

GUIDELINES FOR APPLICATION TO CONDUCT DRUG-RELATED CLINICAL TRIALS IN MALAYSIA

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FOREWORD

The importance of Research and Development in the attainment of national health, social and economic goals is well recognized. The Ministry of Health of Malaysia has always been committed to providing support for the conduct of useful clinical trials in this country. As part of our continuing process of improvement in efforts to facilitate clinical research, we have produced this Guideline to assist clinicians and scientists be familiar with the existing procedures required for the conduct of drug-related clinical trials in Malaysia. This initiative taken by the Ministry of Health, in collaboration with the local Universities, is a positive step towards enhancing and expanding our research capabilities and has been well received by the pharmaceutical industry and the research community.

These guidelines will provide the pharmaceutical industry, sponsors and investigators with a listing of research institutions involved in drug-related research in Malaysia, as well as the specific procedures required in the application for permission to conduct clinical trials in the various research institutions in Malaysia.

The completion of this guideline is timely as it will complement the Ministry of Health's initiative in ensuring that all investigator involved in drug-related research be trained in Good Clinical Practice (GCP) before they undertake to conduct clinical trials.

I would like to take this opportunity to congratulate the "Working Committee on the Guidelines For Application To Conduct Drug-Related Clinical Trial In Malaysia" for their successful effort in the production of this very useful document.

Dato' Dr. Hj. Mohd. Ismail Merican
Deputy Director-General of Health
(Research & Technical Support)
Malaysia.

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(National Pharmaceutical Control Bureau)

INTRODUCTION

The aim of this booklet is to provide a comprehensive guide on the processes involved in obtaining approval to conduct clinical trials in Malaysia. Under the Control of Drugs and Cosmetics Regulation, 1984, a clinical trial is defined as "any investigation or series of investigations on persons conducted by or under the supervision of persons with scientific training or experience for the purpose of finding about or determining the safety, effectiveness and other effects of any product".

The Research Review Committee (RRC) reviews the scientific merit of each research proposal while the Medical Research Ethics Committee (MREC) reviews the ethical aspects of the study to safeguard the rights, safety and well-being of all trial subjects. The RRC/MREC or its equivalent is available at the respective Universities/ Private Institutions to manage applications for research activities.

There are two (2) main processes involved before conducting any clinical trials in Malaysia.

- (i) Application to both the Research and Ethics Committees, and
- (ii) Application to the National Pharmaceutical Control Bureau (NPCB) for clinical trial import licence or similar permits relevant to the drugs under study.

Approval for each of these processes has to be sought before the start of any clinical trial. In Malaysia, parallel submission is allowed for the application of the clinical trial import licence/ permit and the application to the relevant RRC/MREC.

In line with the global harmonization of clinical trial practice, Malaysia will also adopt the ICH-GCP Guidelines with some modifications to suit local requirements. Compliance with this standard provides public assurance that the rights, safety and well being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki. Adhering to GCP Guidelines, enables a unified standard globally and thus facilitates the mutual acceptance of clinical data by the relevant regulatory authorities.

SECTION A: APPLICATION TO THE RESEARCH/ETHICS COMMITTEES

1.0 Clinical Trial Sites

1.1 Clinical Trials in Hospitals under the Ministry of Health (MOH)

Any trial conducted in a government health facility requires the approval of the Director-General of Health, Malaysia.

The executive body for research in the MOH is the Standing Committee for Medical Research (SCMR). The Secretariat to the SCMR (SSCMR) is located in the Institute for Medical Research (IMR), Kuala Lumpur.

1.2 Clinical Trials in Universities/Private Sector

Clinical trials can also be conducted in the Universities, Private Hospitals/ Institutions and private clinics. Principal Investigators are required to apply to the Secretary of both the Research and the Ethics Committee of the respective Universities. In the event that a particular centre has no Research/Ethics Committee, the approval for the trials can be obtained from the RRC/MREC of the Ministry of Health or of the Universities/Private institutions which have such committees.

2.0 Application to conduct clinical trials in the Ministry of Health

2.1 Standing Committee for Medical Research

Applications are to be made on the forms JTP/KKM 1-2, which can be obtained from Dr. Ho Tze Ming, The Secretary, SSCMR, Institute for Medical Research, Kuala Lumpur [Tel no: 03-2935926, Fax no: 03-2935928, (E-mail: hotm@imr.gov.my)]. The form can also be downloaded from the webpage <http://imr.gov.my/formmgmt.htm>

The JTP/KKM 1-2 form consists of 4 parts :

- Part A: Basic information on the project and approval from the Department Head of the Principal Investigator must be obtained.
- Part B : Project costing and source of funding.
- Part C : Consent of all collaborators and their Department Heads.
- Part D : Project Protocol.

The researcher must submit the following to the SSCMR which will then channel the relevant documents to the RRC and the MREC:

- 20 copies of protocol
- 20 copies of patient information sheet and patient informed consent form in English and Bahasa Malaysia
- Product liability letter from drug firm (needed for studies involving new drugs and drugs registered in Malaysia but not in the Ministry of Health 'Blue Book').
- Investigators' curriculum vitae.

2.2 Research Review Committee (RRC)

The RRC examines the scientific merit, relevance and expected benefits of research proposals. The committee meets 6 times a year (i.e. in February, May, July, August, September, November). For further information please contact The Secretary of the RRC, Institute for Medical Research, Kuala Lumpur (Tel. No: 03-4402379 and Fax No: 03-2938306)

The principal investigator is required to defend the proposal concerned at a RRC meeting.

2.3 Medical Research Ethics Committee (MREC)

The principal task of MREC is to ensure that proposals comply with internationally accepted guidelines in the care and treatment of human subjects. The MREC reviews each proposal and recommends approval, changes to the proposal or rejection of proposal. This committee meets 3-4 weeks after RRC meeting. For further information, please contact the Secretary, MREC at the Institute for Medical Research, Kuala Lumpur (Tel. No: 03-4402379, Fax No: 03-2938306).

The principal investigator will be required to defend the proposal.

2.4 Timeline for approval

Comments from the RRC and MREC shall be forwarded to the Director-General of Health, Malaysia, who will then give the final decision. The time frame from submission to the RRC and MREC, to the final approval is usually between 3 to 4 months. The workflow for application to conduct clinical trials in the MOH is displayed in Flowchart I.

3.0 Application to conduct Clinical Trials in Universities/Private Institutions

The application must be submitted to the respective Research/Ethics Committees of the Universities/Institutions as follows:

3.1 University of Malaya

Assistant Registrar
Faculty of Medicine
Universiti Malaya
50603 Kuala Lumpur.
Fax no: 03-7541904, 7568841
Tel. no: 03-7502351, 7502107

The workflow for application to conduct clinical trials at the University of Malaya is as in Flowchart II. The approval normally takes between 4 to 6 weeks depending on the time of submission.

3.2 Universiti Sains Malaysia

Assistant Registrar
Research and Ethics Committee
Pusat Pengajian Sains Perubatan
Universiti Sains Malaysia
16150 Kubang Kerian
Kelantan.
Fax no: 09-7656532
Tel. no: 09-7602004

The workflow for application to conduct clinical trials at the Universiti Sains Malaysia is as in Flowchart III. The Research and Ethics Committee meets once a month and the applicant is notified within one week of the meeting. The approval normally takes between 6 to 8 weeks depending on the time of submission.

3.3 Universiti Kebangsaan Malaysia

Secretariat of Research Committee and Ethics Committee,
Faculty of Medicine
Universiti Kebangsaan Malaysia
Jalan Tenteram, Bandar Tun Razak
56000 Cheras, Kuala Lumpur.
Fax no: 03-9739214
Tel. no: 03-9739064

The workflow for application to conduct clinical trials at the Universiti Kebangsaan Malaysia is as in Flowchart IV. The approval normally takes between 6 to 8 weeks depending on the time of submission.

3.4 International Islamic University Malaysia

Deputy Dean (Postgraduate and Research)
Kulliyah of Medicine,
International Islamic University Malaysia
P.O. Box 141,
25710 Kuantan, Pahang.
Fax no: 09-5133615
Tel. no: 09-5132797

The workflow for application to conduct clinical trials at the International Islamic University Malaysia is as in Flowchart V. The Ethics Committee for research meets once in 2 months.

3.5 National Heart Institute (Institut Jantung Negara)

Secretary of Ethical Committee
National Heart Institute
145, Jalan Tun Razak,
50400 Kuala Lumpur.
Fax no: 03-2982824
Tel. no: 03-2929594

The workflow for application to conduct clinical trials at the National Heart Institute is as in Flowchart VI. The approval normally takes between 3 to 6 weeks depending on the time of submission.

3.6 Universiti Malaysia Sarawak

Deputy Dean (Research)
Fakulti Perubatan dan Sains Kesihatan,
Universiti Malaysia Sarawak,
No. 9 Lot 2341 Bormill Commercial Estate,
93150 Jalan Tun Ahmad Zaidi Adruce
Kuching, Sarawak.
Fax no: 082-427716
Tel. no: 082-428110

The workflow for application to conduct clinical trials at the Universiti Malaysia Sarawak is as in Flowchart VII. The approval normally takes between 4 to 5 weeks depending on the time of submission.

4.0 Multicentre Studies

The Principal Investigator of the respective centres has to obtain approval from their respective RRC and MREC.

For multicentre studies involving any government hospitals, only a single application is required to be submitted to the SCMR but it must be signed by all investigators involved and all relevant directors of institutions.

SECTION B: APPLICATION FOR IMPORT LICENCE/PERMIT FOR PURPOSES OF CLINICAL TRIALS

The sponsor is responsible for applying for the clinical trial import licence or relevant permit to import the drug(s). The application is submitted to the New Chemical Entity/Clinical Trial (NCE/CT) Unit that is located in the National Pharmaceutical Control Bureau (NPCB), Ministry of Health, Jalan Universiti, P.O. Box 319, 46730 Petaling Jaya.

1.0 Types of Licence/Permits

There are 4 (four) types of licence/permits, namely:

- 1.1 Clinical Trial Import Licence (CTIL)
- 1.2 Permit for a clinical trial of an unregistered drug which is manufactured in Malaysia.
- 1.3 Permit for a clinical trial of a registered drug with special labeling.
- 1.4 Permit for a clinical trial of a registered product on a new indication.

1.1 Application for Clinical Trial Import Licence.

1.1.1 Products that require CTIL are those which are not registered with the Drug Control Authority (DCA), and placebos which are intended to be imported for the purpose of clinical trial.

1.1.2 Application for CTIL shall be made on the form BPFK-442.

1.2 Application for a clinical trial permit for an unregistered product to be manufactured in Malaysia for Clinical Trials.

1.2.1 Products which are not registered with the DCA and are to be manufactured in Malaysia for the purpose of clinical trials, shall require a permit from the NPCB for the manufacture of the products and to conduct a clinical trial.

1.2.2 Applications to manufacture unregistered products for the purpose of clinical trials shall be made on the form BPFK-443 and applications to conduct the clinical trials shall be on the form BPFK-442.

1.3 Application of a clinical trial permit for registered drug with special labeling.

1.3.1 Products which are registered with the DCA and require special labeling meaning that the 'product name' is to be substituted with a Protocol Number or to be 'blinded' and the label is for the purpose of clinical trial use only, will require a permit to import the said product.

1.3.2 The application for the permit shall be made on the form BPFK-441.

1.4 Application for a clinical trial permit for a new indication of a registered product.

1.4.1 Products which are registered with the DCA and are to be studied for a new indication will require a permit for the conduct of the clinical trial for locally manufactured drug(s) as well as for imported drug(s).

1.4.2 Applications for the permit shall be made on the form BPFK-441.

2.0 Application Process

2.1 Who must apply/Where to apply

2.1.1 An application for CTIL shall be made by a Principal Investigator or an authorized person from a locally incorporated pharmaceutical company (sponsor) with a permanent address in Malaysia.

2.1.2 Enquiries regarding clinical trial import licence/permits should be directed to:
Principal Assistant Director,
NCE/Clinical Trial Unit,
National Pharmaceutical Control Bureau,
Ministry of Health, Jalan Universiti,
P.O. Box 319,
46730 Petaling Jaya.

Tel. no: 03-7573611

Fax no: 03-7581312

2.1.3 Application forms and guidelines can be obtained from the above office. The application forms can also be downloaded from the National Pharmaceutical Control Bureau website (<http://www.bpfk.gov.my>)

2.2 Documentation required for application of Clinical Trial Import Licence/Permit

2.2.1 One copy of completed application form and checklist (BPFK-002) are to be submitted for each application of CTIL/Permit.

2.2.2 Good Manufacturing Practice (GMP) certificate/statement in the country of manufacture for the product/ placebo.

2.2.3 Product particulars, pharmaceutical data (such as Certificate of Analysis and stability data) and supporting documentation sufficient to establish safety, efficacy and quality. (Please refer to the respective forms)

2.2.4 Approval letter/ certificate by the Research/Ethics Committees of the institution(s) where the clinical trial is to be conducted should be submitted as soon as possible when available.

2.2.5 Processing fee. Please refer to the application forms.

2.3 Comparator Drugs

The documents needed are:

- (i) detailed prescribing information from the manufacturing country;
- (ii) registration status of the drug;
- (iii) registration number (if the drug is registered in Malaysia);
- (iv) the manufacturer's name and address.

2.4 Processing of Applications

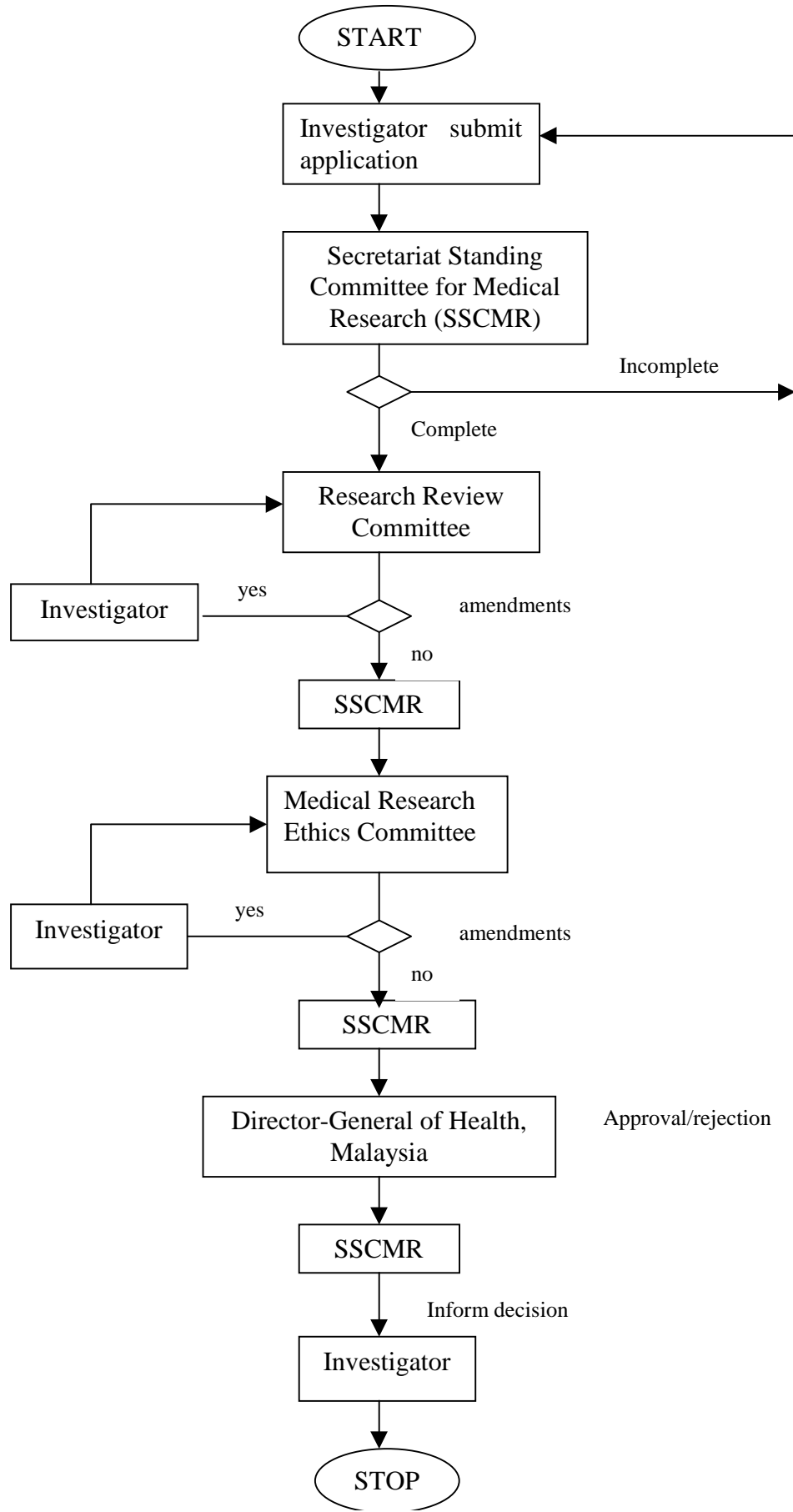
2.4.1 An application for registration of any product will be deemed complete, if

- (i) the application is duly completed and signed;
- (ii) accompanied with GMP certificate/ statement, and appropriate Annexes are submitted; and
- (iii) correct fee is submitted.

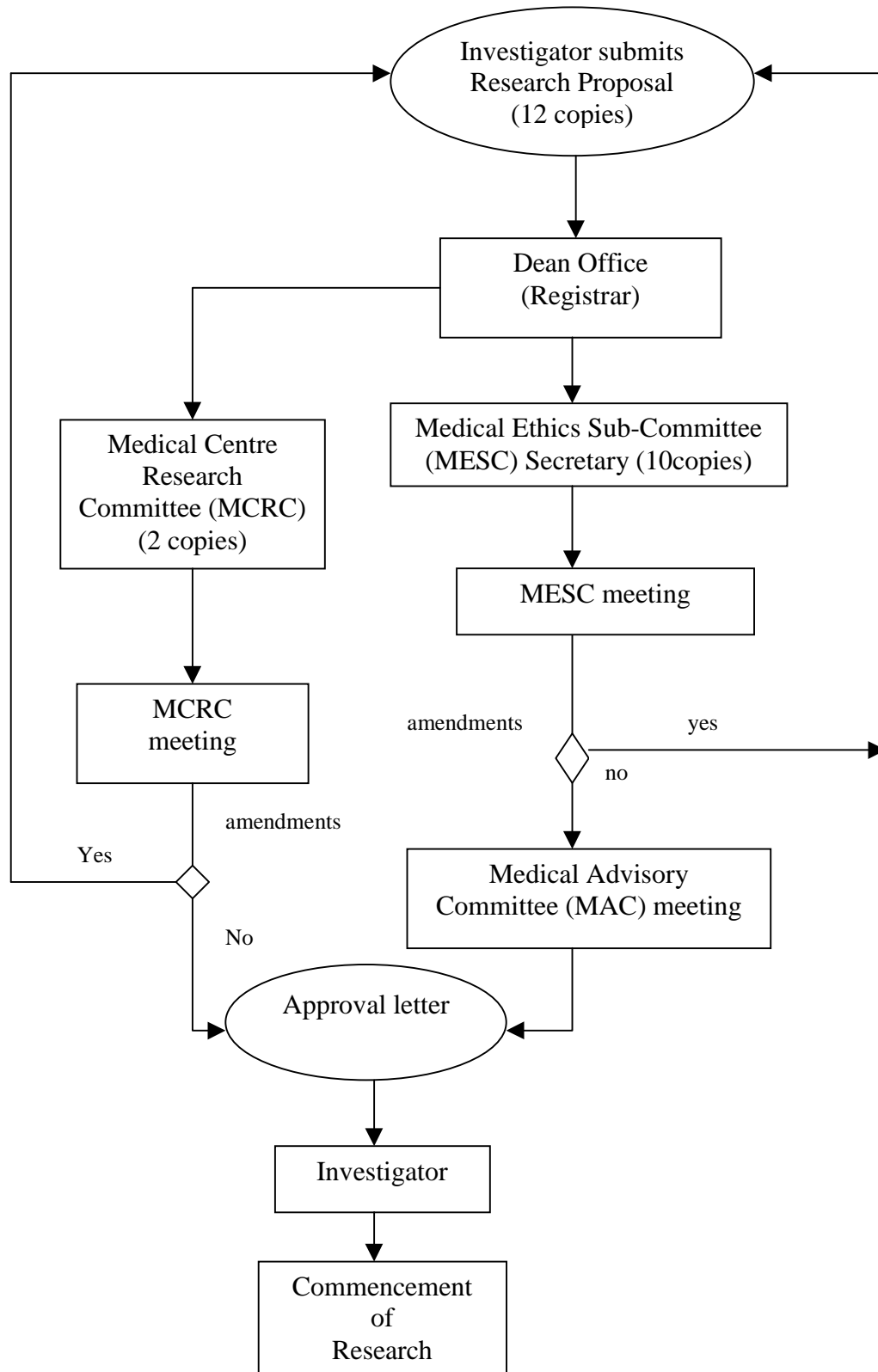
An application, which is incomplete, will not be accepted. The approval process takes between 4 – 8 weeks after submission. The workflow is as in flow chart VIII.

Note: Detailed information regarding the application for CTIL is available in the "Guidelines For Application For Clinical Trial Import Licence"

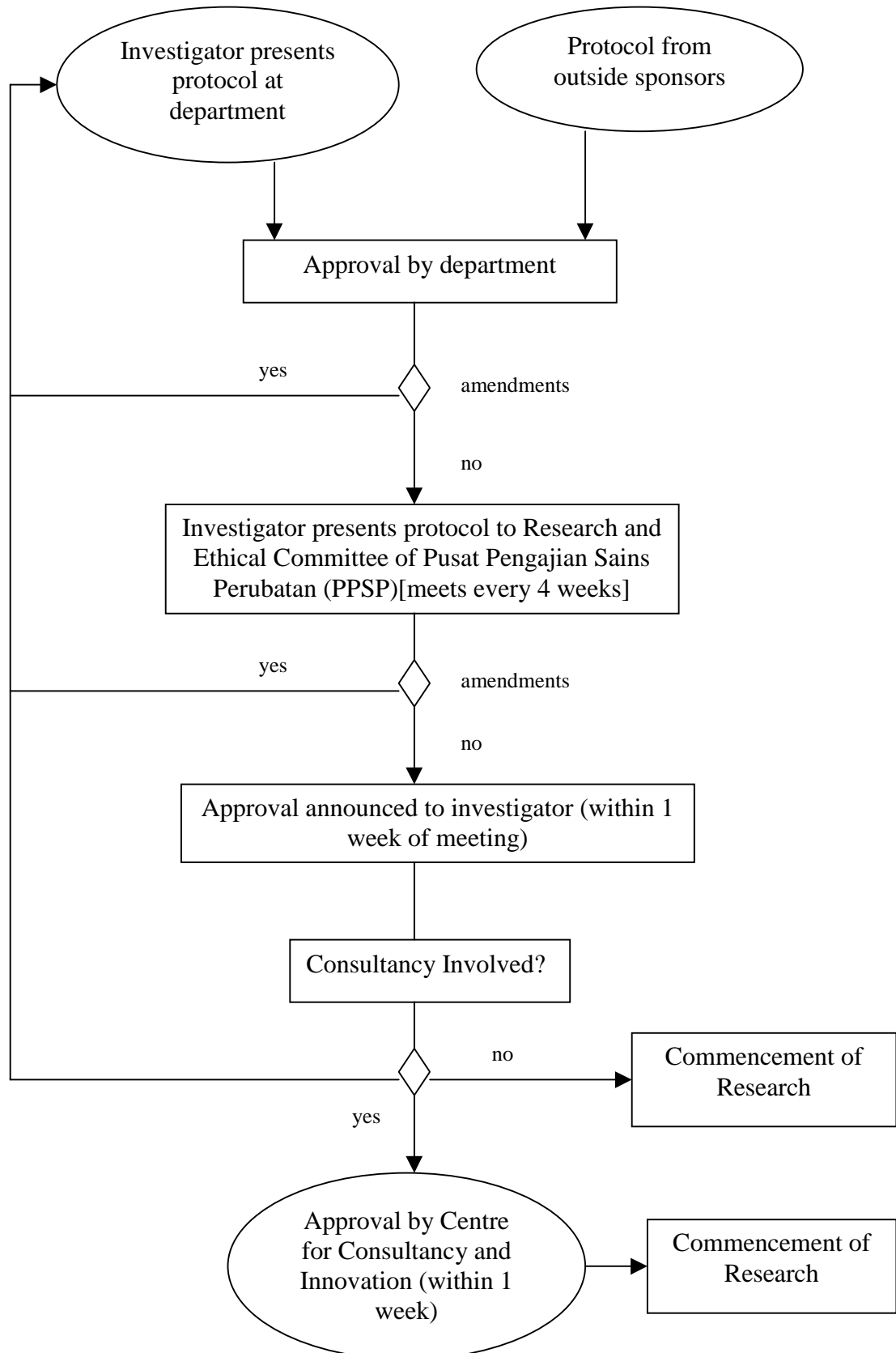
Flow Chart I: Application for Clinical Trial in the Ministry of Health Malaysia



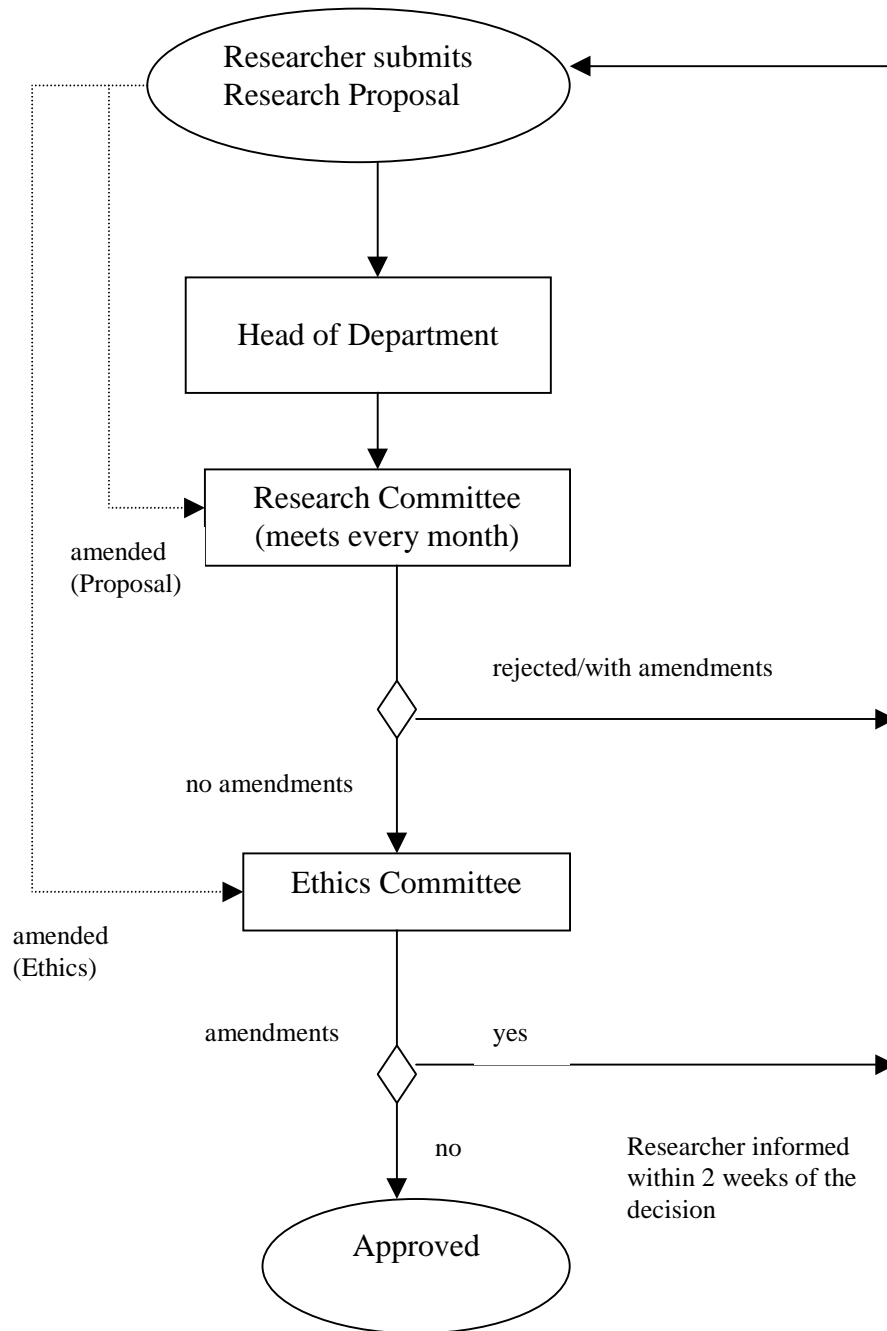
Flow Chart II: The Work Flow For Application To Conduct Clinical Trial At University of Malaya, Kuala Lumpur



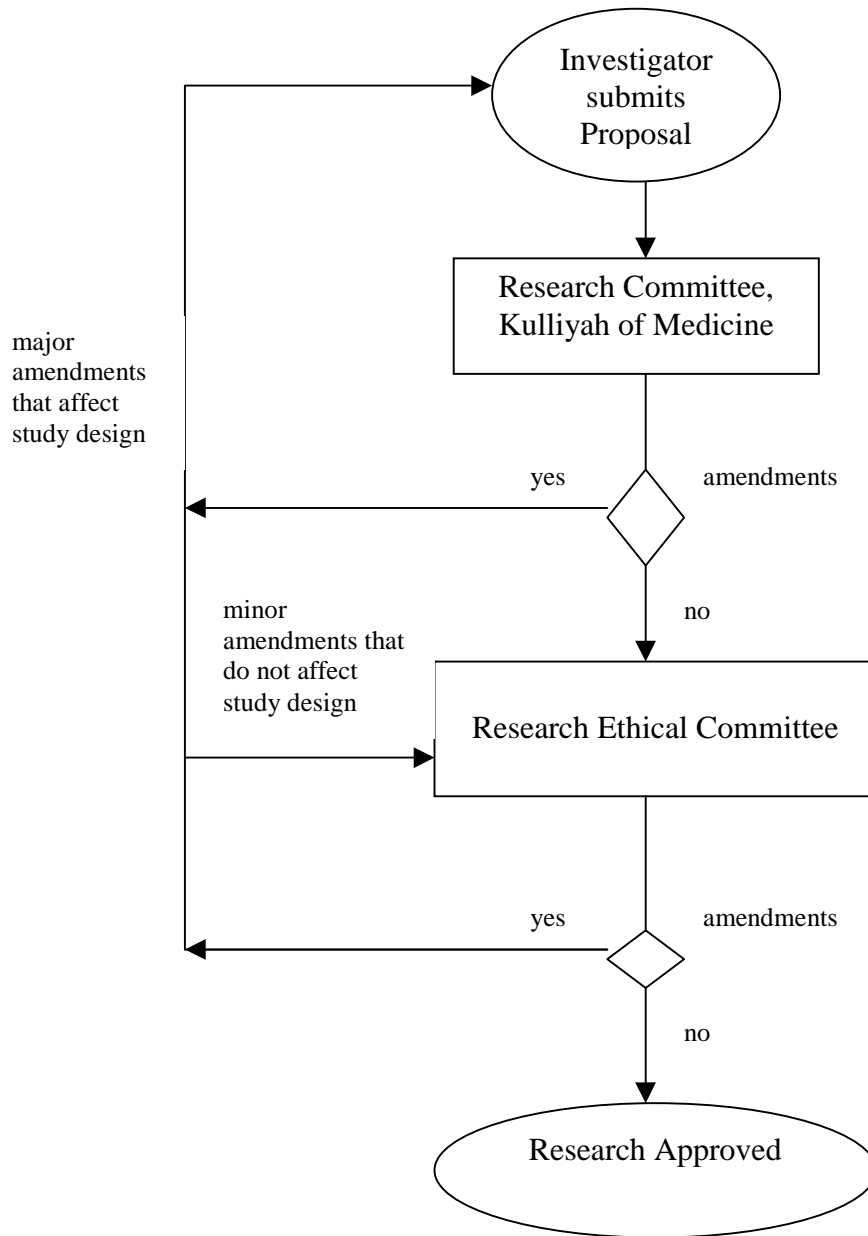
Flow Chart III : The Work Flow For Application To Conduct Clinical Trial At Universiti Sains Malaysia, Kelantan



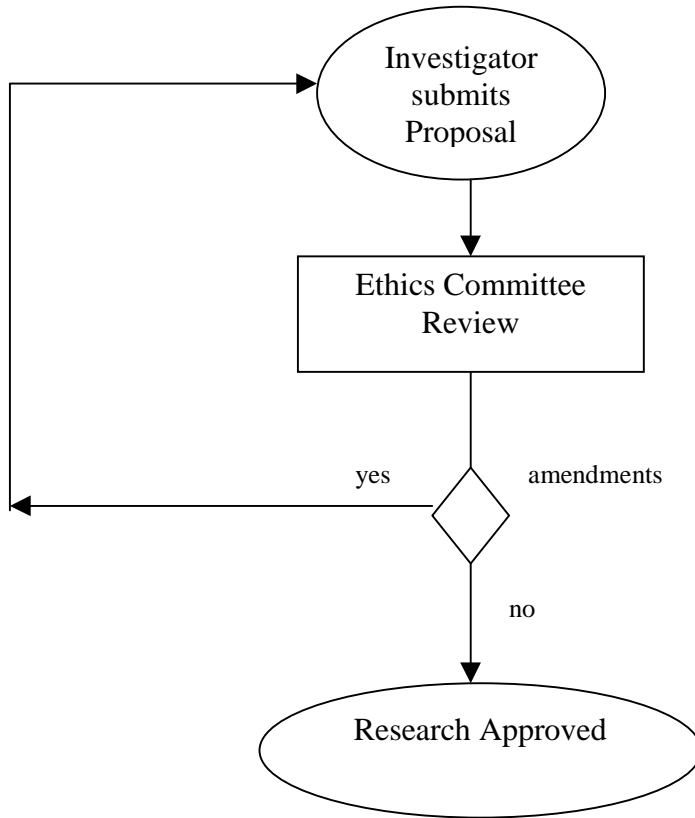
Flow Chart IV: The Work Flow For Application To Conduct Clinical Trial At Universiti Kebangsaan Malaysia, Kuala Lumpur



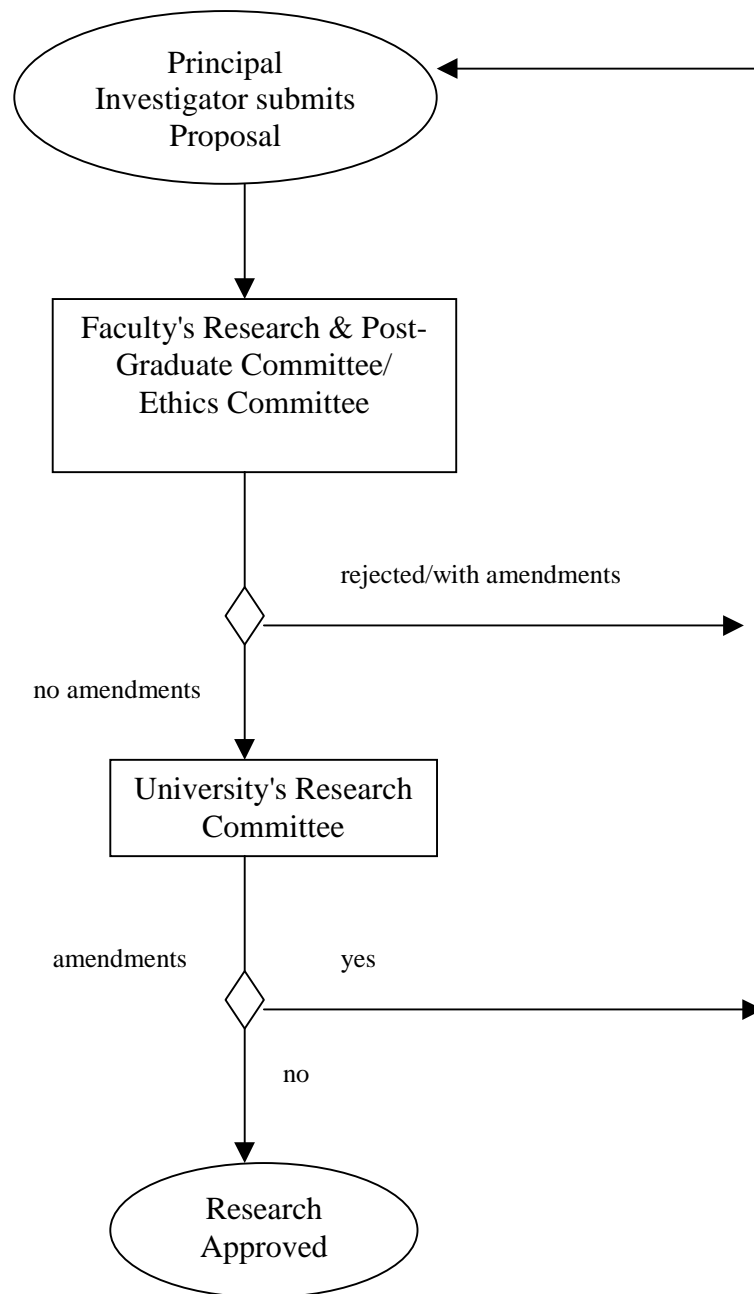
Flow Chart V: The Work Flow For Application To Conduct Clinical Trial At International Islamic University Malaysia, Kuantan, Pahang.



Flow Chart VI: The Work Flow For Application To Conduct Clinical Trial At National Heart Institute (Institut Jantung Negara), Kuala Lumpur.



Flow Chart VII: The Work Flow For Application To Conduct Clinical Trial At Universiti Malaysia Sarawak, Sarawak.



Flow Chart VIII: Application For Clinical Trial Import Licence/Permit from the National Pharmaceutical Control Bureau, Petaling Jaya.

