

GUIDELINES FOR ETHICAL REVIEW OF CLINICAL RESEARCH OR RESEARCH INVOLVING HUMAN SUBJECTS

**Research Ethics Committee (REC)
Universiti Kebangsaan Malaysia**

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PURPOSE AND SCOPE OF GUIDELINES

The purpose of these guidelines is to ensure that research involving humans carried out in UKM, is conducted in a scientific and ethical manner. Participants involved in the research should be accorded the respect and protection that is due to them and the research must be of benefit to the participant and/or the community. These guidelines outline the responsibilities of:

- researchers for the ethical design, conduct and dissemination of results of human research
- **Research Ethics Committee UKM (RECUKM)** in the ethical review of research

It is hoped that these guidelines will help researchers and the RECUKM to meet their responsibilities: to identify issues of ethics that arise in the design, review and conduct of human research, to deliberate about those ethical issues and justify decisions about them. The responsibilities set out in these guidelines are intended to be consistent with the existing national guidelines on human research. Consistent with the intent and purpose of these guidelines, researchers should conform to the current research guidelines in the relevant fields. In addition, good research governance also requires compliance with legal obligations (statutory or otherwise). It is the responsibility of the RECUKM and researchers to adhere to general and specific legal requirements, wherever relevant.

What is human research?

Human research is any study that is conducted with or about people, their data or biological specimen. This includes studying of humans through:

- surveys or interviews
- psychological, physiological or medical testing or treatment
- observation by researchers
- access to their personal document or other materials
- the collection and use of their body organs, tissues or fluids (eg. skin, blood, urine, saliva, hair, bones, tumour, and other biopsy specimens)
- access to their information (in individually identifiable, re-identifiable or non-identifiable form) as part of an existing published source or database

1.0 VALUES AND PRINCIPLES OF ETHICAL CONDUCT

The values on ethical conduct of research rest on four guiding principles: respect for persons, beneficence, justice and research merit and integrity.

1.1 Respect For Persons

The principle of respect for persons involves recognizing that each human being has value in himself or herself. Researchers must equally respect the dignity of those involved in research. The moral requirement is based on the acknowledgement of the participant's autonomy and protecting those with diminished autonomy. It is the duty of the researcher to obtain informed consent from study participants and to maintain confidentiality on their behalf. Due scope must be given throughout the research process to the capacity of human beings to **make their own decision (voluntariness)**. Where the participants are unable to make their own decisions or have diminished capacity to do so, respect for them involves empowering them where possible and providing for their protection as necessary. Researchers should respect the **privacy, confidentiality and cultural sensitivities** of participants and where relevant, of their communities. Any specific agreement made with the participants or the community should be fulfilled.

1.2 Beneficence

1.2.1 The principle of beneficence weighs between the potential benefit and harm of participation. The likely benefit of the research must justify any risks of harm or discomfort to participants and/or the wider community. Researchers have an obligation to maximize possible benefits and minimize possible harm. Researchers are responsible for:

- (a) designing the research to minimize the risks of harm or discomfort to participants
- (b) clarifying to participants the potential benefits and risk, and
- (c) the welfare of the participants in the research context

1.2.2 Where there is no likely benefit to participants, the risk to participants should be lower than would be ethically acceptable where there are such likely benefits.

1.3 Justice

1.3.1 The principle of justice involves regard for human sameness that each person share with others, that equals should be treated equally. It means a fair distribution of the burdens and benefits of research and encompasses fair treatment in recruitment of participants and in the review of research. Researchers must ensure that the vulnerable are not exploited and that eligible candidates who may benefit from participation are not excluded without good cause.

1.3.2 The principle of justice raises 3 questions:

- (a) Who ought to receive the benefits of the research?
- (b) Who ought to bear its burden?
- (c) Is it just to use public funds for this research?

- In research that is just:
 - (a) the selection, exclusion and inclusion of research participants is fair and accurately described in the research reports
 - (b) the process of recruiting participants is fair
 - (c) there is no unfair burden of participation in research on particular groups
 - (d) there is fair distribution of benefits of participation in research
 - (e) there is no exploitation of participants in the conduct of the research; and
 - (f) there is fair access to the benefits of research

1.3.3 Research outcomes may be made accessible to research participants.

1.4 Research merit and integrity

1.4.1 The involvement of human participants in the research cannot be ethically justifiable unless the proposed research has merit and the researchers have integrity.

1.4.2 Research that has **merit** is

- (a) justifiable by its potential benefit (contribution to knowledge, understanding, skill or expertise of researchers and improvement in social welfare and/or individual wellbeing)
- (b) designed using methods appropriate for achieving the aims of the proposal
- (c) based on current and previous literature . This does not exclude the possibility of novel research for which there is little or no literature available, or research requiring a quick response to an unforeseen situation
- (d) designed to ensure that respect for participants is not compromised by the aims of the research, by the way it is conducted, or by the results
- (e) conducted or supervised by persons or teams with experience, qualifications and competence that are appropriate for the research
- (f) conducted using facilities and resources appropriate for the research

Integrity of researcher (to refer to GRP)

2.0 RISK AND BENEFIT, CONSENT

2.1 RISK AND BENEFIT

2.1.1 Risk

A risk is a potential for **harm, discomfort or inconvenience**.

2.1.1.1 Harm

The list of harm is not exhaustive but may include:

- (a) physical harm: including injury, illness and pain
- (b) psychological harm: including feelings of worthlessness, distress, guilt, anger or fear(for example, to disclosure of sensitive or embarrassing information, or learning about the genetic possibility of developing an untreatable disease)
- (c) devaluation of personal worth: including being humiliated, manipulated or treated disrespectfully or unjustly
- (d) social harm: including damage to social networks or relationships with others; discrimination in access to benefits, services, employment or insurance; social stigmatization; and findings of previous unknown paternity status
- (e) economic harm: including the imposition of direct or indirect costs on participants
- (f) legal harm: including discovery and prosecution of criminal conduct.

2.1.1.2 Discomfort

Discomfort is less serious than harm and can involve body and/or mind. Examples:

- (a) minor side-effects of medication
- (b) discomforts related to venepuncture
- (c) anxiety induced by an interview.

Where a person's reactions exceed discomfort and become distress, they should be viewed as harm.

2.1.1.3 Inconvenience

Less serious than discomfort is inconvenience. Examples of inconvenience may include:

- (a) having to travel to participate in the research
- (b) filling in a form
- (c) participating in a survey, or
- (d) giving up time to participate in research.

Research may also pose risks to non-participants and these may include risk of distress for a participant's family members identified with a serious genetic disorder, the possible effects of a biography on family or friends, or infectious disease risks to the community. Some social research may carry wider social or economic risks; for example, research in a small

community into attitudes to specific subpopulations may lead to unfair discrimination or have effects on social cohesion, property values, or business investment.

Harm that may arise from research misconduct or fraud, and harm to members of research teams from other forms of misconduct (for example, harassment or bullying). These forms of misconduct may also lead to potential harm to participants.

2.1.1.4 Low and negligible risk research

‘Low risk research’ describes research in which the only foreseeable risk is one of discomfort and ‘negligible risk research’ is one when any foreseeable risk is no more than inconvenience. Research in which the risk for participants is more serious than discomfort is not low risk.

2.1.1.5 Assessment of risks

Assessment of risks engages:

- (a) the **researchers**, who need to identify, gauge, minimize and manage any risk involved in their project
- (b) **RECUKM** in reviewing research proposals and making judgment on whether risks are justified by potential benefits including taking into consideration participants’ perception of risks and benefits.

2.1.1.6 Gauging and minimising risk

Gauging risk involves taking into account:

- (a) the **kind** of harm, discomfort or inconvenience that may occur
- (b) the **likelihood** of these occurring
- (c) the **severity** of any harm that may occur

In designing a research project, researchers have an obligation to minimise the risks to participants. Minimising risk involves an assessment of the research aims, their importance, and the methods by which they can be achieved.

2.1.1.7 Managing risk

When risks have been identified, gauged and minimised, and the research has been approved, the risks must then be managed. This requires that:

- (a) researchers include, in their research design, mechanisms to deal adequately with any harm that occur; and
- (b) a monitoring process is in place and carried out

The greater the risk to participants in any research for which ethical approval is given, the greater the need for certainty that the risks are well managed, and the participants clearly understand the risks they are assuming.

2.1.2 Benefit

Benefits of research may include, for example, gains in knowledge, insight and understanding, improved social welfare and individual wellbeing, and gains in skill or expertise for individual researchers, teams or institutions. Some research may offer direct benefits to the research participants, their families, or particular group/s with whom they identify. Where this is the case, participants may be ready to assume a higher risk than otherwise. For example, people with cancer may be willing to accept research risks (such as treatment side-effects) that would be unacceptable to people who are well. Such willingness should be taken into account in deciding whether the potential benefits of the research justify the risks involved.

2.1.3 Guidelines

Risks to research participants are ethically acceptable only if they are justified by potential benefits of the research. Steps to arriving at judgment on the ethical acceptability of risks should include:

- (a) identification of the risks, if any
- (b) assessment of the likelihood and severity of risks (researcher and reviewers of research should base their assessments on the available evidence, whether qualitative or quantitative. They should consider whether to seek advice from others who have the experience with the same methodology, population and research domain)
- (c) identification of who (participants and/or others) the risks may affect
- (d) establishment of the means to minimize risks
- (e) identification of the potential benefits (whether potential benefit justify the risk involved). Research reviewers should take into account any willingness by participants to assume greater risks because of the potential benefits to them, their families, or groups to which they belong.
- (f) identification of whom the benefits are likely to accrue.

2.2 GENERAL REQUIREMENTS FOR CONSENT

2.2.1 Guidelines

- The guiding principle for researchers is that a person's decision to participate in research is to be voluntary, and based on sufficient information and adequate understanding of both the proposed research and the implications of participation in it (purpose, methods, demands, risks and potential benefits of the research)
- This information must be presented in a way that is easily understood by the participant.
- The process of communicating information to participants and seeking their consent must aim towards a mutual understanding between researchers and participants. This aim requires an opportunity for participants to ask questions and to discuss the information and their decision with others if they wish.
- Consent may be expressed orally, in writing or by some other means (for example, return of a survey, or conduct implying consent), depending on:
 - (a) the nature, complexity and level of risk of the research; and
 - (b) the participant's personal and cultural circumstances.
- The subject information sheet must contain:
 - (a) Title of research;
 - (b) Introduction (purpose, the sources of funding for the research);
 - (c) Subject's involvement;
 - Method and procedure (the amount and quantity of tissue, fluids, or body parts to be taken and from where; if the tissues, fluids or body parts to be taken for research are part of standard medical procedure or specifically harvested for the research)
 - (d) Benefits of research;
 - (e) Potential risks;
 - provision of services to participants adversely affected by the research
 - (f) Privacy and confidentiality, as well as any alternatives to participation;
 - (g) A clear statement regarding voluntary participation;
 - (h) The participant's right to withdraw, along with any implications of withdrawal, and on withdrawal, participants will not be deprived of the standard medical care;
 - (i) Any payments and compensation to participants;
 - (j) The likelihood and form of dissemination of the research results, including publications;
 - (k) Contact details of the researchers;
 - (l) Contact details of RECUKM;
 - (m) Any other relevant information.

2.2.1.1 Coercion and pressure

No person should be subject to coercion or pressure in deciding whether to participate. Even where there is no overt coercion or pressure, consent might reflect deference to the researcher's perceived position of power, or to someone else's wishes.

2.2.1.2 Reimbursing participants

Participants may be reimbursed for the costs of taking part in research, such as travelling cost. However, payment that is disproportionate, or any other inducement that is likely to encourage participants to take risks, is ethically unacceptable.

2.2.1.3 Where others need to be involved in participation decisions

Where a potential participant lacks the capacity to consent (*children and young people, people highly dependent on medical care who may be unable to give consent, people with a cognitive impairment, an intellectual disability, or a mental illness*), a person or appropriate statutory body exercising lawful authority for the potential participant should be provided with relevant information, and decide whether subject will participate. Within some communities, decisions about participation in research may involve not only individuals but also properly interested parties such as formally constituted bodies, institutions, families or community elders. Researchers need to engage with all properly interested parties in planning the research.

2.2.1.4 Consent to future use of data and tissue in research

Consent may be:

- (a) 'specific': limited to the specific project under consideration;
- (b) 'extended': given for the use of data or tissue in future research projects that are:
 - i. an extension of, or closely related to, the original project; or
 - ii. in the same general area of research (for example, genealogical, ethnographical, epidemiological, or chronic illness research);
- (c) 'unspecified': given for the use of data or tissue in any future research.

Extended or unspecified consent is also required if data is to be entered into a data bank or the tissues collected to be kept in a tissue bank. When unspecified consent is sought, its terms and wide-ranging implications should be clearly explained to potential participants. When such consent is given, its terms should be clearly recorded. Data or tissue additional to those covered by the original extended or unspecified consent will sometimes be needed for research. Consent for access to such additional data or tissue must be sought from potential participants unless the need for this consent is waived by an ethical review body.

2.2.1.5 Declining to consent and withdrawing consent

Persons who elect not to participate in a research project need not give any reason for their decision. Researchers should **ensure** those who decline to participate will suffer no disadvantage as a result of their decision. Participants are entitled to withdraw from the

research at any stage. Before consenting to involvement in the research, participants should be informed about any consequences of such withdrawal.

2.3 QUALIFYING OR WAIVING CONDITIONS FOR CONSENT

The requirement for consent may sometimes be justifiably waived. In this case, research participants will characteristically not know that they, or perhaps their tissue or data, are involved in the research. **'Limited disclosure'** to participants of the aims and/or methods of research may also sometimes be justifiable. This is because in some human research (for example, in the study of behaviour), the aims of the research cannot be achieved if those aims and/or the research methods are fully disclosed to participants. Research involving limited disclosure covers a spectrum, from simply not fully disclosing or describing the aims or methods of observational research in public contexts, all the way to actively concealing information and planning deception of participants. Examples along the spectrum include: observation in public spaces of everyday behaviour; covert observation, for example of the hand-washing behaviour of hospital employees; undisclosed role-playing by a researcher to investigate participants' responses; telling participants the aim of the research is one thing when it is in fact quite different. For some limited disclosure research (for instance, observation in public spaces), waiver of consent might be sought.

2.3.1 Limited disclosure

Where limited disclosure does not involve active concealment or planned deception, ethical review bodies may approve research provided researchers can demonstrate that:

- (a) there are no suitable alternatives involving fuller disclosure by which the aims of the research can be achieved;
- (b) the potential benefits of the research are sufficient to justify both the limited disclosure to participants and any risk to the community's trust in research and researchers;
- (c) the research involves no more than low risk to participants and the limited disclosure is unlikely to affect participants adversely;
- (d) the precise extent of the limited disclosure is defined;
- (e) whenever possible and appropriate, after their participation has ended, participants will be:
 - provided with information about the aims of the research and an explanation of why the omission or alteration was necessary; and
 - offered the opportunity to withdraw any data or tissue provided by them.

Where limited disclosure involves active concealment or explicit deception, and the research does not aim to expose illegal activity, researchers should in addition demonstrate that:

- (a) participants will not be exposed to an increased risk of harm as a result of the concealment or deception;
- (b) a full explanation, both of the real aims and/or methods of the research, and also of why the concealment or deception was necessary, may subsequently be made available to the participants; and
- (c) there is no known or likely reason for thinking that participants would not have consented if they had been fully aware of what the research involved.

Where research involving limited disclosure, aims to expose illegal activity the adverse effects on those whose illegal activity is exposed must be justified by the value of the exposure.

2.3.2 Waiver

RECUKM may grant waiver of consent for research using personal information in any human research. Before deciding to waive the requirement for consent (other than in the case of research aiming to expose illegal activity), RECUKM must ensure that:

- (a) involvement in the research carries no more than low risk to participants;
- (b) the benefits from the research justify any risks of harm associated with not seeking consent;
- (c) it is impracticable to obtain consent (for example, due to the quantity, age or accessibility of records);
- (d) there is no known or likely reason for thinking that participants would not have consented if they had been asked;
- (e) there is sufficient protection of their privacy;
- (f) there is an adequate plan to protect the confidentiality of data;
- (g) in case the results have significance for the participants' welfare, there is, where practicable, a plan for making information arising from the research available to them (for example, *via* a disease-specific website or regional news media);
- (h) the possibility of commercial exploitation of derivatives of the data or tissue will not deprive the participants of any financial benefits to which they would be entitled;
- (i) the waiver is not prohibited by law.

Before deciding to waive the requirement for consent in the case of research aiming to expose illegal activity, the UKM- REC must be satisfied that:

- (a) the value of exposing the illegal activity justifies the adverse effects on the people exposed;
- (b) there is sufficient protection of their privacy;
- (c) there is sufficient protection of the confidentiality of data; and
- (d) the waiver is not otherwise prohibited by law

3.0 ETHICAL CONSIDERATIONS SPECIFIC TO RESEARCH METHODS OR FIELDS

3.1 QUALITATIVE METHODS

3.1.1 Introduction

Qualitative research involves disciplined inquiry that examines people's lives, experiences and behaviours, and the life stories individuals ascribe to them. It can also investigate organisational functioning, relationships between individuals and groups, and social environments.

Commonly used approaches to data collection in qualitative research include:

- **Interviews;** are usually audio- or video-taped, or documented. These records are research data in themselves, but also may be transcribed. Interviews may be *structured*, *semi-structured*, or *unstructured*. Interviews also vary according to the type of interviewee, e.g. *key informant interviews* (conducted with individuals or groups with specific knowledge or expertise about the issue being studied), *sample informant interviews* (conducted with people whose experience or expertise is taken as representative of a broader group).
- **Life story or oral history;** commonly undertaken in studies in humanities.
- **Focus groups;** participants discuss a set of research questions or topics, with the researcher as moderator.
- **Observation;** the researcher observes participant/s in their own environment, or in the study environment.
- **Archival research;** it involves materials usually kept in official or private libraries or archives.
- **On-line research;** includes conducting on-line real-time group discussions using web-based chat-room technology through the use of electronic bulletin boards and moderated email groups. Data collection and dissemination can also be utilized online.
- **Action research;** is often community or organization-based and is carried out in the field to test ideas in practice as a means of increasing knowledge and improving social, economic or environmental conditions.

3.1.2 Guidelines

- A range of relationships between participants and researchers may develop as a result of the duration and nature of the interaction. Where such relationships threaten to compromise the research, researchers must consider whether to modify those relationships, or to modify or even discontinue the research.

- Where a researcher has professional skills (e.g. counseling) that become relevant to the relationship with a participant, the researcher needs to decide, when continuing the research, whether:
 - (a) it is ethically acceptable to exercise those skills; or
 - (b) to refer that participant to another professional.
- Researchers have a duty to inform participants whenever they are acting in a non-research professional role.
- Qualitative research emphasises the significance of particular contexts and settings. It is not necessary to be able to generalize the results of qualitative research. Even so, qualitative research should aim to provide a sufficiently detailed account and/or analysis to enable others to determine whether there are other circumstances to which the findings may be applicable.
- If a sampling strategy is used, the most common type is purposive sampling, which aims at the selection of information-rich cases relevant to the research question. While random and representative sampling are not excluded in qualitative studies, many sampling frames are required to achieve the objectives of the study.
- The strength of a qualitative study should not be judged on sample size. When sampling is appropriate, the objectives and theoretical basis of the research should determine the size of the sample and the sampling strategy. For example, some qualitative methods use a principle of 'saturation', where sampling occurs until no new information is being obtained. This is only one of several criteria for assessing sample size.
- Research proposals that include sampling should clearly describe the recruitment strategy and criteria for selecting participants.
- The strength of a qualitative research should be assessed primarily by criteria of quality and credibility of data collection and analysis, and not by matters of validity and reliability as defined in research designs that employ quantitative methods.
- The criteria for inclusion and exclusion of participants in qualitative research are often complex. For this reason, researchers should state these criteria clearly and be able to justify them.
- Participants are often easily identifiable (e.g. as members of small communities or groups, or as key informants), and the information they provide may be sensitive. For these reasons, care should be taken that participants are not identifiable by the information they provide, unless they have agreed to be identified. Special care should be taken to protect the identity of participants when disseminating information and storing material.
- Where possible, participants should be informed about any potential to be identified in the results of research even if identifiers, such as name and address, are removed.

- Qualitative research that explores sensitive topics in depth may involve emotional and other risks to both participant and researcher. There should be clear protocols for dealing with distress that might be experienced by participants.
- Predicting what topics are likely to lead to distress will not always be easy. Researchers should have sufficient training to help them in making such predictions.
- Qualitative research may involve methods of data collection that require the development of personal relationships with participants. Researchers should reflect on the impact that they may have on the participants and vice versa, and as far as possible should describe in the research proposal any anticipated impact of this nature.
- Researchers should consider whether respect for the participants requires that the accuracy or completeness of each interview transcript should be verified by the relevant participant before analysis is complete.
- The method of providing consent in qualitative research depends on various factors including the type of research, its level of sensitivity, its cultural context and the potential vulnerability of the participants.
- A written informed consent is usually required, however in certain circumstances, consent may be implied by participation e.g. the return of a survey or the answering of a verbal question.

3.2 DATABANKS

3.2.1 Introduction

Types of research that commonly make use of databanks include epidemiology, pathology, genetics and social sciences. The term 'databanks' includes databases. Data include:

- (a) what is said in interviews, focus groups, questionnaires, personal histories and biographies;
- (b) analysis of existing information (clinical, social, observational, etc);
- (c) information derived from human tissue, e.g. blood, bone, muscle, urine.

3.2.1.1 Data identifiability

Data may be collected, stored or disclosed in the following mutually exclusive forms:

- (a) **Individually identifiable data**, where identifiers exist.
- (b) **Re-identifiable data**, where identifiers have been removed and replaced by codes that can be linked back to the identifiers.
- (c) **Non-identifiable data**, where labeling was never done or have been permanently removed. A subset of non-identifiable data is those that can be linked with other data so it can be known that they are about the same data subject, although the person's identity remains unknown.

3.2.1.2 Tissue and data

Human tissue samples should always be regarded as, in principle, re-identifiable, so as to enable researchers to match individuals in different data sets without being able to identify the person. These data may or may not have originally been obtained for research purposes.

3.2.1.3 Banking

While most data are collected, aggregated and stored for a single purpose or activity, permission may sometimes be sought from participants to 'bank' their data for possible use in future research projects.

3.2.2 Guidelines

- When planning a databank, researchers should clearly describe how their research data will be collected, stored, used and disclosed.
- Researchers' use of data from databanks must comply with conditions specified by the providers of the data;
- Where research involves linkage of data sets, approval may be given to the use of identifiable data to ensure that the linkage is accurate, even if consent has not been given for the use of identifiable data in research. Once linkage has been completed, identifiers should be removed from the data to be used in the research unless consent has been given for its identifiable use.
- It is the duty of the custodian to ensure that the data are used responsibly and respectfully, and that the privacy of participants is safeguarded.
- Whenever research using re-identifiable data reveals information that bears on the wellbeing of participants, researchers have an obligation to consider how to make that information available to the participants. Where individual notification is warranted, the custodian of the data will need to take all reasonable steps to re-identify those data.
- Some uses of data in a databank may be detrimental to people to whom the data relate. Researchers and/or custodians should consider denying or restricting access to some or all of the data for those uses,
- When collecting data for deposit in a databank, researchers should provide clear and comprehensive information about:
 - (a) the form in which the data will be stored (identifiable, re-identifiable, non-identifiable);
 - (b) the purposes for which the data will be used and/or disclosed; and
 - (c) whether they will seek:
 - (i) specific, extended or unspecified consent for future research or
 - (ii) permission from a review body to waive the need for consent.

- Any restrictions on the use of participants' data should be recorded and the record kept with the collected data so that it is always accessible to researchers who want to access those data for research.
- Researchers and custodians of the databank should observe any confidentiality agreement about stored data with the participant, and custodians should take every precaution to prevent the data becoming available for uses to which participants did not consent.

3.3 INTERVENTIONS AND THERAPIES, INCLUDING CLINICAL AND NON-CLINICAL TRIALS, AND INNOVATIONS

3.3.1 Introduction

3.3.1.1 Clinical research

This chapter focuses on randomised clinical trials.

3.3.1.2 Innovations in clinical practice

Innovations in clinical practice and complementary medicine include a new diagnostic or therapeutic method that aims to improve health outcomes but have not yet been fully assessed for safety and/or efficacy. The spectrum of innovations may range widely from minor variations or extensions of existing methods, to new indications, through to completely novel technologies. Where a proposed intervention is innovative and/or experimental, this should always be made clear to those who might be subject to it.

Whether a change in an individual's investigation or treatment is simply an innovation or actually constitutes clinical research is generally a matter for the responsible clinician's judgment, guided by institutional policies. Systematic evaluation of an innovation is research and requires ethical review.

3.3.1.3 Clinical and other trials

A clinical trial is a form of human research designed to find out the effects of an intervention, including a treatment or diagnostic procedure. A clinical trial can involve testing a drug, a surgical procedure, other therapeutic procedures and devices, a preventive procedure, or a diagnostic device or procedure.

Clinical trials of new therapeutic substances are typically categorised into Phase I, II, III or IV trials. The following definitions, adapted from the Therapeutic Goods Administration (TGA), describe these phases in trials of medications:

- Phase I studies involve the first administration of the medicine to humans. Medicines are usually given to small numbers of healthy volunteers, but sometimes to people affected by the disease the medicine is intended to treat. The purpose may be to determine the medicine's safety, pharmacokinetics, pharmacological activity, side effects, preferred routes of administration, or appropriate doses (for later studies). The studies are usually

undertaken in centres equipped for specialised monitoring and a high degree of surveillance.

- Phase II studies are typically the first trials of the medicine in people with the health condition for which the medicine is intended. The principal aim is to determine efficacy and safety, and establish an appropriate dosing regimen. These studies are undertaken in a small number of closely supervised patients and conducted by researchers regarded as specialists in the health condition and its treatment.
- Phase III studies are undertaken if the Phase II studies indicate the medicine has potential benefits that outweigh any harm. The studies involve greater numbers of patients with the health condition under study, and aim to determine whether the medicine confers clinical benefit in that health condition and whether the incidence and nature of adverse effects are acceptable. These trials are usually randomised, concurrently comparing new therapy(ies) versus the standard of care.
- Phase IV studies are those undertaken after the medicine has been approved for marketing for the treatment of a particular disease or for a particular indication. They may include studies to compare the medicine with a wider range of therapies, and may also further investigate the use of the medicine in the normal clinical setting of the disease (which may differ markedly from the conditions under which pre-marketing trials were conducted). Such studies also gather more comprehensive safety data, adding to the information known from the premarketing studies.

In pharmaceutical trials there are established codes of good clinical research practice that define clearly what is meant by a clinical trial for those purposes (see the Guideline of The Malaysian Medical Council on Clinical Trials and Biomedical Research 009/2006, the Malaysian Guidelines for Good Clinical Practice of the Ministry of Health of Malaysia 2004, Guidelines for Application of Clinical Trial Import License and Clinical Trial Exemption in Malaysia and any other related guidelines). This chapter's main application is to biomedical clinical trials, but it also applies to any other interventions claiming therapeutic benefit.

3.3.1.4 Application of randomised trial methods to other areas of human research

Research methods intended to avoid or reduce bias include randomisation and 'blinding' participants and researchers to the identity of agents being compared. These research methods were first applied to the study of new therapies, and are now used in various other fields including, for example, psychology and education. Researchers who propose to use such methods should be aware of the ethical issues that may arise in the design and conduct of such research.

Research to which this chapter applies must be reviewed, presented and approved by a formal meeting of the RECUKM.

3.3.2 Guidelines

- Researchers should show that:
 - (a) the research is directed to answering a specific question or questions;

- (b) there is a scientifically valid hypothesis being tested that offers a realistic possibility that the interventions being studied will be at least as beneficial overall as standard treatment, taking into account effectiveness, burden, costs and risks;
 - (c) the size and profile of the sample to be recruited is adequate to answer the research question;
 - (d) the research meets the relevant requirements of the Malaysian Good Clinical Practice Guidelines.
- Researchers must inform the UKMREC of:
 - (a) any business, financial or other similar association between a researcher and the supplier of a drug or surgical or other device to be used in the trial;
 - (b) any other possible conflicts of interest; and
 - (c) any restrictions on publication.
 - In any clinical research, UKMREC should be satisfied that:
 - (a) funding is sufficient to conduct and complete the trial as designed;
 - (b) any payment in money or kind, whether to institutions, researchers or participants, will not adversely influence the design, conduct, findings or publication of the research; and
 - (c) the facilities, expertise and experience available are sufficient for the trial to be conducted safely.
 - The research methodology should provide a rationale for the selection of participants and a fair method of recruitment.
 - In research without likely benefit to participants, any known risk to participants should be lower than would be ethically acceptable in research where there are likely benefits. In 'first-time-in-humans' (phase I) research projects, where risks are uncertain, recruitment into the study should be gradual and monitored with special care.
 - In clinical research, where patient care is combined with intent to contribute to knowledge, any risks of participation should be justified by potential benefits which are appreciated by the participants.
 - The prospect of benefit from research participation should not be exaggerated, in order to justify to the UKMREC and participant to accept a higher risk than that involved in the participant's current treatment.
 - The use of a placebo alone or the incorporation of a non-treatment control group:
 - (a) is ethically unacceptable in a controlled clinical trial where:
 - i. other available treatment has already been clearly shown to be effective and readily available; AND
 - ii. there is known risk of significant harm in the absence of treatment.
 - (b) may be considered if there is genuine uncertainty as to whether currently available treatments have a net clinical benefit.

- Data should be accurately recorded in a durable form that complies with established legislation, policies and guidelines. Where a trial is using materials of biological origin, or other materials where there is limited experience of their long-term use, records should be preserved for long enough to enable participants to be traced in case evidence emerges of late or long-term effects.
- Before beginning the clinical phase of the research, researchers should register clinical trials in the National Medical Research Registry (NMRR).
- Due to the potential complexity of information to be provided to participants, the requirements of voluntary participation based on sufficient information that requires adequate understanding of the purpose, methods, demands, risks and potential benefits of the research should be carefully considered and followed.
- Written information should not be unduly long or complex. Adequate time should be allowed for prospective participants to read and take in what is proposed, and they should be encouraged to ask questions.
- Particular care should be taken to make it clear to participants whether any therapeutic benefit to them is intended from the trial.
- It should always be made clear to potential participants to a proposed intervention
 - whether it is innovative and/or experimental.
 - that they will be randomly allocated to one treatment arm which may be a placebo arm, in the case of a randomised clinical trial.
- In clinical research, where patient care is combined with an intent to contribute to knowledge, the following matters should be carefully weighed:
 - (a) the seriousness of the condition being treated;
 - (b) the risks involved in the proposed research; and
 - (c) the possible repercussion to the participants in an unequal or dependent relationship with the treating health professional or researcher
- Where the researcher is also the treating health professional, it should be considered whether an independent person should seek the consent of potential participants.
- RECUKM should be satisfied that:
 - (a) payment in money or incentives of any kind, whether to researchers or participants, does not result in pressure on individuals to consent to participate;
 - (b) research participants are adequately informed of the funding arrangements of the research;
 - (c) it has been made clear to participants whether they will have continued access after the trial to treatments and other aspects of management they have received during the trial, and on what terms.

3.3.2.1 Monitoring of approved clinical research

- UKMREC is responsible for monitoring the conduct of approved research. In clinical research, and especially clinical trials, research sponsors also have such responsibilities. This involves;
 - (a) monitoring arrangements that commensurate with the risk, size and complexity of the trial;
 - (b) mechanisms for reporting and reviewing for each project:
 - i. reporting of serious adverse events (SAEs), at any site for which the institution is responsible;
 - ii. reporting of serious adverse drug reactions (ADRs) serious unexpected suspected adverse reactions (SUSARs), and serious adverse device events from any site for which the institution is responsible.
 - (c) *for a large multi-centre trial, a Data and Safety Monitoring Board (DSMB) is used and there is a mechanism for informing the RECUKM of any relevant emerging data from the DSMB;
 - (d) *for a local trial, there is an identified person/s or committee with suitable expertise to assist and advise the RECUKM about reports of serious adverse events.

- In addition to the requirements stated in the approval letter from the RECUKM, the researcher shall:
 - (a) conduct the trial in compliance with the approved protocol;
 - (b) provide reports of the progress of the trial to the RECUKM, at a frequency directed by the RECUKM (at least annually), and related to the degree of risk to participants;
 - (c) inform the RECUKM, and seek its approval, of amendments to the protocol that:
 - i. are proposed or undertaken in order to eliminate immediate risks to participants;
 - ii. may increase the risks to participants; or
 - iii. significantly affect the conduct of the trial;
 - (d) duly notify the RECUKM of any protocol deviation during the conduct of the trial;
 - (e) notify, in the manner and form specified by the RECUKM, any serious adverse events at any trial sites;
 - (f) inform the RECUKM as soon as possible of any new safety information from published or unpublished studies, or clinical use that may have an impact on the continued ethical acceptability of the trial, or may indicate the need for amendments to the trial protocol;
 - (g) inform the RECUKM, giving reasons, if the trial is discontinued before the expected date of completion; and
 - (h) for trials with implantable medical devices, confirm the existence of, or establish, a system for tracking the participant, with consent, for the lifetime of the device; and report any device incidents to the RECUKM.
 - (i) inform UKMREC of any decision to leave the institution temporarily or permanently, and of the appropriate arrangement pertaining to the research.

3.3.2.2 Discontinuation of trials

- The trial should be discontinued by the researchers if:
 - (a) there are or have been substantial deviations from the trial protocol;
 - (b) side-effects of unexpected type, severity, or frequency are encountered; or
 - (c) as the trial progresses, one of several treatments or procedures being compared appears to be so much better or worse than the other/s that the continuation of the trial would disadvantage some of the participants. The clearer it becomes that one treatment is substantially better or worse than the others, the stronger the need to consider discontinuing the trial.
- The RECUKM reserve the right to discontinue the trial in the light of the above three circumstances.

3.3.2.3 Insurance

- RECUKM must be satisfied that sponsors of trials have made the indemnity or insurance and compensation arrangements. The researcher should inform the RECUKM of any compensation claims. For all investigator-initiated clinical trials, individual researchers must ensure that there is insurance coverage for researchers and subjects.

3.4 HUMAN TISSUE SAMPLES

3.4.1 Guidelines

3.4.1.1 Institutional policy

- The institution has a policy for the collection, storage, use and disposal of human tissue including blood and body fluids in research. This policy is stated below:
 - (a) The researcher should record the source, nature and reason for collection of the tissue.
 - (b) Informed and written consent must be obtained from the participants. However, there may be circumstances where waiver of consent may be justified.
 - (c) Researchers should not transfer tissue samples or related information to any other researcher not involved in the research project unless participants have been informed and consented or have given unspecified consent or if the RECUKM has waived the need for consent and approves the transfer.
 - (d) Researchers should ensure the privacy and confidentiality of the information/results of the research with regard to both family members and others are in accordance with the plan for disclosing and withholding information.
 - (e) Access to samples and information is limited to the purpose of the stated research.
 - (f) The researcher should have a clear statement pertaining to the proper storage and disposal of the samples collected, according to the requirements of the institutions' laboratory.
 - (g) The researcher must take into account socio-cultural considerations bearing on these issues.

- The researcher shall comply with the information stated in the Human Tissues Act 1974.
- Researchers should demonstrate that tissues will be collected, stored, used and disposed of, in accordance with this policy.
- This policy applies to all tissues, whether primarily collected for research or for clinical purpose including archival specimens.

3.4.1.2 Imported tissue

- Where tissue is imported from another country for use in Malaysia, researchers should try to establish whether there are ethical and professional policies in that country, or the relevant institution, governing the collection of tissue for use in research.
 - (a) Where such a policy exists, and reasonable enquiry reveals no reason to believe the collection of the tissue contravened it, RECUKM may consider waiving consent for the use of this tissue.
 - (b) Where it cannot be established that a policy exists, or where it exists but enquiry reveals reason to believe the tissue was not collected in accordance with it, the tissue should not be used for research in Malaysia.
- Participants should receive clear information about whether their tissue samples will be identified, and if so, how.
- If the research is likely to produce information relevant to the health and wellbeing of the person from whom the tissue was derived, procedures to allow participants to be identified for appropriate follow-up should, wherever possible, be included in the research protocol.
- Consent for the use of tissue may be specific, extended or unspecified. When consent is given for the use of human tissue in specific research only, that tissue should not be used for any other purpose without the consent of the tissue donor unless RECUKM has waived the requirement to seek further consent.

3.4.1.3 Cadaveric tissue

- Any wish expressed by a person about the use of his or her post-mortem tissue for research should be respected. If no such wish is discovered, consent for the use of the tissue should be sought from the next of kin. RECUKM reserves the right to waive consent on research carried out on unclaimed bodies. (Refer to Human Tissue Acts 1974).
- At the time of seeking this consent it should be agreed with the next of kin how the tissue is to be disposed of when the research has been completed. Researchers should try to accommodate any reasonable wishes of the next of kin about this. In instances where the next of kin is unknown or untraceable, the tissue can be disposed of according to the institutions' laboratory guidelines.

3.4.1.4 Commercialisation

- There should be no trade in human tissue for research purposes.

3.5 HUMAN GENETICS

3.5.1 Introduction

The genome contains genes that determine an individual's biological traits upon interaction with the environment. Research in genetics may involve characterisation of the gene structures and functions, study of the gene-gene or gene-environment interactions, epigenetics, gene abnormalities or effects of the genes and their products of normal and disease conditions in individuals, relatives, families and populations.

There are ethical issues specific to genetic researches because:

- (a) many of the genes are shared with biological or blood relatives
- (b) findings from genetic research may reveal information about predispositions to disease. This information may affect the individual's access to employment, education and to certain services such as insurance. This issue of privacy and confidentiality may also have similar implications for the blood relatives.

Research results may be beneficial to the blood relatives of the participants because testing for specific genetic abnormalities may help in making important decisions in life including those with potential to improve health. Family members, who are not blood relatives such as spouses, may have an interest because of concerns about the health of their offspring. Genetic research can also reveal information about previously unknown paternity or maternity. The potential ability to identify all human genes and their mutations has profound social implications. Misunderstanding or misuse of the results of genetic testing has the potential to interfere with an individual's self identity and sense of self-worth, and to stigmatize the entire group to which that individual belongs.

3.5.2 Guidelines

- The researchers should indicate in their proposal, a plan to disclose or withhold information of potential importance to the participants, or their blood relatives.
- This plan must take into consideration the clinical relevance, methods and results of the genetic tests.
 - (a) Research participants should be allowed to decide whether they wish to know the result and who else may be given the information.
 - (b) Participants should be informed that the genetic information is potentially identifiable. Measures will be taken to protect the confidentiality of the participants.
 - (c) If participants or their relatives are to be informed of genetic information that may be important for their health, the researcher must have a plan for them to seek clinical advice and genetic counseling.

- (d) For participants or relatives who prefer not to be notified of their genetic information, their decision should be reconfirmed when the results of the research are available.
 - (e) Where the potential relevance of genetic information is not clear until after further analysis of the research results, participants should again be notified of the existence of that information or given the option of receiving the information and/or access to counseling about the implications of their decisions.
- Researchers should state in their proposal the known potential harm of the findings of the genetic testing to participants and family members. Steps should be taken to avoid misrepresentation or misuse of the results which may lead to prejudice, disrespect or other harm to participants or communities.
 - Researchers should not transfer genetic material or related information to any researcher not involved in the research project unless participants have been informed and consented or have given unspecified consent or if the RECUKM has waived the need for consent and approves the transfer.

3.5.2.1 Family involvement

- The researcher should first seek consent from the participant if the researcher requires to include other family members or blood relatives in the research. The opportunity to make initial contact should be given to the participant or someone else he or she chooses.
- Researchers should ensure the privacy and confidentiality of their genetic information with regard to both family members and others in accordance with the plan for disclosing and withholding information.
- If the result shows that a family member may be at risk of a serious illness for which treatment is available, this information may, with the approval of the RECUKM, be disclosed to the family member, even if the research participant does not consent to this. This must be stated in the participant's information sheet.
- The potential to detect previously unknown paternity or maternity or non-blood relationship should be explained to participants.

3.5.2.2 Community involvement

- Consent should also be sought from appropriate community representatives (e.g. Orang Asli) and relevant authorities as well as from the individuals concerned in cases where researchers propose to collect genetic material and information from participants who are chosen because of their membership of a particular community, the research involves sensitivities for that community and there is known to be a culturally relevant community structure involved in such matters.

3.5.2.3 Other information to be given

- Participants whose genetic material and information are collected and/or used for research should also be informed:
 - (a) if the research has potential to generate information that a participant may be legally required to disclose to a third party, such as for the purposes of insurance, employment, finance or education;
 - (b) that genetic material and data may have uses unrelated to research. Participants should be advised that their material and data will not be released for such uses without their consent unless required by law.
 - (c) about any proposal, subject to participants' consent, to store their genetic material and data because it might be useful for as yet unspecified future research. If such consent is not given, the genetic material and data will be disposed of at the end of the research, once the sample storage and record keeping of good research practice have been met.
 - (d) the possibility that the genetic material and the information derived from its use may have potential commercial uses and that the participant will have no claim on any proceeds resulting from this.
 - (e) that they are free to withdraw from the research at any time. Participants should be informed of any consequences of such withdrawal, including that they may request their genetic material and data to be disposed of, if the samples can be identified, and
 - (f) that, in research studying large numbers of genes simultaneously, participants will not be given the names of all the individual genes to be studied.
- Researchers must ensure that the genetic information or research results are protected from access by third parties unless informed consent is given by the participant. Researchers should be aware of the potential risks to confidentiality that arise from DNA banking and publication of data.
- The rarity of some genetic disorders might allow certain families or individuals to be identified by other researchers and in some cases by members of the community. For this reason, where genetic data are stored, confidentiality might sometimes require restrictions on the release of data for future research use.

3.6 HUMAN STEM CELLS

3.6.1 Introduction

There are two major areas in the stem cell research:

- (a) Development of new therapies which includes clinical trials and innovative therapy involving stem cells or their products;
- (b) Research on the stem cells themselves such as pluripotentiality of stem cells, drug metabolism and therapeutics, and studies of specific diseases.

The guidelines cover research using derived human stem cells or stem cell lines, whether embryonic, somatic or derived from primordial germ cells. Researchers and RECUKMs

should refer to national '**GUIDELINES FOR STEM CELL RESEARCH AND THERAPY**' on clinical research that proposes novel uses of stem cells.

3.6.2 Guidelines

- Clinical trials involving the grafting, transplant or activation of human stem cells in humans should be conducted only where there is substantial evidence, from pre-clinical models, of safety and efficacy.
- Identifiers should not be removed from stem cells without the consent of the donor if the removal would make it difficult to communicate information that could benefit the donor or his or her blood relatives.
- Potential donors of material from which stem cells are derived should be informed that the individual donor may remain identifiable.
- Those conducting research involving stem cells derived from a human embryo or fetus should have no involvement in the clinical care of the woman from whom an ovum, embryo or fetus was obtained.
- In addition to the information given to the participant (on the purpose, method, demands, risks and potential benefits of the research), those who are considering donating embryos or tissue for the derivation of stem cells for research should also be given:
 - (a) an explanation of the research for which the stem cells are to be used;
 - (b) an explanation of the implication of removing identifiers from stem cells, including loss of a say in the use of the stem cells and, potentially, loss of their use for treatment for the participant or his or her blood relatives;
 - (c) an assurance that they are free to decline to participate in research and entitled to withdraw from research at any time before identifiers are removed and a cell line is created;
 - (d) an explanation that the research could result in the production of a stem cell line that could be maintained for many years, distributed to other parts of the world, and used for various research purposes; and
 - (e) an explanation that the research participants will not benefit financially from any future commercialisation of cell lines, and that the donor will not have any authority over any cell lines created once their identifiers have been removed.
- If stem cell lines have been produced in another country, their use in research in Malaysia shall be GMP certified and registered by the National Pharmaceutical Control Bureau (NPCB) (refer **GUIDELINES FOR STEM CELL RESEARCH AND THERAPY**)

4.0 ETHICAL CONSIDERATIONS SPECIFIC TO PARTICIPANTS

4.1 WOMEN WHO ARE PREGNANT AND THE HUMAN FETUS

4.1.1 Introduction

The guidelines in this chapter are meant for the ethical conduct of research involving women who are pregnant, the human fetus *ex utero*, and human fetal tissues after the separation of the fetus from the woman. They do not apply to research involving:

- (a) gametes, embryos (*refer to National guidelines for stem cell research and therapy*) and/or participants in assisted reproduction;
- (b) embryos excess to the needs of those for whom they were created using assisted reproductive technology.

Research to which this chapter applies must be reviewed and approved by the Research and Ethics Committee, except where that research uses collections of non-identifiable data and involves negligible risk, and may therefore be exempted from ethical review.

4.1.2 Guidelines

4.1.2.1 The woman who is pregnant and the fetus *in utero*

- The wellbeing and care of the woman who is pregnant and of her fetus always takes precedence over research considerations.
- The research participation of a young person who is pregnant should be guided by the requirements of *Chapter 4.2: Children and young people*.
- Research involving the woman may affect the fetus, and research involving the fetus will affect the woman. The risks and benefits to each should be carefully considered in every case, and should be discussed with the woman and spouse/partner. This must include the effect of the research on the fetus *in utero* (including consideration of fetal stress) and on the child who may subsequently be born.
- The possibility of providing access to counseling for the woman about these issues should be part of this discussion.
- Researchers should ask the woman whether, in her decisions about the research, she wishes to involve others for whom the research may have implications.
- Except in the case of therapeutic innovative therapy, the process of providing information and obtaining consent for involvement in research should be separate from clinical care.
- If it is consistent with promoting the life and health of the fetus, research on the fetus *in utero* may be ethically acceptable. Such research may, for example, provide information about the health of the fetus.

- Research should be designed so as to minimize pain or distress to the fetus, and should include steps for monitoring for signs of fetal distress, and steps for suspending or ceasing the research if necessary.
- ‘Innovations in clinical practice’, in *Chapter 3.3: Interventions and therapies, including clinical and non-clinical trials, and innovations*, should be considered for any innovative therapy involving the fetus.
- Non-therapeutic research that involves administering drugs or carrying out a procedure on the woman or her fetus must be subjected to review by the RECUKM.

4.1.2.2 The human fetus, or fetal tissue, after separation

- Those conducting research involving the human fetus *ex utero* or fetal tissue, after termination of pregnancy, should have no involvement in the clinical care of the woman from whom the fetus or fetal tissue was derived, and no financial or legal relationships with those who are so involved. Whenever it is practicable, the attending physician responsible for the infertility treatment and the investigator deriving or proposing the use of fetal tissue should not be the same person. If it is not practicable, the ethics committee in allowing compromise shall determine the best means to avoid conflict of interest.
- Researchers should demonstrate that there are no suitable alternatives by which the aims of research using the separated human fetus or fetal tissue can be achieved.
- There should be no trade in human fetal tissue.
- Those who conscientiously object to being involved in conducting research with separated fetuses or fetal tissue should not be compelled to participate, nor should they be put at a disadvantage because of their objection.
- Where research involves a separated fetus, researchers should ask the woman whether, in her decisions about the research, she wishes to involve others for whom the research may have implications.
- A fetus or fetal tissue may become available for research as the result of termination. The process through which the woman is approached, informed about, and her consent sought for research on that fetus should be separate from the process under which she decides whether to terminate her pregnancy, and should not begin until a decision to terminate has been made. Consenting to the research must not compromise the woman’s freedom to change that decision.
- Where research involves her separated fetus or its fetal tissue, arrangements should be made for the woman to have access to counseling and support.
- Research on a terminated fetus or its tissues, including the timing and content of the process of seeking the woman’s consent for the research, should be designed so as not to compromise the woman’s decisions about the timing and method of termination.

- A woman's wishes, her physical, psychological and emotional welfare should be considered:
 - (a) When a decision is made to approach her about proposed research involving her, her separated fetus or its tissue; and
 - (b) the way information is provided about the research and her consent is sought.
- The woman should also be informed:
 - (a) that she should consider whether to seek consent to the proposed research from any other person;
 - (b) whether it is possible to store the fetus or fetal tissues for later use in research;
 - (c) that she is free to withdraw her consent to the research at any time, whether before or after a termination or other loss of a fetus;
 - (d) whether there is potential for commercial application of outcomes of the research, including the development of cell lines;
 - (e) that she will not be entitled to a share in the profits of any commercial applications; and
 - (f) whether fetal organs or stem cell lines developed from them will be exported to another country.
- A fetus delivered alive after 22 weeks period of gestation and weighing more than 500 gm, is a child, and should be treated as a child and receive the care that is due to a child.
- Organs and tissues may be removed from a fetus delivered dead and used for research only if the conditions are met, and:
 - (a) the woman and any others she wishes to involve have given consent to the removal and the research;
 - (b) the fetus is available for research only as a result of separation by natural processes or by lawful means; and
 - (c) death of the fetus has been determined by a registered medical practitioner who has no part (or financial interest) in the research.
- If, for research purposes, fetal cells are to be derived from the fetal tissue and stored or propagated in tissue culture, or tissues or cells are to be used in human transplantation, the woman's consent is required. Others whom the woman identifies may also need to be involved in decisions about these matters.

4.2 CHILDREN AND YOUNG PEOPLE

4.2.1 Introduction

Research involving children and young people raises particular ethical concerns about:

- (a) their capacity to understand what the research entails, and therefore whether their consent to participate is sufficient for their participation;
- (b) their possible coercion by parents, peers, researchers or others to participate in research; and

(c) conflicting values and interests of parents and children.

Researchers must respect the developing capacity of children and young people to be involved in decisions about participation in research. The child or young person's particular level of maturity has implications for whether his or her consent is necessary and/or sufficient to authorize participation. Different levels of maturity and levels of the corresponding capacity to be involved in the decision include:

- (a) infants, who are unable to take part in discussion about the research and its effects;
- (b) young children, who are able to understand some relevant information and take part in limited discussion about the research, but whose consent is not required;
- (c) young people of developing maturity, who are able to understand the relevant information but whose relative immaturity means that they remain vulnerable. The consent of these young people is required, but is not sufficient to legally authorise research.

4.2.2 Guidelines

- The research and its methods should be appropriate for the children or young people participating in the research.
- In the research design researchers should:
 - (a) specify how they will judge the child's vulnerability and capacity to consent to participation in research;
 - (b) describe the form of proposed discussions with children about the research and its effects, at their level of comprehension; and
 - (c) demonstrate that the requirements of this chapter will be satisfied.
- In educational research, discussion with the school community should be built into the research design.
- When children and young people are not of sufficient maturity to consent to participation in research, it is justifiable to involve them only when:
 - (a) it is likely to advance knowledge about the health or welfare of, or other matters relevant to, children and young people; or
 - (b) children's or young people's participation is indispensable to the conduct of the research.
- The circumstances in which the research is conducted should provide for the child or young person's safety, emotional and psychological security, and wellbeing.
- Researchers should be attentive to the development level of children and young people when engaging them in understanding the nature and likely outcomes of research, and when judging their capacity to consent to the research.
- Except in the circumstances described, specific consent to a child's or young person's participation in each research project should be obtained from:

- (a) the child or young person whenever he or she has the capacity to make this decision; and
 - (b) either
 - i. one parent, except when, in the opinion of the review body, the risks involved in a child's participation require the consent of both parents; or where applicable
 - ii. the guardian or other primary care giver, or any organisation or person required by law.
- A review body may also approve research to which only the young person consents if it is satisfied that:
 - (a) he or she is mature enough to understand the relevant information and to give consent, although vulnerable because of relative immaturity in other respects; and the research involves no more than low risk; and
 - (b) the research aims to benefit the category of children or young people to which this participant belongs; and
 - (c) either
 - i. the young person is estranged or separated from parents or guardian, and provision is made to protect the young person's safety, security and wellbeing in the conduct of the research. (In this case, although the child's circumstances may mean he or she is at some risk, for example because of being homeless, the research itself must still be low risk); or
 - ii. it would be contrary to the best interests of the young person to seek consent from the parents, and provision is made to protect the young person's safety, security and wellbeing in the conduct of the research.
 - Before including the child or young person in research, researchers must establish that there is no reason to believe that such participation is contrary to that child's or young person's best interest.
 - A child or young person's refusal to participate in research should be respected wherever he or she has the capacity to give consent to that same research but may be overridden by the parents' judgment and/or estimation as to what is in the child's best interest.

4.3 PEOPLE IN DEPENDENT OR UNEQUAL RELATIONSHIPS

4.3.1 Introduction

Examples may include relationships between:

- (a) Carers and people with chronic conditions or disabilities, including long-term hospital patients, involuntary patients, or people in residential care or supported accommodation;
- (b) Health care professionals and their patients or clients;
- (c) Teachers and their students;
- (d) Prison authorities and prisoners;
- (e) Governmental authorities and refugees;

- (f) Employers or supervisors and their employees (including members of the police and defence forces);
- (g) Service-providers (government or private) and especially vulnerable communities to whom the service is provided.

4.3.2 Guidelines

- Being in a dependent or unequal relationship may influence a person's decision to participate in a research. While this influence does not necessarily invalidate the decision, it always constitutes a reason to pay particular attention to the process through which consent is negotiated.
- In the consent process, researchers should, whenever possible, invite potential participants to discuss their participation with someone who is able to support them in making their decision. Where potential participants are especially vulnerable or powerless, consideration should be given to the appointment of a participant advocate.
- In the research design, researchers should identify and take steps to minimize potentially detrimental effects of:
 - (a) an unequal or dependent relationship on the conduct of the research; and
 - (b) the research on participants involved in the relationship.
- People in the categories of relationship described above are vulnerable to being over-researched because of the relative ease of access to them as research populations.
- Where participants are in a relationship of dependency with researchers, researchers must take particular care throughout the research to minimise the impact of that dependency.
- Researchers need to be mindful that in some relationships of dependency, participants may have an unrealistic expectation of the benefits of research.
- A person declining to participate in, or deciding to withdraw from, research should not suffer any negative consequences, such as unfair discrimination, reduction in the level of care, dismissal from employment, or any other disadvantage.
- The design of research involving those in dependent relationships should not compromise respect for them.
- Where the researcher has a pre-existing relationship with potential participants, it may be appropriate for their consent to be sought by an independent person.
- Researchers should take special care to safeguard confidentiality of all information they receive, particularly in settings such as shared workplaces, hospital rooms or rooms in residential care.

4.4 PEOPLE HIGHLY DEPENDENT ON MEDICAL CARE WHO MAY BE UNABLE TO GIVE CONSENT

4.4.1 Introduction

Significant ethical issues are raised by research conducted in the following settings:

- (a) Neonatal intensive care;
- (b) Terminal care;
- (c) Emergency care;
- (d) Intensive care; and
- (e) The care of unconscious people.

4.4.2 Guidelines

- Research involving people who are highly dependent on medical care may be approved where:
 - (a) it is likely that the research will lead to increased understanding about, or improvements in, the care of this population;
 - (b) the requirements of relevant jurisdictional laws are taken into account; and
 - (c) either
 - i. any risk or burden of the proposed research to this particular participant is justified by the potential benefits to him or her; or
 - ii. where participants have capacity to consent, any risk or burden is acceptable to them and justified by the potential benefits of the research.
- People highly dependent on medical care may be exposed to severe threats to their lives so that recruiting them into research might seem unfair. However, those people are entitled to participate in research and provided they meet the above criteria.
- The distinguishing features of *neonatal intensive care research* are the small size and unique developmental vulnerability of the participants and the potential for very long-range impact on their growth, development and health. In this research, risks and potential benefits should be assessed with particular care by individuals or groups with relevant expertise.
- The distinguishing features of *terminal care research* are the short remaining life expectancy of participants and their vulnerability to unrealistic expectations of benefits. Terminal care research should be designed so that:
 - (a) the benefits of research to individual participants or groups of participants, or to others in the same circumstances, justify any burden, discomfort or inconvenience to the participants;
 - (b) the prospect of benefit from research participation is not exaggerated;
 - (c) the needs and wishes of participants to spend time as they choose, particularly with family members, are respected; and
 - (d) the entitlement of those receiving palliative care to participate is recognised.

- People involved in research to which this chapter applies may have impaired capacity for verbal or written communication. Provision should be made for them to receive information, and to express their wishes, in other ways.
- In *emergency care research*, recruitment into a research project often has to be achieved rapidly. Where the research involves emergency treatment and meets the requirements, consent for the research may be waived.
- In *intensive care research*, heavy sedation may impair participants' cognition, and communication is difficult with people receiving ventilatory assistance. Whenever possible, consent to intensive care research, based on adequate information, should be sought from or on behalf of potential participants before admission to that level of treatment. When prior consent to research is not possible, the process described in paragraphs 4.4.2.1 should be followed.
- In *research with unconscious people*, the participants cannot be informed about the research and their wishes cannot be determined. Those who are unconscious should be included only in minimally invasive research, or in research designed both to be therapeutic for them and to improve treatment for the condition from which they suffer.

4.4.2.1 Process to be followed

- Consent should be sought from people highly dependent on medical care wherever they are capable of giving consent and it is practicable to approach them.
- Where it is not practicable to approach a person highly dependent on medical care, or the person is not capable of making such a decision, consent should be sought from the participant's guardian, or person or organisation authorised by law, except under the circumstances described in paragraph 5 in 4.4.2.1.
- When consent is to be sought, either from the potential participant or another on his or her behalf, steps should be taken to minimise the risk that:
 - (a) stress or emotional factors may impair the person's understanding of the research or the decision to participate; and
 - (b) the dependency of potential participants and their relatives on the medical personnel providing treatment may compromise the freedom of a decision to participate.
- Where the researcher is also the treating health professional, it should be considered whether an independent person should make the initial approach and/or seek consent from potential participants or from others on their behalf.
- When neither the potential participant nor another on his or her behalf can consider the proposal and give consent, the RECUKM may, having taken account of relevant jurisdictional laws, approve a research project without prior consent if:

- (a) there is no reason to believe that, were the participant or the participant's representative to be informed of the proposal, he or she would be unwilling to consent;
 - (b) the risks of harm to individuals, families or groups linked to the participant, or to their financial or social interests, are minimised;
 - (c) the project is not controversial and does not involve significant moral or cultural sensitivities in the community; and, where the research is interventional, only if in addition:
 - (d) the research supports a reasonable possibility of benefit over standard care;
 - (e) any risk or burden of the intervention to the participant is justified by its potential benefits to him or her; and
 - (f) inclusion in the research project is not contrary to the interests of the participant.
- As soon as reasonably possible, the participant and/or the participant's relatives and authorised representative should be informed and documented of the participant's inclusion in the research and of the option to withdraw from it without any reduction in quality of care.

4.5 PEOPLE WITH COGNITIVE IMPAIRMENT, INTELLECTUAL DISABILITY OR MENTAL ILLNESS

4.5.1 Introduction

People with cognitive impairment, intellectual disability or mental illness are entitled to participate in research. While research involving these people need not be limited to their particular impairment, disability or illness, their distinctive vulnerabilities as research participants should be taken into account. Even when capable of giving consent and participating, people with these conditions may be more-than-usually vulnerable to various forms of discomfort and stress.

4.5.2 Guidelines

- The study design should consider factors that may affect the capacity to receive information, to give consent, or to participate in the research.
- Care should be taken to determine whether participants' cognitive impairment, intellectual disability or mental illness increases their susceptibility to some forms of discomfort or distress. Ways of minimising effects of this susceptibility should be described in the research proposal.
- People with cognitive impairment, an intellectual disability, or a mental illness, are entitled to participate in research.
- Because of the participants' distinctive vulnerability, care should be taken to ensure that the risks and any burden involved in the proposed research are justified by the potential benefits of the research.
- Consent to participation in research by someone with a cognitive impairment, an intellectual disability, or a mental illness should be sought either from that person if he

or she has the capacity to consent, or from the person's guardian or next of kin or legal representatives.

- The process of seeking the person's consent should include discussion of any possibility that his or her capacity to consent or to participate in the research may vary or be lost altogether. The participant's wishes about what should happen in that circumstance should be followed unless changed circumstances mean that acting in accordance with those wishes would be contrary to the participant's best interests.
- Consent should be witnessed by a person who has the capacity to understand the merits, risks and procedures of the research, is independent of the research team and, where possible, knows the participant and is familiar with his or her condition.
- Where consent has been given by a person authorised by law, the researcher should nevertheless explain to the participant, as far as possible, what the research is about and what participation involves. Should the participant at any time recover the capacity to consent, the researcher should offer him or her, the opportunity to continue participation or to withdraw.
- Researchers should inform RECUMs how they propose to determine the capacity of a person with a cognitive impairment, an intellectual disability, or a mental illness to consent to the research. This information should include:
 - (a) how the decision about the person's capacity will be made;
 - (b) who will make that decision;
 - (c) the criteria that will be used in making that decision, and
 - (d) the process for reviewing, during the research, the participant's capacity to consent and to participate in the research.
- Refusal or reluctance to participate in a research project by a person with cognitive impairment, an intellectual disability, or a mental illness should be respected.

4.6 PEOPLE WHO MAY BE INVOLVED IN ILLEGAL ACTIVITIES

4.6.1 Introduction

Research may in some instances discover illegal activity (including notifiable activity) by participants or others, or may discover information indicating future illegal activity.

Such research may:

- (a) be intended to study, and perhaps to expose, illegal activity;
- (b) be not specifically intended to discover illegal activity, but likely to do so;
- (c) discover illegal activity inadvertently and unexpectedly.

4.6.2 Guidelines

- Research designed to expose illegal activity should be approved only where the illegal activity bears on the discharge of a public responsibility or the fitness to hold public office.
- Participants may be subject to risks because of their involvement in research that discovers illegal activity. It should be clearly established that these risks are justified by the benefits of the research.
- Where research discovers information about illegal activity by participants or others, researchers and institutions may become subject to orders to disclose that information to government agencies or courts.
- Consideration should be given to the use of pseudonyms, or to the removal of links between names and data, for participants whose illegal activity may be revealed or discovered in research.
- Researchers, who may have contact with those participants professionally, should ensure that the research is not compromised by their professional contact with the participants. On the other hand, their professional obligations to participants should not be compromised by the research activity.
- In research where it is not designed to expose illegal activity, researchers should explain to participants:
 - (a) the likelihood of such discovery and of any resulting legal obligation of disclosure; and
 - (b) the extent to which the researcher will keep confidential any information about illegal activity by participants or others, and the response the researcher will make to any legal obligation or order to disclose such information.
- Researchers should be satisfied that participants who are subject to criminal justice processes:
 - (a) are aware that the research may discover illegal activity; and
 - (b) do not have unrealistic expectations of benefit from their participation.

4.7 PEOPLE IN OTHER COUNTRIES

4.7.1 Introduction

When a researcher from UKM proposes to conduct research in another country, additional ethical considerations may arise. In some situations, regard for the beliefs, customs and cultural heritage of participants will require recognition of values other than those of this guidelines. Sometimes these values will differ with one or more of the ethical values of these guidelines.

Sometimes the legal, regulatory or ethical review processes of another country may also demand conduct that differs with the ethical values of these guidelines.

4.7.2 Guidelines

- Local cultural values should be acknowledged in the design and conduct of the research.
- As far as is necessary, the design and conduct of the research should reflect continuing consultation with the local participant population and the communities to which they belong.
- Researchers should inform RECUKM:
 - (a) whether, in the country in which they intend to do research, there are ethics approval processes that are relevant to that research, and whether any such processes are mandatory or voluntary in relation to the proposed research; and
 - (b) how such processes function, the values and principles on which they rely, and whether they require reports of the RECUKM.
- Where there are no ethics approval processes in an overseas country, these guidelines may provide the only applicable process for ethical approval. In this case, the RECUKM should take account of the available resources and means to conduct the research and avoid imposing unrealistic requirements, providing always that research participants are accorded no less respect and protection than this guidelines require.
- Some funding or national requirements will direct researchers and review bodies to conform to the ethics guidelines of local institutions or to recognized international guidelines or instruments. Research conducted under those guidelines or instruments should be approved only if participants will be accorded no less respect and protection than this guideline requires.
- Researchers should have enough experience or access to expertise to enable them to engage with participants in ways that accord them due respect and protection.
- When research is to be conducted overseas by a researcher who is subject to academic supervision, researchers should inform the RECUKM of how that supervision is to be effected so that due respect and protection will be accorded to participants.
- When co-researchers are to be recruited in an overseas country, researchers should inform RECUKM of how the capacity and expertise to conduct that part of the research assigned to the co-researchers will be established.
- It is the responsibility of researchers to satisfy themselves that those co-researchers will carry out the research in a way that accords participants no less respect and protection than these guidelines requires.
- The distribution of the burdens and benefits of research in overseas countries, for the participants and in some instances the broader community, should be fair and the research should not be exploitative.

- The conduct of the research in other countries should take into account the opinions and expectations of participants and their communities about the effect of any limits of resources on:
 - (a) the way the research will be conducted;
 - (b) participants' post-research welfare; and
 - (c) application of the results of the research.
- Institutions and researchers should find out whether research they are planning to do in another country is lawful in that country.
- Researchers need to inform RECUKM when participants will be in dependent relationships with researchers, whether through previous or proposed arrangements
- Researchers need to know enough about the communities, and how to engage with them, to be able to assess the burdens and benefits of their research to the communities. Political and social factors that may jeopardise the safety of participants need to be taken into account. Researchers should inform RECUKM about these likely burdens and benefits.
- A local, readily accessible contact should be available to participants to receive responses, questions and complaints about the research. Responses and questions should be handled by the researcher. Researchers should ensure that there is a process independent of the researcher for dealing with complaints.
- In proposing mechanisms for monitoring research, researchers should take account of local circumstances.
- Conducting research in other countries can expose researchers to risks of harm. Institutions and researchers should try to identify and evaluate any such risks, and make provision for dealing with them, for instance by establishing local academic or institutional affiliations.
- Respect for participants in other countries requires having due regard for their beliefs, customs and cultural heritage, and for local laws.
- Local beliefs and practices regarding recruitment, consent, and remuneration to participants or contributions to communities for participating in research should be taken into account in the design and the conduct of the research, and in the ethical review process.
- It should be clearly established that the processes to be followed in recruiting participants and through which they choose whether to be involved are respectful of their cultural context.

5.0 RESEARCH REQUIRING ETHICS REVIEW

- All research that involves human subjects (including biological materials and /or patients' data) requires review and approval by a UKM Human Research Ethics Committee (RECUKM) before the research is started.

- Research requiring such review includes:
 - (a) Research by university members, both full and part time, who apply for external and/or internal grant funds.
 - (b) Research by university members, both full and part time, who conduct research not requiring funds.
 - (c) Research conducted by UKM graduate and undergraduate students as part of formal course requirements.
 - (d) Research conducted by UKM students or staff that makes use of university resources or facilities, either on-site or off-site.
 - (e) Research that has already been approved but subsequently requires significant changes in the original protocol or in collecting, storing, analyzing, or reporting data; or research in which ethical issues have arisen.
 - (f) Research that is conducted by non-UKM researchers and students, both undergraduate and postgraduate, wishing to access UKM students, staff or patients (including biological materials and /or patients' data) as a study population in the proposals that have been approved at another institution.
 - (g) Research that is conducted by non-UKM researchers in collaboration with UKM staffs and using UKM resources that have been approved by another institution.

- All research involving emergency health situations, involving either physical or psychological characteristics, must conform to the guidelines stipulated in RECUKM Guidelines.

- Research that does not require RECUKM review includes:
 - (a) Research about a living individual involved in the public arena, or about an artist, based exclusively on information available in the public domain.
 - (b) Quality assurance studies.
 - (c) Performance reviews that are carried out as part of the routine activity.
 - (d) Testing within normal educational requirements.
 - (e) Activities emerging from professional practice training (e.g., teacher-in-training; clinicians-in-training).
 - (f) Consultations with colleagues that are not part of research projects.

5.1 MEMBERSHIP

5.1.1 RECUKM Permanent Members

5.1.1.1 Principle

- The committee members must collectively possess the competence and the technical know-how to consider and take into account the consequences of the participation of patients or healthy volunteers on their health and welfare.
- The members from the medical profession must have the experience and exposure in medical research. They must be well-respected, trustworthy, always promote sound scientific research and show no compromise to the ethical conduct of human research. Members of the committee must be able to evaluate research proposals from the viewpoint of the research subjects and not the researcher. Representation from the public is important in the evaluation of the consent form and the subject information sheet.
- Committee member who is involved directly with any research which is being discussed is required to be out or not involved in that research ethical discussion in order to prevent conflict of interest.

5.1.1.2 The composition of the RECUKM

The recommended number of members is 16, and as far as possible it shall include 5 members from non-medical disciplines.

- (a) There should be fair representation of men and women.
- (b) Members from the medical profession, should include at least three with research experience in clinical trials. There must be at least one member from each discipline (medicine, surgery, pediatrics, obstetrics and gynaecology, pre-clinical disciplines, public health and genetics & molecular biology). The majority of the members from the medical profession must be active in clinical service and medical research.
- (c) At least one non-medical scientist
- (d) At least one lay person who has no affiliation to the institution and is not currently engaged in medical scientific, legal or academic work.
- (e) At least one lawyer who is not engaged to advise the institution.
- (f) At least one person with knowledge and experience in the professional health care and/or counseling.
- (g) At least one person who is qualified in religious knowledge. (the priority goes to Islam since it is the religion of the majority of citizens of Malaysia)

5.1.1.3 Meeting Attendance and Quorum

- Meeting attendance will be determined by Chairman of RECUKM according to specialties required.
- The quorum for meeting is 5 members. This must include;
 - (a) At least 1 layperson.
 - (b) At least 2 medical Doctors.
 - (c) A member from non-medical discipline.
- Chairman reserves to invite an expert (non-member) in relevant fields to the proposal to attend the meeting.
- When there is less than full attendance, decisions will be adopted only under quorum conditions with a minimum number of 5 members.
- Where there is less than full attendance of the quorum at a meeting, the Chairman should be satisfied, before a decision is reached, that the views of those absent who belong to the quorum have been received and considered.

5.1.1.4 Appointment

- Chairman is nominated among members by the members of Medical Faculty Administration Meeting and designated by UKM Vice Chancellor.
- Committee members are nominated by faculty and designated by UKM Vice Chancellor.
- Appointment term is for the period of 3 years and all members are eligible to be reappointed for 2 years in every reappointment.
- Members can be stripped of position if they do not attend 3 consecutive meetings or less than 50% attendances a year.
- Members also may withdraw from membership on any reason after being agreed by the Chairman of RECUKM.
- Member that lay off or pull out, replacement may be made by nomination by faculty and designated by UKM Vice Chancellor.
- RECUKM members will need to provide a copy of their curriculum vitae.
- RECUKM Members will be asked to sign a *Confidentiality & Conflict of Interest Form* indicating their required assurance to maintain reasonable confidentiality in relation to the information they may become aware of while performing their duty and to report to the Chair of the RECUKM any conflict of interest related to their position as soon as they become aware of it. Confidentiality however, should not compromise the need for transparency and governance.

- UKM should provide an assurance of legal protection to all those involved in ethical review of research, for liabilities that may arise in the course of *bona fide* conduct of their duties in this capacity.

5.1.2 Term of References

5.1.2.1 The Roles and Responsibilities of RECUKM

- Evaluate proposal from research ethical angle based on “Helsinki Declaration, International Conference on Harmonisation (ICH), Malaysian GCP Guidelines and others, where related”
- Discuss and resolve ethics issues which arose and make decision whether the research proposal should be approved, amended or rejected.
- Drafting and provide relevant research ethics guidelines.
- Give annual report to university's management and this report can be accessed publically.
- Monitor the progress of research and make decision whether that research could be continued, amended or terminated if there is any ethical problem.
- Discuss and provide policies and new guidelines which are related, if required.
- Review RECUKM Guidelines from time to time and give advice to the university management on policy related to ethical procedures.

5.1.2.2 The Roles and Responsibilities of the Chairman of RECUKM

- Determining the dates for the RECUKM meeting periodically at least once a month
 - In the event that a meeting cannot be scheduled within a calendar month or a scheduled meeting is cancelled, then a notice and reason for cancellation shall be given to all UKM staff (through electronic portal via UKM bulletin).
- Chair the meetings as well as ensuring that the meetings proceed according to meeting ethics.
- Ensure the active participation of the committee members in all discussions and the decision-making process.
- Arrange and/or call for ad-hoc committee members whenever their expertise is needed in evaluating research proposals.
- Prepare and sign the letter of approval for all research proposals involving human.
- Explains to the researcher, if necessary, the reasons for the rejection of research proposals.

- Raise other relevant issues such as research that contravenes the code of ethics, appeal and the rejection of proposals, complaints about researchers and research projects, and any other issues related to ethics.
- Represent UKM and act as spokesman for the committee at relevant meetings or forums in and outside the university.
- Withdraw the approval of projects that contravene the rules and conditions provided by the RECUKM.
- Provide advice to relevant organizations and authorities on all matters relating to research ethics which involve humans.

5.1.2.2 The Role and Responsibilities of the RECUKM Members

- Attend and actively participate in RECUKM meetings.
- Evaluate research proposals involving human in the relevant institutions.
- Monitor the progress of research projects with respect to the appearance of side effects and deviations from the approved protocol.
- Independently evaluate the ethics of all research projects involving human.
- Prepared to act as chairman of the committee during the absence of the chairman.

5.1.3 RECUKM Replacement Members

- Replacement members have task and responsibility just like permanent members. They are required to attend RECUKM meeting when permanent members unable to attend that meeting.

5.2 PRINCIPLES UNDERLINING RESEARCH REVIEW

- RECUKM adopt the principle of proportionate review; that is, the more invasive the research, the greater the scrutiny should be in the review.
- For approval, research proposals must address the applicable principles outlined in RECUKM Guidelines and any other relevant documents.

5.2.1 Review Procedure: RECUKM

- The RECUKM meets face-to-face, year-round, on a regular basis, at least once a month. Communication about reviews may take place between meetings.
 - In the event that a meeting cannot be scheduled within a calendar month or a scheduled meeting is cancelled, then a notice and reason for cancellation shall be given to all UKM staff (through electronic portal via UKM bulletin).

- Proposals should be reviewed within thirty (30) days of submission to the MRIS in accordance with the scheduled monthly meetings.
 - For initial review, the reviewer will be given approximately 3 weeks to complete the review.
 - If a reviewer is unable to complete the review within the time line, the research proposal will be given to the RECUKM Chairman or a second reviewer.
- All applicants are required to use the Ethics Review Application Form developed by the MRIS. For undergraduate and graduate students, application must be made by the Supervisor unless the applicants are UKM staffs who are doing research outside UKM.
- The RECUKM reviews proposals that exceed minimal risk. In the case of expedited review for minimal risk studies, the Chair will make a full report to the RECUKM of all decisions made between meetings.
- All decision made between meetings will be endorsed at the scheduled meetings.
- Member(s) of the RECUKM are required to disclose any conflict of interest and to exclude themselves from the discussion and vote. When a research proposal involves the Chairman, then a member of RECUKM will take over the role of the Chairman for the said research proposal
 - Conflicts of interest and change of Chair will be noted in the minutes of the meeting
- Approval will be reached on the basis of consensus, or if this is not possible, then through majority vote. There will be no retrospective approval projects.
- The Chair of the RECUKM decides if a proposal warrants expedited review.
- Expedited review may be activated when a research proposal clearly involves no more than minimal risk, in which case one member of the RECUKM will review and recommend approval of the proposal to the Chairman. In the instance there are minor changes to a proposal, the Chair may approve the revision.
 - When amendments have been made to a research project involving the Chairman, then a member of the RECUKM will review the changes for approval. The Chairman will then endorse the approval.
- RECUKM may invite researchers to be present for discussion of their proposed research.
- Communication between a research sponsor and a RECUKM should be avoided where it may, or may be perceived to, influence the ethical review and approval of the project.
- Researchers who have submitted proposals shall be informed of the RECUKM decision, by written notice, which will outline the necessary changes for proposals requiring modifications, usually within ten (10) working days of the scheduled meeting. For a proposal that requires amendment, a letter containing the proposed changes will be sent to the researcher. Once a study is approved, a letter of approval will be issued by RECUKM.
 - A Certificate of approval will be attached with the letter.

- For studies which required formal presentation, the list of attendees at the meeting will be included with the letter of approval.
- Researchers may ask to have their proposals reconsidered, and/or they may meet with the Chairman of RECUKM for discussion. Both researchers and the RECUKM may activate this invitation in the spirit of resolving outstanding concerns.

5.2.1 Record Keeping

- Minutes/records/notes of the meetings of the RECUKM will be maintained. Minutes/records/notes must document reasoned decision. The minutes must be accessible to authorized representatives of the institution, researchers, and funding agencies.
 - The date of approval of minutes shall be at the next scheduled meeting when the minutes are verified (or to state deadline for minutes to be approved.)
- Any other documents that are submitted to permit review of a proposal will be kept on file. Written feedback about the results of a review must be provided to the faculty member(s) involved in the research.
- In the event that an internal or external audit is performed to determine whether ethical practices are upheld, documents and records about decisions must be stored for the specified period, after which time the material may be shredded, five years after completion of the study.

5.2.2 Appeals

- Faculty researchers have a right to appeal negative decisions.
- An appeal regarding a negative decision about a graduate or undergraduate project must be activated by the faculty member responsible for the project.
- Appeal Committee will consist of 3 members of the RECUKM, 2 of whom were not involved in the primary review and 1 is the original reviewer. Members of the Appeal Committee will be decided by RECUKM.
- The Chair of the Appeal Committee will be appointed by members of RECUKM. Appeals must be made in writing and include all supporting documents. The appeal must be forwarded to MRIS within two (2) weeks of issuance of the letter that outlines the reasons for the negative decision. MRIS will forward these documents to the appeals committee as indicated above.
- Committee adjudicating the appeal reserves the right to invite the researcher to appear before the committee. Appeals will be settled in a timely fashion and the appeal decision is final.

5.2.3 Procedures For Changes To Protocol

- Any changes made to already approved research proposals, related documents, or instruments must be approved by the RECUKM prior to their implementation. To request a review of proposed changes, the researcher must write a letter with the amended document.

- Minimal risk applications are vetted by the Chair of the RECUKM or a member of RECUKM delegated by the Chair for expedited review. These include research involving :-
 - History taking and clinical examination
 - Behavioural or psychological testing
 - Quality of Life assessment
 - Venipuncture, heel or finger prick
 - Collection of small volumes of blood samples (less than 20 mls) at any one time and not too often (not more than 3 times for whole duration of study, and not more than twice a week) by venipuncture, finger prick, heel prick, etc.
 - Collection of specimen by non-invasive means
 - Urine, saliva or sputum collection.
 - Hair or nail samples
 - Monitoring test such as blood pressure, electroencephalography, electrocardiography
 - Vision or hearing test, ophthalmoscopy
 - Tympanometry
 - Oral glucose tolerance test
 - Anthropometric measurements
 - Surveys based on questionnaires or interviews of a non-confidential nature not likely to be detrimental to the status or interests of subjects, and not likely to offend the sensibilities and sensitivities of subjects.
 - Modification or amendment of approved protocol:
 - Administrative revisions such as correction of typographical errors.
 - Addition or deletion of non-procedural items such as addition of study personnel names, laboratories, etc.
 - Research involving data, documents or specimens that have already been collected or will be collected for ongoing medical treatment or investigation

(Source MREC KKM 2014 & EU Paediatric Guideline 2008)

- For those applications that exceed minimal risk, the appropriate number of copies of the amended document and applicable attachments must be submitted for approval by the RECUKM.

5.2.4 Monitoring

- It is not practical for the committee to monitor all research projects in great detail, but the committee must monitor the general conduct of research. However, the committee will scrutinize all essential research documents, particularly in relation to multi-centre clinical trials.

- Monitoring through the submission of periodic progress report and a final report, based on the format provided.
- With regards to clinical trials, all information about adverse events have to be documented using a standard form (CIOMS form) and reported to the committee.
- Reporting timeframe for local serious adverse events, a verbal report should be made within 48 hours of event occurrence or discovery. A written report should be submitted as soon as possible but no later than seven (7) calendar days upon awareness of occurrence or discovery. An updated written report must be submitted within thirty (30) additional calendar days since the initial notification.
- Reporting timeframe for foreign serious adverse events, ALL FATAL OR LIFE-THREATENING serious adverse events as soon as possible but no later than seven (7) calendar days upon receipt from sponsor or the Contract Research Organization (CRO). OTHER serious adverse events, reports submitted within fifteen (15) calendar days upon receipt from sponsor or the Contract Research Organization (CRO).
- Reporting timeframe for Oversea suspected unexpected serious adverse reactions (SUSAR) reports, reports are submitted within thirty (30) calendar days upon receipt from the sponsor or the Contract Research Organization (CRO).
- Annual reports and requests for renewals must be sent to the RECUKM thirty (30) days **prior** to the expiry date of the letter of ethics approval.
- No research with human participants shall take place without a valid letter of ethics approval.
- All the researches which have been approved by the RECUKM must provide the RECUKM with a final report within 30 days of the expiry date of the letter of ethics approval.

5.2.5 Handling Complaints

- To handle complaints about researchers or the conduct of research, MRIS/RECUKM should:
 - (a) identify a person, accessible to participants, to receive these complaints; and
 - (b) establish procedures for receiving, handling and seeking to resolve such complaints.
- In the case of research misconduct, the approval by the RECUKM can be withdrawn or cancelled at any time after formal discussions with the researcher.
- The RECUKM shall report to the relevant authority (Faculty, Institution, Hospital or University), if researchers fail to heed the advice of the committee, conduct the research project in an unethical way or contravene the stipulated rules.

5.2.6 Conflict Of Interest

- RECUKM should require its members, and also any experts whose advice it seeks, to disclose any actual or potential conflict of interest in research to be reviewed, including any:
 - (a) personal involvement or participation in the research;
 - (b) financial or other interest or affiliation; or
 - (c) involvement in competing research.
- The RECUKM should adopt measures to manage such conflicts. In the case of members these measures may include exclusion from a meeting, or from some or all of the committee's deliberations, or in the case of expert advisors, requesting only written advice from them.
- Sometimes a researcher who discloses the fact that he or she has a conflict of interest may have an ethically acceptable reason for not disclosing what the conflict is, for example, that this might breach another person's privacy. The researcher may then remain involved in the research only if RECUKM is satisfied that the conflict can be managed without its nature being disclosed.
- Measures to manage conflicts of interest involving researchers include:
 - (a) the information be disclosed to research participants;
 - (b) a person other than the researcher make the initial approach to participants;
 - (c) the information be disclosed in any report of the research;
 - (d) the research be conducted by another researcher; or
 - (e) the research not be conducted.
- Where RECUKM becomes aware that there may be a conflict of interest, the review body should notify the relevant authority.

REFERENCES

1. Australian National Statement on Ethical Conduct in Human Research, Endorsed March 2007, Reprinted October 2007
2. Mount Saint Vincent University: Policies and Procedures: Ethics Review of Research Involving Humans, As Approved by Senate on November 5, 2005
3. Operational Guidelines for Ethics Committees That Review Biomedical Research (WHO 2000)
4. Guidelines For Application Of Clinical Trial Import License And Clinical Trial Exemption In Malaysia, Fifth Edition (Version 1) June 2009
5. Malaysian Guideline for Good Clinical Practice (GCP) October 1999
6. Guidelines for Stem Cell Research and Therapy, MOH/P/PAK/177.08(GU) July 2009
7. Guideline Of The Malaysian Medical Council, MMC Guideline 009/2006, Clinical Trials And Biomedical Research
8. MREC KKM 2014 & EU Padiatric Guideline 2008

GLOSSARY

Child

Subject to law in the relevant jurisdiction, a minor who lacks the maturity to make a decision whether or not to participate in research. Under the Malaysian law, a child is any person under the age of 18 years.

Young person

In the context of this guidelines, a minor who (subject to the law in the relevant jurisdiction) may have the maturity to make a decision whether or not to participate in research. Under the Malaysian Young Person's Act, a young person is any person between the age of 14 and 18 years.

Negligible risk

Research in which there is no foreseeable risk of harm or discomfort, and any foreseeable risk is of inconvenience only.

Low risk

Research in which the only foreseeable risk is one of discomfort.

Beneficence

Doing good to others: here also includes "non-maleficence", avoiding doing harm.

Benefit

That which positively affects the interests or welfare of an individual or group.

Confidentiality

The obligation of people not to use private information – whether private because of its contents or the context of its communication – for any purpose other than that for which it was given to them.

Consent

A person's or group's agreement based on adequate knowledge and understanding of relevant material, to participate in research.

Discomfort

A negative accompaniment or effect of research, less serious than harm.

RECUKM

Human Research Ethics Committee.

Justice

Regard for the human sameness shared by all human beings, expressed in a concern for fairness or equity. Includes three aspects of justice: procedural justice, involving fair methods of making decisions and settling disputes; distributive justice, involving fair distribution of the benefits and burdens of society; and corrective justice, involving correcting wrongs and harms through compensation or retribution.

Monitoring

The process of verifying that the conduct of research conforms to the approved proposal.

Non-identifiable data

Data that have never been labeled with individual identifiers or from which identifiers have been permanently removed, and by means of which no specific individual can be identified. A subset of non-identifiable data are those that can be linked with other data so it can be known they are about the same date subject, although the person's identity remains unknown.

Non-therapeutic (intervention)

An intervention not directed towards the benefit of the individual but rather towards improving scientific knowledge or technical application, or the benefits of others.