Short Review: Implementation of Biomedical Ethics in Malaysia

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ABSTRACT: This literature review focuses on the implementation of biomedical ethics in Malaysia based on the government and institutional settings. Insights of the development of biomedical ethics and the responsible entities, particularly the clinical trials that become the emerging field of interest by the government to boost the biomedical research in Malaysia are provided. Some issues and their implications for research and ethical review process in Malaysia are also elucidated. The review indicates the advancement of policies by the government in implementing the biomedical ethics with some affairs that should be a matter to be concerned.

Keywords: Biomedical, ethics, implementation, standards, research ethic committee, good laboratory practice.

Brief history of biomedical ethics

“In civilised life, law floats in a sea of ethics” by Earl Watson reflects the prerequisite of coexistence of ethics and law (Tomić-Petrović, 2015). Although ethics and law are coexisting but they are not synonymous (Pera, 2011). As science advances, the requirement for ethical and legal control and their continuous review have become an obligation, serving as the guide in research against ethical issues and research misconduct. In this review, we discuss the establishment of biomedical ethics, the principles and its implementation in Malaysia at institutional and national level.
As derived from Greek word, *ethikos*, ethics can be labeled as the various ways of understanding and examining the moral life (Beauchamp and Childress, 2001), besides defining it as the standard or belief of particular group of individuals (Pera, 2011). Through enquiry, the moral dimension of human conduct can be understand which is based on two approaches, normative and non-normative approaches (Beauchamp and Childress, 2001). Within those approaches lie the reasoning that lead to the foundation of morality. Morality derives from Latin *morales* which is about the right or wrong of the human conduct which reflect one’s characters, including the dimension of human decision-making and behavior (Pera, 2011). Literally, morality covers the ‘rights’, ‘responsibilities’ and ‘virtues’ and adjectives such as ‘good’ and ‘bad’ (or ‘evil’), ‘right’ and ‘wrong’, ‘just’ and ‘unjust, thus defining it as the matter of action whereas ethics as the matter of knowing (Williams, 2009).

As years past, the understanding of biomedical research is compounding and implicates the organisms especially the human communities. Here, research ethics serves as guidelines for the responsible conduct of biomedical research by educating and monitoring the scientists and research conduct. Research ethics are defined specifically as *the moral problems encountered in connection with scientific or other academic research, by the researcher, their subjects or their social environment* (Berg, 1983). Some literatures refer bioethics as biomedical ethics explaining that it is a very broad subject, concerning on moral issues raised by advancements of biological sciences (Williams, 2009).

The birth of modern research ethics began with a desire to protect human subjects involved in scientific research. The primary event was started in the end of World War II, with the establishment of Doctors Trial in 1946-1947. The Doctors Trial was a segment of the Nuremberg Trials for Nazi war criminals. In the Doctors Trial, 23 German Nazi physicians were accused of conducting horror and torturous “experiments”. The accused physicians tortured and murdered thousands of victims in the name of science. Some of their experiments involved gathering scientific information about the limits of the human body by exposing victims to extreme temperatures and altitudes. The most cruel and destructive experiments tested how quickly a human could be euthanatised. The experiments that done to the prisoner were conducted without consent. Hence, the doctors who convicted murders were claimed for being unethical researchers. Consequently, a list of ethical guidelines for the conduct of research were developed known as the Nuremberg Code. With ten basic ethical
principles, the guidelines were created in order to satisfy moral, ethical and legal concepts, allowing for permissible medical experiments with justifications (Table 1) (Shuster, 1997; Elnimeiri, 2008).

Table 1: The ten principles in Nuremberg Code (Shuster, 1997; Elnimeiri, 2008)

<table>
<thead>
<tr>
<th>The Nuremberg Code</th>
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<tr>
<td>1. The voluntary consent of the human subject is absolutely essential.</td>
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<td>2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.</td>
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<td>3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.</td>
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<td>4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.</td>
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<td>5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur, except, perhaps, in those experiments where the experimental physicians also serve as subjects.</td>
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<tr>
<td>6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.</td>
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<tr>
<td>7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.</td>
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<tr>
<td>8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.</td>
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<tr>
<td>9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.</td>
</tr>
<tr>
<td>10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probably cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.</td>
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The Nuremberg Guidelines eventually initiated the Helsinki Declaration, developed by the World Medical Association and has been revised and kept updated since 1964, to promote responsible research with human subjects. The document outlines basic ethical principles for conducting biomedical research and specifies guidelines to conduct research either by a physician, as well as medical care, or within a clinical setting. These principles are 1) the importance of good research design formulated in an experimental protocol, 2) qualifications/competence of the research investigator, 3) risk/benefit assessment and balance, 4) informed consent of prospective participants, 5) protection of a legally
incompetent participant or a participant incapable of giving consent, 6) the role of an independent ethical review committee, 7) safeguarding privacy of research participants and confidentiality of research data, 8) ethical obligations of authors and journal editors, and 9) request for public scrutiny and transparency regarding economic incentives involved in research (Bošnjak, 2001). The Helsinki Declaration contains all the basic ethical elements comprised in the Nuremberg Code but then progressively design it further specifically to address five unique vulnerabilities of human subjects solicited to participate in clinical research projects.

Another distinguished research ethics guidelines is Belmont Report of 1978, which is a short form of moral guidelines by National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Beauchamp, 2008). It provides the basic framework with the purpose is to protect subjects and participants in medical research. The three Belmont principles are beneficence, justice, and respect for persons. However, Beauchamp (2008) addressed the limitations in Belmont principles as he introduced the four ethical principles known as Beauchamp and Childress’ Four Principles (Beauchamp and Childress, 2001; Beauchamp, 2003), which are autonomy, beneficence, nonmaleficence and justice (Table 2).

The Nuremberg, Helsinki, and Belmont guidelines provide the foundation of ethically uniform research with stringent rules and consequences for violation. Since then, governmental laws and regulations concerning the conduct of research have been developed for biomedical research that involves both human and animal subjects. It is important to note that the issues concerning research with human subjects involve topics ranging from voluntary participation in research to fair selection and justice.
Table 2: Beauchamp and Childress’ Four Principles (Source: Beauchamp and Childress, 2001; Beauchamp, 2003)

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<th>Beauchamp and Childress’ Four Principles</th>
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<tr>
<td><strong>Autonomy</strong></td>
<td>Individuals should be treated as autonomous agent by respecting their decision-making capacities and affirming them to make reasoned informed choice in self-awareness.</td>
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<td><strong>Beneficence</strong></td>
<td>An obligation to act in ways that promote good by providing benefits. Still, the benefits have to be balanced with deficits to produce the best result.</td>
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<td><strong>Nonmaleficence</strong></td>
<td>The principle require the act of avoiding the causation of harms and inflicting evil as one’s should not cause avoidable or intentional harm. If the harm is unavoidable, it should be balanced to the benefits.</td>
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<td><strong>Justice</strong></td>
<td>People are treated in fairly manner based on the resources and rights</td>
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International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was incepted since 1990 to gather the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration (Baber, 1994). ICH has devised the Good Clinical Practice (GCP) as the international ethical and scientific quality standard that responsible for the designing, implementation, performance, supervision, analyses and reporting of clinical trials (Guideline, 1997) with the aim to ensure that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial subjects are respected and protected.

Since the implementation of the ICH-GCP guidelines, many countries in the Asia-Pacific region realised the need to formulate guidelines of their own based on the framework of the original guideline (Vadivale, 1999). Clinical trials in Malaysia are operated in strict compliance with the ICH-GCP Guideline, which is almost identical to the original ICH-GCP Guideline with very few minor amendments (Ministry of Health, 2004). Compliance with ICH-GCP standards is essential and crucial as the Malaysian ICH-GCP Guideline requires that all investigators to acquire approved GCP training and workshops by the Ministry of Health which implement the original ICH-GCP Guideline.
Everything that constitutes in ethical research is crucial to be understood and implemented when conducting research. Researchers should be familiar and kept updated about the policies and procedures that solely designed to prevent unsystematic or irresponsible research. Research is a public trust which must be handled ethically as it gives impacts to the society. All components of the research project ranging from the project design to result submission for peer review, must be considered ethical and research integrity should be uphold.

**Ethics in clinical trials and biomedical research in Malaysia**

Clinical trial is defined as any research study that prospectively involves human participants or groups of humans to one or more health-related intervention (such as drugs, biological products and devices) to evaluate the effects on health outcomes (World Health Organisation, 2015). Biomedical research is an approach used towards solving medical problems by dealing with the beliefs or theories which can be proven or disproved through observations and experimentation. According to Malaysian Medical Council (MMC), the objectives in clinical trial and biomedical research is to discover or verify the clinical, pharmacological and, or other pharmacodynamics effects of an investigational product(s), including also to identify the adverse reactions, pharmacokinetics and pharmacodynamics of the products without abstaining its safety and efficacy. Prior to humans participation in testing, researchers are required to use animals whose living systems best represent that of humans. Once the safety of a product has been established through animal research, research may then be extended to human beings under very strict protocols and safety net (MMC, 2007).

The clinical research scenario in Malaysia has changed dramatically since 20 years ago. According to the National Pharmaceutical Control Bureau report and National Medical Research Registered (Figure 1), the numbers of clinical trials registered have increased over years after the establishment of the Masters of Medicine and Masters of Surgery programs by local public universities in 1990s such as Universiti Malaya and Universiti Sains Malaysia. These institutions produced more than 3,000 qualified medical specialists who will go through clinical training and also they have to involve in research project for their dissertation.
The government also supports the promotion of Malaysia as a clinical trial hub, thus the Clinical Research Centre (CRC) was introduced under Ministry of Health (MOH) in 2007. In the 8th Malaysian Plan, approximately RM30 million was allocated to the Ministry of Science, Technology and Innovations (MOSTI) for research purposes. The Ministry of Education (MOE) allocated RM100 million into the Fundamental Research Grant Scheme (FRGS) in 2002. This fund was invested to increase the knowledge on the basis and fundamental sciences. In 9th Malaysian Plan also indicated that the main emphasis was to invest in long-term human development in the field of sciences and technology to boost biotechnology and medical sciences in Malaysia (Zabidi-Hussin, 2007).

According to MMC (2007), all proposals on biomedical research including clinical trials involving human participant have to be cleared by the ethics committee prior to initiation of the project. Besides, all studies that require additional investigative testing, invasive procedures, or medication above normal standard practice of medicine also have to review. This is also applied to the questionnaire studies even though it might give only minimal risk.
effect to the participants. All studies using patient data outside of the researcher’s professional custody are also required for reviewing by ethics committee.

Three research standards involve in clinical trials and biomedical research in Malaysia are The Malaysian Guidelines for Good Clinical Practice, The Guidelines for Application of Clinical Trail Import License (CTIL) and Clinical Trial Exemption (CTX) in Malaysia, and The National Institutes of Health (NIH) Guideline for Research conduct in MOH. Nevertheless, there is no law in Malaysia that specifically regulates the running of clinical trials and biomedical research. The only relevant legislation is the Sale of Drugs Act 1952 and Control of Drugs and Cosmetics Regulations 1984. Thus, ethics guidelines are crucial as the main framework to govern biomedical research in Malaysia.

**Implementation of biomedical ethics in Malaysia**

In the wide overview, bioethics signifies the field of ethical enquiry regarding on ethical issues and dilemmas arising from health, health care and research involving humans. In brief, research involving human participants includes any social science, biomedical, behavioural or epidemiological activity that necessitates systematic collection or analysis of data with the intent to generate new knowledge. According to Council for International Organisations of Medical Sciences (CIOMS), the human participants may expose to manipulation, intervention, observation or other interaction with investigators, either directly or through alteration of their environment. In addition, the participants may be individually identifiable through investigators’ collection, preparation or use of biological materials or medical records or other records (CIOMS, 2003).

In medical research, research ethics approval and the requirement for informed consent are critically significant in order to protect human subjects under the ICH-GCP Guideline. Therefore, the ethics review and deliberation are necessary before approval. One of the core principles of ICH-GCP is to warrant a trial to be conducted in compliance with the protocol that has received prior Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approval or favourable opinion (Vijayananthan and Nawawi, 2008). IRB or IEC is research ethics committee (REC) that consist of a group of individuals who commence the ethical review of research protocols involving humans, applying agreed ethical principles. As
participant of GCP, REC is appointed by institution, or if unavailable, the authoritative health body in that country will be responsible (Vijayananthan and Nawawi, 2008). CIOMS in International Ethical Guidelines for Biomedical Research Involving Human Subjects emphasises ethical review committees as the second guideline that is fundamental in biomedical research (Table 3).

**Table 3:** Ethical review committees as the second guideline in International Ethical Guidelines for Biomedical Research involving Human Subjects

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<th><strong>Guideline 2: Ethical review committees</strong></th>
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<td>All proposals to conduct research involving human subjects must be submitted for review of their scientific merit and ethical acceptability to one or more scientific review and ethical review committees. The review committees must be independent of the research team, and any direct financial or other material benefit they may derive from the research should not be contingent on the outcome of their review. The investigator must obtain their approval or clearance before undertaking the research. The ethical review committee should conduct further reviews as necessary in the course of the research, including monitoring of the progress of the study.</td>
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New guidelines have also been devised by World Health Organization (WHO). Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants have been introduced in 2011, which is the revised edition of Operational Guidelines for Ethics Committees that review biomedical research. This guideline has been developed for individuals and organisations involved in health-related research and providing guidance to the REC for ethical reviews and the investigators who design and carry out health research. According to the first standard in the guideline, REC and relevant authorities with adequate legal framework for independent ethics review system of health-related research must be established at national, subnational, and/or institutional (public or private) levels. Nevertheless, the quality and effectiveness of review by REC should always be monitored to ensure that the system is appropriate and sustainable.
Implementation of biomedical ethics in Malaysia at national level

In Malaysia context, medical research is conducted by two settings which are at MOH facilities at national level, and universities or the private sector at institutional level. At the national level, National Institutes of Health (NIH), a network of MOH research institutes, has been established in 2003 with its primary role to conduct and support medical research in Malaysia. In 2005, Secretariat National Institutes of Health (NIHSec) was founded to conduct research management for MOH, with its aim role to process approval prior to conducting research, process applications for research grants, monitor approved research, process approval for publication of research findings, provide consultation on research management, provide liaison with non-MOH agencies, coordinate priority setting, develop research guidelines and procedures, manage contents of NIH web page as well as to document and disseminate research findings. Two important units under NIH are National Medical Research Register (NMRR) and Medical Research Ethics Committee (MREC) where guidelines for conducting research in the MOH institutions and facilities are set. Research commenced by MOH personnel, conducted in MOH facilities or funded by MOH require registration at NMRR, review and approval of the research by a designated entity to whom authority has been delegated for the purpose. Significantly, researches involving human subjects require prior review and approval by the MREC and all research publications by the NIH initially, and thereafter by the Director General of Health Malaysia. In addition, all research presentations (oral and poster) must also obtain approval from the Director General of Health Malaysia prior perusal.

Medical Research Ethics Committee (MREC) is the authority to review all health research involving human subjects that been conducted by MOH researchers and non-MOH researchers using facilities and resources of the MOH. Like other research committees, any reviews by MREC are in accordance to Declaration of Helsinki (2013), besides national and international ethical guidelines for biomedical research involving human subjects such as CIOMS and the Belmont Report. MRES employs guidance from Operational Guidelines for Ethics Committees that review biomedical research/standards and operational guidance for ethics review of health-related research with human participants by WHO, ICH and Malaysian Guidelines for Good Clinical Practice (Malaysian GCP) to design and establish its own standard operating procedure to review and oversee the ethical aspects of research. To
date, there are 40 MREC members from multidisciplinary and multisectoral fields which consists of medical reviewer, scientific reviewer, independent member and lay person. Besides MREC members, MREC is also supported by MREC Secretariat through its administrative roles and Independent Experts, in which the latter is responsible for reflections on specific protocols or requests for advice on specific ethical issues.

One of six research institutes under the NIH is Clinical Research Centre (CRC), a clinical research division of the NIH. CRC is the main clinical research organisation in the country. Through the Clinical Trial Unit (CTU), CRC supports Investigator Initiated Clinical Trials by providing sophisticated facility and equipment, state of the art technology, and the trained human resources such as project managers, epidemiologists, statisticians, information technology professionals and other technical supporting staff skilled in clinical databases and registry operations. In addition, CRC is responsible to organise training, workshops and clinical trial courses in GCP.

Clinical Research Malaysia (CRM), previously under CRC is a government own company which is established under the National Key Economic Area (NKEA) Entry Point Project 2. CRM aims to grow and promote clinical research, and to establish Malaysia as the preferred destination for contract research and clinical trials by attracting foreign investment. CRM manages clinical trials based on Malaysia’s Regulatory and Ethics Committee. The regulatory body that administer clinical trials in Malaysia are National Pharmaceutical Control Bureau (NPCB) and Medical Device Authority (MDA). As there is specific law in Malaysia that regulates the clinical trials, NPCB is given task to ensure the quality, efficacy and safety of pharmaceuticals through the registration and licensing scheme. In addition, universities and private institutions are involved as ethics committee for approving clinical trials in Malaysia.

NPCB involves in National Committee for Clinical Research (NCCR), the organisation that is responsible in establishing policies and plan clinical trial activities in Malaysia. Besides that, NCCR significant roles are to establish the guidelines for accreditation of CRC. Due to strict compliance of clinical trials with ICH-GCP Guideline, NCCR has devised and published the Malaysian version of the ICH-GCP Guideline and Guidelines for Applications to Conduct Drug-Related Clinical Trials in Malaysia. Malaysian GCP has become important guidelines and all public institutions or institutions that receive public funding, require
approval by the guidelines issued by the NCCR. With the Guideline, it is hoped that all drug related clinical trials conducted in Malaysia are in accordance with the highest international ethical and scientific standards while at the same time taking into consideration the national issues and local realities without compromising the standards (MOH, 2011).

Besides ethical guidelines in clinical trials and pharmaceuticals, several research standards were established which are the Guideline on the Use of Human Biological Tissues for Research (2006), Medical Genetics and Genetic Services MMC Guidelines 010/2006, and Checklist for Research on Stem Cell and Cell-Based Therapies.

**Implementation of biomedical ethics in Malaysia at university and research institutions**

Human REC has been established in local public universities and other institutions in Malaysia to create guidelines and doing review for biomedical research that being held in the institutions. For instance, Jawatankuasa Etika Penyelidikan (Manusia), renamed as JEPeM after 2007, was established under School of Medical Science, Universiti Sains Malaysia (USM) in 1987. This organisation was responsible to review and examine research proposals for short and long term research grants. In 1994, this committee was included in vetting on ethical issues on clinical trials. In brief, JEPeM vet and regulate on research involving human subjects, human samples, data derived from humans and also research using products which will be tested on humans. Since 2004, JEPeM has started to do more clinical trials involving international pharmaceutical companies, the Federal-Wide Assurance (FWA) and the Institutional Review Board (IRB). The Committee adopts research ethics guidelines outlined by the Helsinki Declaration agreed by the CIOMS.

In Universiti Malaya (UM), the University Malaya Research Ethics Committee (UMREC) undertakes ethics review of all research involving human participants including funded and unfunded research which is non-medical. The UMREC members conduct ethics review prior to the beginning of any research involving human participants. The committee examines the ethics components of the research such as, sound methodology, possible risks to the subjects, recruitment of subjects, consent from the subjects, confidentiality or anonymity for the subjects, the way in which the data is handled, and how feedback can be provided for the subjects.
In Universiti Putra Malaysia (UPM), human ethics committee was started in 1998 as the Medical Research Ethics Committee but it included the animal ethics committee. After that, the animal ethics committee has been made as an independent committee under the official name of IACUC (Institutional Animal Care and Use Committee). In 2011, The Ethics Committee for Research Involving Human Subjects (JKEUPM) was established under the authority of the Senate of UPM, with the aim to protect research participants and to ensure that the basic principles regarding the use of human subjects are observed in the research. All the decisions and guidance are expressed in the Declaration of Helsinki. JKEUPM is also guided by the National and International Ethical Guidelines for Biomedical Research Involving Human and has the authority to approve, disapprove or modify studies based upon consideration of aspects related to human subject protection. It is also responsible to monitor and oversee the conduct of the study, suspend or terminate the approval of a study also place restrictions on a study.

International Islamic University Malaysia (IIUM) Research Ethic Committee (IREC) was first established in 2004. This committee is responsible to safeguard the interests, rights, dignity, welfare, health and wellbeing of patients and research participants. Following the advice and decision by the ethical principles of the Declaration of Helsinki, The Malaysian Good Clinical Practice Guidelines issued by the Ministry of Health Malaysia, International Ethical Guidelines like the European Convention on Human Rights and Biomedicine 1977 and International Ethical Guidelines for Biomedical Research Involving Human Subjects and also based on the vision and mission of the IIUM, the committee protects the rights and welfare of human participants who take part in research conducted under the auspices of the University. IREC provides guidance to researchers and ensure that research involving persons is carried out safely with considered consent and respect to autonomy and privacy of the subjects.

The Research Ethics committee of Universiti Teknologi MARA (UiTM) was established by the vice chancellor of UiTM in 2004. This committee is currently managed by Research Management Institute (RMI). The objectives of this committee is to examine ethical issues in research proposals and also to ensure that research projects conducted at UiTM are in
compliance with the national and international conditions and guidelines stipulated in the Good Clinical Practice Guideline, MOH, Malaysia and the Declaration of Helsinki, World Medical Association (WMA). REC also protects the rights and wellbeing of human subjects, ensures no intentional harm inflicted on them and protects the rights of the researcher and the university.

Independent Ethic Committee of Ramsay Sime Darby Health Care or IEC RSDHC is the member of clinical research Malaysia. It was established under the Ramsay Sime Darby Health Care Group policies. This committee was constituted of medical professionals and non-medical members with the aim to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and also to provide public assurance of that protection, by reviewing, approving or providing favourable opinion on the trial protocol, the suitability of the investigators, facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects. All the clinical trials that will conduct or review by IEC RSDHC are request to follow the ethical principles based on the Declaration of Helsinki, consistent with GCP and also applicable with Malaysia regulatory requirements.

**Issues on biomedical ethics implementation in Malaysia**

Clinical trials and other facets of biomedical development are enthusiastically been promoted by the government, resulting great increase in the number of industry-sponsored multinational trials in Malaysia. Edis (2013) delineated the clinical trials landscape in Malaysia with ethnically diverse population with high prevalence of ‘first world’ disease, such as coronary artery disease (CAD) and type II diabetes, Malaysia has emerged to be one of preferred destination for clinical research in South East Asia by providing decent quality and lower financial costs compared to other places like Taiwan, Singapore and Hong Kong. The current movement of conducting clinical trials is expanding to developing countries due to several factors such as recognition by Food and Drug Association (FDA) and emergence of the ICG guidelines, low financial costs due to low salaries paid to investigators as well as easy and fast patient recruitment. In addition, CRM provides experienced investigator teams with GCP certificate, thus delivering high quality clinical research. Hence, this scenario
encourages the aim of NIH to attract foreign investment and to make Malaysia as region's preferred clinical trial destination.

The ethical implementation in Malaysia is favours clinical trials due to its transparent review process and short start-up timelines. For instance, a complete application without queries can be approved within 30 working days and the investigator site initiation can be less than three months (Figure 2). Furthermore, there is no national template for clinical trial agreement (CTA). Consequently, the process for review and sign-off of CTAs in Malaysia is relatively fast compared to other countries in the Asia pacific.

![Figure 2](image.png)

**Figure 2:** At the Asia Pacific region, Malaysia has the shortest regulatory and start-up timelines (Elegant, 2013)

There are, nonetheless, limitation issues regarding on the implementation of biomedical ethics in Malaysia. An important reason for the expansion of clinical trials to developing countries is due to increasingly complexity and expensive ethics and research regulatory environment in many developed countries, in contrast to the regulatory regimes in Malaysia which is less complicated with faster approval (Glickman *et al.*, 2009). In addition, this scenario encourages the injection of money and technology from developed countries into local health care system. Although this provides positive impact towards the promotion of Malaysia as clinical trial centre, on the other hand, this reflects the extent of biomedical ethics implementation in handling ethical reviews regarding on clinical trials. Several issues
were highlighted by Kaur (2011) regarding on the impact of globalisation of critical trials and questioning the adequacy of ethics review process in Malaysia.

In order for cooperative international clinical research between the funding institutions (developed countries) and the clinical trial host countries, there are four objectives to be agreed for the bilateral agreements. These include research aims in developing therapeutic, preventive or diagnostic methods targeting health problems that are a priority for the populations of the host countries, the targeted populations are given the possibility to have access to the outcome of the research, the human rights of the participants are respected and it contributes to the development of research capacity of the countries involved (Garrafa et al., 2010).

Due to encouragement of clinical trial industry by Malaysian government, exploitation of vulnerable group resulting human subject protection might be compromised or harmed. Furthermore, the weakening of international normative standard for research such as the latest revisions of the Declaration of Helsinki, 2008 (Garrafa et al., 2010), with some incompetency in ethics guidelines in Malaysia allow the exploitation of human subject to perform clinical trials that has been considered unethical in the developed countries.

An example is the application of placebo-controlled trials in which the efficacy of a new drug is tested against a placebo. This trial is considered to be unethical if there is a known effective treatment for that same condition. It can be a biased issue when the subjects are offered with a placebo in place of an effective treatment. However, placebo-controlled are permitted where no current proven intervention exists. Still, this is unfair as developing countries including Malaysia are unable to afford the proven interventions as standard intervention, hence, permitting the placebo-controlled trials to be conducted (Kaur, 2011).

Although ethics committee has been relatively firmly established in the Malaysian context, the deliberations and decisions made during the course of ethics review may be disputed, whether it can fulfill the role in protecting human subject protection. Besides that, the competencies and lack of training of the research ethics members result in lack of ability to comprehend and construct a meaningful discourse. In addition, the current ethical
frameworks that exist in the local research landscape can be unreliable to provide coherent and workable frameworks for decision-makers and lead to research misconduct (Kaur, 2011).

According to Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants (WHO, 2011), the Standard 5 (Table 4) highlights the requirement of training for the REC.

**Table 4:** Standard 5 of Standards and guidance for entities that establish research ethics committees

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<th>Standard 5: Training the research ethics committee</th>
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<td>Training on the ethical aspects of health-related research with human participants, how ethical considerations apply to different types of research, and how the REC conducts its review of research, is provided to REC members when they join the committee and periodically during their committee service.</td>
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As the GCP workshop that has been mandatory to the investigators, the REC members should be obligated to undergo training, either directly by the appointing entity or through cooperative arrangements with other RECs and/or organisations that provide education on research ethics. However, according to the MREC membership requirements, there is no prerequisite for the members to undergo training, prior or after being appointed as MREC members. As been highlighted by Kaur (2011), formal training that include initial courses and continuous programme, should be compulsory to the REC members.

Standard 5 in the guidelines for entities that establish research ethic committee emphasises that the training should focus on the role and responsibilities of the research and its role vis-à-vis other relevant entities, according to relevant international guidelines such as CIOMS, ICH-GCP, national laws and institutional policies, the full range of ethical considerations relevant to research with human participants, the application of such ethical considerations to different types of research, basic aspects of research methodology and design (for members who lack such background, the impact of different scientific designs and objectives on the ethics of a research study and the various approaches for recognizing and resolving the tensions that can arise among different ethical considerations and modes of ethical reasoning. Therefore, the REC members should also be able to understand the local context in which the
research is being carried out and recognise the particular issues raised by conducting research in Malaysia, which is a developing country that is at the same time, multi-cultural and multi-religious.

Another concern regarding the implementation of biomedical ethics in Malaysia is the conflict of interest and the independence of the local REC, as well as the institutional REC. Standard 4 of the same guideline stresses the independence of REC (Table 5).

**Table 5**: The Standard 4 of Standards and guidance for entities that establish research ethics committees

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<td>Policies governing the REC include mechanisms to ensure independence of the REC’s operations, in order to protect decision making from influence by any individual or entity that sponsors, conducts, or hosts the research it reviews. Such policies provide at a minimum that REC members (including the Chair) remove themselves from the review of any research in which they or close family members have a conflicting interest.</td>
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</table>

It is predicted that the MREC and institutional REC may expose to potential situation of conflicts of interests where employees may feel inclined to make decisions that favour the interests of the institution. In MREC, the committees are made up primarily medical and scientific reviewers, whereas only six layman people are appointed in the committee. This condition may lead the ethical review to be inclined towards personal interests that may influence the committee decisions. In addition, the chairpersons of REC are appointed from high administration of the institution, hence creating potential vulnerability for the committees to make decisions that will favour the interests of the institutions. For instance, more than half of USM JePEM committees are from USM employees while only two members are being appointed as layman people. Furthermore, the Chairperson is appointed by the Vice Chancellor.

According to Standard 2 (Table 6), the lay people and other members, whose primary background is not in health research with human participants, should be appointed in sufficient numbers to ensure that they feel comfortable voicing their views. This is important in order to enhance independence through injection of more lay members drawn from a larger
and more diverse pool of society. Besides that, the employees of the institution carrying out the research should comprise of less than half of the entire membership of the committee (Kaur, 2011). The REC must ensure that the members cannot be pressured by the policy of the senior decision-makers of the entity creating the REC. Instead, the entity that establishes the REC should ensure that REC members are protected from retaliation based on positions taken with respect to REC-related matters or review of research projects.

**Table 6:** The Standard 2 of Standards and guidance for entities that establish research ethics committees

<table>
<thead>
<tr>
<th>Standard 2: Composition of research ethics committees</th>
</tr>
</thead>
<tbody>
<tr>
<td>The research ethics committee (REC) is constituted according to a charter or other document that establishes the manner in which members and the Chair will be appointed. The appointing entity ensures that the REC has a multidisciplinary and multisectoral membership, that it composition is gender balanced, that it reflects the social and cultural diversity of the communities from which research participants are most likely to be drawn, and that it includes individuals with backgrounds relevant to the areas of research the committee is most likely to review.</td>
</tr>
</tbody>
</table>

**Final remarks**

Following the policy makers, government of Malaysia has introduced a number of policies and set up several institutions and research centers to attract foreign sponsors for contract research organization in clinical research. The government’s enthusiasm in making Malaysia as hub for clinical trials might intimate the implementation of biomedical ethics in Malaysia. As been mentioned earlier, the transparent review process in Malaysia might enquire the extent of ethical disclosure between government, investigators, the funding organization and the participants. Another major cause for concern in clinical research is the source of funding and researchers’ conflicts of interest (Buffel du Vaure et al., 2014). In addition, implications of financial relationship among industry, scientific investigators and academic institutions on the presentation and interpretation of clinical trial results might become an ethical issue that should be pondered.
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References


