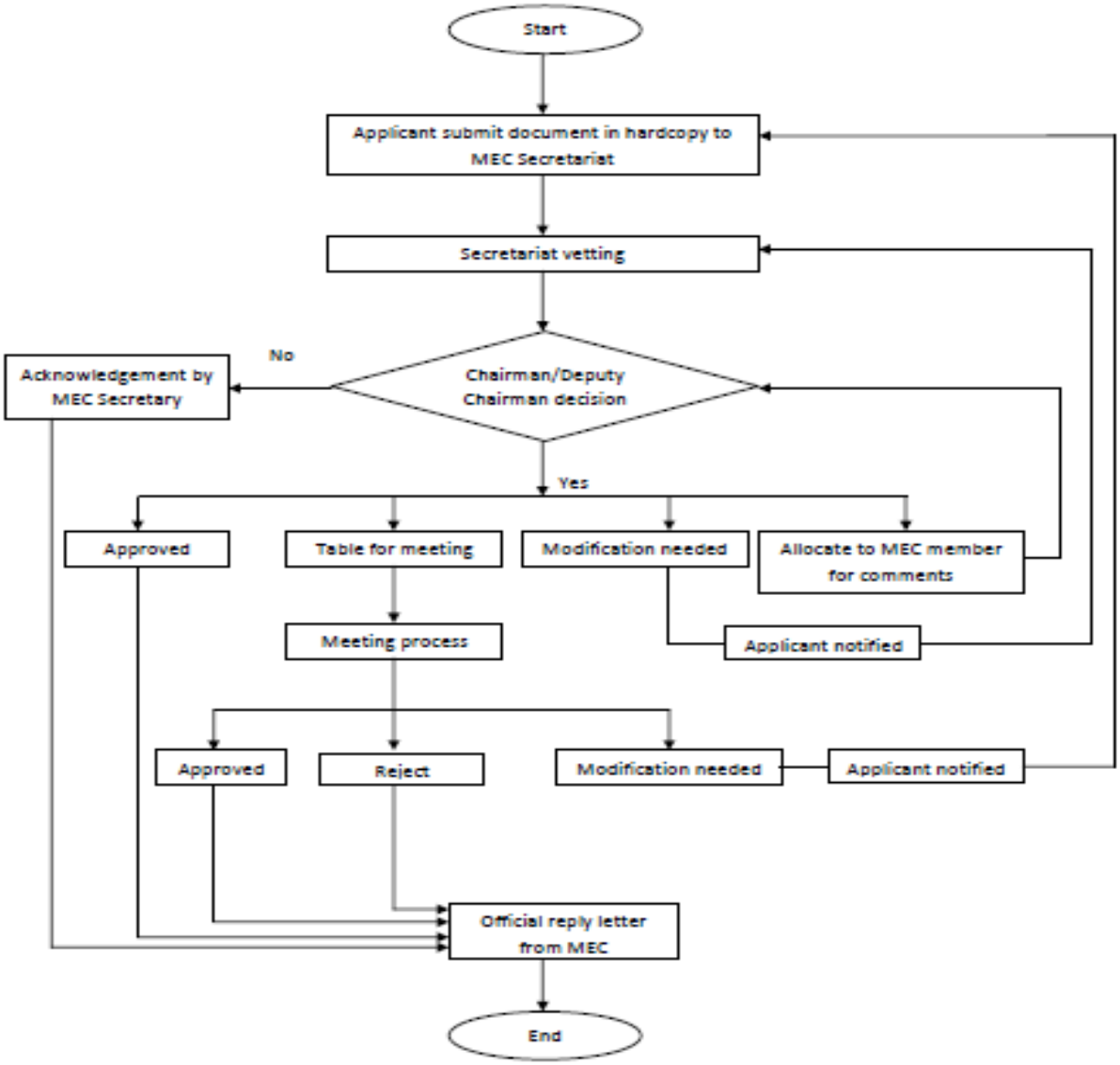
No.	Record	Location	Duration	Responsibility
9.1	Minutes of MEC meetings	Office of the Secretary of MEC	7 years	Secretary of MEC
9.2	Notification of MEC decisions to Principal Investigators	Office of the Secretary of MEC	3 years after termination of study	Secretary of MEC
9.3	Application forms and accompanying documents: (BK-MIS-1116), (BK-MIS-1117), (BK-QSU-026),	Office of the Secretary of MEC	3 years after termination of study	Secretary of MEC
9.4	Report forms: (BK-QSU-025), (BK-MIS-1118)	Office of the Secretary of MEC	3 years after termination of study	Secretary of MEC
9.5	Records of correspondence including e-mail	Office of the Secretary of MEC	3 years after termination of study	Secretary of MEC

10.0 FLOW CHART




Yes
Need further action?
Yes
Allocate to committee member for comments
No
Approved
Yes
Expedited approval?
No
Table for meeting
Application open to MEC member
Meeting process
Approved
Reject
Modification needed
No
Require NMRR ID?
Yes
Applicant get notified to provide NMRR ID
CIC check the validity of NMRR ID
No
Applicant get notified to provide valid NMRR ID
Valid/Not valid?
Yes
Official reply letter from MEC
End

MEDICAL ETHICS COMMITTEE - PROCESS FLOWCHART [PROTOCOL AMENDMENT, ADDITIONAL DOCUMENTATION, NOTIFICATION, ETC]



11.0 APPENDICES

11.1 COMPOSITION OF THE MEDICAL ETHICS COMMITTEE (MEC)

Chairman:

A clinical academic staff of Faculty of Medicine, University Malaya, appointed by the Board of Management, University Malaya Medical Centre, upon advice of the Dean, Faculty of Medicine, University Malaya.

Deputy Chairman:

A clinical academic staff of Faculty of Medicine, University Malaya, appointed by the Board of Management, University Malaya Medical Centre, to deputize for the Chairman of MEC, upon advice of the Dean, Faculty of Medicine, University Malaya.

Members:

(i) Director, University Malaya Medical Centre or his nominated representative, appointed by the Board of Management, University Malaya Medical Centre.

(ii) Head, Department of Medicine or his nominated representative, appointed by the Board of Management, University Malaya Medical Centre.

(iii) Head, Department of Psychological Medicine or his nominated representative, appointed by the Board of Management, University Malaya Medical Centre.

(iv) Head, Department of Surgery or his nominated representative, appointed by the Board of Management, University Malaya Medical Centre.

(v) Dean, Faculty of Law, University of Malaya or his nominated representative, appointed by the Board of Management, University Malaya Medical Centre.

(vi) Head, Department of Pharmacy / Pharmacology, Faculty of Medicine, University Malaya, or their nominated representative, appointed by the Board of Management, University Malaya Medical Centre, on rotation through a two yearly term.

(vii) Head of Pharmacy, Department of Pharmacy, UMMC or his nominated representative, appointed by the Board of Management, University Malaya Medical Centre.

(viii) Public representative(s): At least two (2) persons, appointed by the Board of Management, University Malaya Medical Centre, upon advice of the Director, UMMC.

(x) Secretary: An officer of UMMC, appointed by the Director, UMMC.

11.2 Details of quality records:

(i) Investigator's checklist (BK-QSU-027)

(ii) Application to conduct research project (BK-QSU-024)

(iii) Application for amendment to research project (BK-QSU-026)

(iv) Patient Information Sheet (English version) BK-MIS-1116)

(v) Consent form (BK-MIS-1117)

(vi) Serious Adverse Event Report (BK-MIS-1118)

(viii) Annual Study Report / Study Closure Report Form (BK-QSU-025)

(ix) Application For Permission To Conduct A Research Involving Patients At UMMC (BK-QSU-028)