

GUIDELINE OF THE MALAYSIAN MEDICAL COUNCIL

MMC GUIDELINE 009/2006

CLINICAL TRIALS AND BIOMEDICAL RESEARCH



Malaysian Medical Council

PRELUDE

This Guideline complements, and should be read in conjunction with, the Code of Professional Conduct of the Malaysian Medical Council (MMC) and the Malaysian Guideline for Good Clinical Practice (GCP) of the Ministry Of Health Malaysia (1999) and any other related Guidelines.

In this Guideline, the words “doctor”, “physician”, “medical practitioner” and “practitioner” are used interchangeably, and refer to any person registered as a medical practitioner under the Medical Act 1971. The words “hospital” and “healthcare facility and service” are used interchangeably and refer to any premises in which members of the public receive healthcare services. Words denoting one gender shall include the other gender. Words denoting a singular number shall include the plural and vice versa.

Adopted by the Malaysian Medical Council on 14 November 2006

FOREWORD

The Malaysian Medical Council, with the objective of ensuring that registered medical practitioners are fully aware of the codes of professional medical practice, issues directives and guidelines from time to time. The purpose of these codes, guidelines and directives is to safeguard the patient and members of the public, to ensure propriety in professional practice and to prevent abuse of professional privileges.

The Guidelines are designed to complement, and should be read in conjunction with, the Medical Act and Regulations, Code Of Professional Conduct of the Malaysian Medical Council and other Guidelines issued by the Council or any related organisation, as well as any statute or statutory provisions in force and all related statutory instruments or orders made pursuant thereto.

This Guideline on **Clinical Trials and Biomedical Research** has been prepared with careful attention to details, cognisant of the current international stand on the subject. The draft has been reviewed numerous times by the Malaysian Medical Council includes valuable from individuals, organisations and professional bodies in the country, before formal adoption by the Council.

The Guideline is available in the printed form as well as in the MMC website. Registered medical practitioners are advised to familiarise themselves with the contents, as they will serve as documents to refer to or to seek clarifications from, when they need guidance on matters of professional ethics, codes of professional conduct and medical practice in general.

Tan Sri Datuk Dr. Hj. Mohamed Ismail Merican

MBBS(Mal), MRCP(UK), FRCP(London)(Edinburgh)(Glasgow),

FAMM, FACP(Hon), FRACP(Hon)

President

Malaysian Medical Council

January 2007

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CLINICAL TRIALS & BIOMEDICAL RESEARCH

INTRODUCTION

The genocidal human experimentation during World War II awakened the world's need to lay down strict guidelines on biomedical research and the Nuremberg Code was the fore-runner. The medical profession endorsed the principles embodied in that Code, culminating in the Declaration of Helsinki, drawn up by the World Medical Association in 1964, and revised in 1996, and represents the single essential document of reference for all biomedical research and clinical trials involving human beings.

Excerpts from the Declaration of Helsinki are annexed to this Guideline.

This Guideline on Clinical Trials and Biomedical Research adopts the basic principles outlined by the International Committee on Harmonisation of Good Clinical Practice (ICH-GCP), with modifications to suit the local requirements.

The principles for the establishment of Clinical Trials and Biomedical Research for trial on medical products in human beings was primarily developed and directed towards the pharmaceutical industry.

A properly planned and executed clinical trial is a powerful experimental technique for assessing the effectiveness of an intervention.

The involvement of the human subject in clinical trials of therapeutic agents as well as in interventions of new procedures raises important ethical considerations.

Basic issues range from the relevance of the proposed study, getting approval, insurance and liability, informed consent, as well as proper collection, analysis and complication of data, and subsequently to disposal of the reports.

This Guideline on Clinical Trials and Biomedical Research sets the ethical principles and the code of professional conduct for clinical trials involving human subjects, and outlines the role and functions of an institutional Ethical Committee in regulating the research.

1. BRIEF HISTORY

- 1.1 Biomedical experimentation using human subjects had initially proceeded almost without comment. The researchers justified their activities as benefitting mankind; the subjects were generally happy to ‘oblige’ and to be reasonably recompensed; and research was of manageable quantity. However, it was not long before attitudes and conditions started to change. The reaction against paternalistic medicine gained momentum *pari passu* with an increasing concern for the rights of the individual and the explosive development of new therapeutic agents.
- 1.2 The greatest single impulse to regulate experimentation on human beings sprang from the shocking realisation of the depths to which human dignity was plummeted during the genocidal era of the Second World War. During this period biomedical data of dubious significance were nonchalantly gathered. The sufferings of human victims in experimentation in the prison laboratories had so scarred the human conscience in the post-war years, and the morality of profiting from such results had become an issue needing some control and codification. It was in such circumstances that international codes on the ethics of research were thought to be necessary and were formulated in great urgency to prevent further diabolical travesties on human beings in the guise of research.
- 1.3 The first internationally accepted set of ethical guidelines in this context was known as the Nuremburg Code and was a direct result of the war–crimes trials. There were ten clauses in this Code and researcher and the medical profession soon endorsed the principles expressed in them, which in turn became the basis for the Declaration of Helsinki (which was drawn up by the World Medical Association in 1964 and revised several times

between 1975 and 1996). Since then many national authorities had attempted to explain or expand upon the basic principles established at Nuremburg.

- 1.4 The Royal College of Physicians of London in 1990 and the Medical Research Council of Britain in 1992 and the Council of Europe's Convention on Human Rights and Biomedicine in 1997, further expanded upon the basic principles embodied in the Nuremberg Code. They set out the broad principles under which research may be undertaken on human subjects, including those who are unable to give or incapable of giving consent, and on human embryos.
- 1.5 The International Covenant on Civil and Political Rights, which forms part of the International Bill of Rights, includes the provision:

‘No one shall be subjected to torture or to cruel, inhuman, or degrading treatment or punishment. In particular, no one shall be subjected without his free consent to medical or scientific experiment.’
- 1.6 In the US, the predominant ethical framework for biomedical research was set out by the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research in the Belmont Report in 1979.
- 1.7 The Ethics of Medical Research is addressed in the Malaysian Medical Council Code of Professional Conduct, 1987.

2. THE PHILOSOPHY OF CLINICAL TRIALS AND BIOMEDICAL RESEARCH

- 2.1 Clinical Trials and Biomedical Research should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki (Revised 1996) which lays down “the recommendations guiding physicians in biomedical research involving human subjects” and that are consistent with good clinical practice requirements and the applicable regulatory requirements.

The Declaration of Helsinki, in laying down the Basic Principles in Biomedical Research, states: “Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific tradition.”

- 2.2 Good Practice in Research (GPR) refers to the international ethical and scientific standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials that involve the participation of human subjects.
- 2.3 Compliance with GPR provides public assurance that the rights, safety, well-being and confidentiality of trial subjects are protected, consistent with the principles of the Declaration of Helsinki, and that data and reported result are credible and accurate.
- 2.4 Essential to all the above procedures is the prerequisite inclusion of a good statistical design. This is necessary for two reasons:

- (a) to protect the credibility of the data generated; and
 - (b) to recognise that it is unethical to enlist the cooperation of human subjects in trials which are not adequately designed.
- 2.5 The most significant impact of Clinical Trials and Biomedical Research on medicine is their influence on treatment choices. Reliable knowledge (derived from well designed randomised controlled trials) of which treatments do, or do not, work has become the basis for evidence based practice.

A properly planned and executed clinical trial is a powerful experimental technique for assessing the effectiveness of an intervention.

3. DEFINITION

This Guideline adopts the following definitions:

- 3.1 **“Clinical Trial”** - in which the objective of the trial/research is of essentially diagnostic or therapeutic value to the patient.
- 3.2 **“Biomedical Research”** - an approach used towards solving medical problems. It deals with beliefs or theories which can be proven or disproved through observations and experimentation. Before humans can be asked to participate 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 such animal research, research may then be extended to human beings under very strict protocols and safety net.

There is, however, little conceptual difference between clinical trials and biomedical research in relation to ethical requirements and procedural protocols.

4. THE OBJECTIVES IN CLINICAL TRIAL/BIOMEDICAL RESEARCH

Any investigation in human subjects intended:

- (a) to discover or verify the clinical, pharmacological, and/or other pharmaco-dynamic effects of an investigational product(s); and/or
- (b) to identify any adverse reactions to an investigational product(s); and/or
- (c) to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

It implies a pre-determined protocol with a clearly defined end-point.

5. ETHICAL PRINCIPLES OF RESEARCH ON HUMANS

Research investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in Malaysia as well as applicable international requirements. No national ethical, legal or regulatory requirements should be allowed to reduce or eliminate any of the protections for human subjects.

The Declaration of Geneva of the World Medical Association (1994) binds the physician with the words, “The health of my patients will be my first consideration.”

The International Code of Medical Ethics declares: “A physician shall act only in the patient’s interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient.”

The MMC Code of Professional Conduct covers the ethics of Medical Research in the Section on Neglect or Disregard of Professional Responsibilities, in subsection 1.9 of the Code.

Research involving human subjects raises complex ethical, legal and social issues. Researchers sometimes find that their obligations with respect to a research project come into conflict with their obligations to individual patients. The field of research ethics is devoted to the systematic analysis of such questions to ensure that the study participants are protected and, ultimately, that clinical research is conducted in a way that serves the needs of such participants and of society as a whole.

The ethical conduct of research rests on three guiding principles: respect for persons, beneficence and justice.

Respect for persons implies the duty to obtain informed consent from study participants and to maintain confidentiality on their behalf.

Beneficence demands a favourable balance between the potential benefits and harms of participation.

Justice requires an equitable distribution of the burdens and benefits of research. Researchers must ensure that the vulnerable not be exploited and that eligible candidates who may benefit from participation not be excluded without good cause.

The principle for the establishment of standards of practice for trials on medical products and human beings (biomedical research) was primarily developed and directed towards the pharmaceutical industry, with the objective of improving prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Since then this has also benefited all those who were involved in the generation of clinical data for inclusion in regulatory submission for medical products. Besides, even the best proven prophylactic, diagnostic and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.

6. ETHICS COMMITTEES/ INSTITUTIONAL REVIEW BOARDS FOR RESEARCH

6.1 The philosophy of peer-review

Accountability is a necessary facet of modern society, as much as the ethical conduct of medical practitioners in all areas of practice is a necessary expectation of the public. The minimum standards of professional conduct of registered medical practitioners are assessed by their peers in the profession, assembled as the Malaysian Medical Council. Similarly, medical research is subject to peer-review by Research Ethics Committees (Institutional Review Boards) along guidelines and regulatory procedures laid down by the Malaysian Medical Council.

6.2 Role of the Ethics Committee

The Ethics Committee (Institutional Review Board) is defined as an independent body of medical/scientific professionals and non-medical/non-scientific members that reviews, approves and

provides continuing review of human research/study protocols and amendments, and of the methods and materials to be used in obtaining and documenting consent of the study subjects.

The Ethics Committee is normally appointed by the institution in which the Clinical Trial or Research is conducted, and composed of members who must collectively have the qualifications and experience to review and evaluate the science, medical aspects, and ethics of the proposed study. Review must be independent, competent and timely.

The Committee should be empowered to approve a proposed study, require modification of the study, disapprove the proposed study, suspend or terminate any previously approved study, and approve or disapprove protocol amendments to approved any study.

6.3 Monitoring of studies

The following must be promptly reported to the Ethics Committee in order to reduce /eliminate risk to study subjects:

- All changes to the approved protocol
- All serious adverse events and serious adverse reactions
- All deviations from the approved protocol
- New information that may adversely affect the safety of subjects or the conduct of the trial
- When a study is discontinued prematurely
- When a study is completed

6.4 Ethics Committee Approval

No subject should be admitted to a trial before the Ethics Committee issues a written approval.

No changes to an approved protocol should be initiated without prior written approval of the Ethics Committee, except:

- to eliminate immediate hazard to subjects, and
- when changes are merely logistic or administrative.

7. TYPES OF RESEARCH REQUIRING ETHICAL REVIEW

In principle, studies requiring Ethics Committee clearance can be categorized into:

7.1 All clinical trials and biomedical research involving human subjects, whether patients or healthy volunteers. This refers to any investigation in human subjects intended:

- (a) to discover or verify the clinical, pharmacological, and/or other pharmaco-dynamic effects of an investigational product(s)
- (b) to identify any adverse reactions to an investigational product(s)
- (c) to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of
 - (i) ascertaining its safety and/or efficacy
 - (ii) assessing the utility of any drug or procedure that is not yet accepted in routine medical practice.

- 7.2 All studies requiring additional procedures on human subjects. This refers to studies that require additional investigative testing, or additional invasive procedures, or additional medication over and above the normal standard practice of medicine, even though the tests or procedures or medication involved are not by themselves new.
- 7.3 All questionnaire studies involving patients or their relatives. This is to safeguard unnecessary distress and inconvenience to patients.
- 7.4 All studies using patient data outside of the researcher's professional custody. It is recognized that the medical practitioner is already bound by the Code of Professional Conduct to safeguard the integrity and confidentiality of his own patients' records, and the Code would still apply when any data regarding his patient is included in a research study. Hence, a study based solely on routine data from the practitioner's own patients would not require additional Ethics Committee review. However, if he intends to assess information from records of patients other than his own patients, then such a study should be subject to Ethics Committee review.
- 7.5 During the review of proposed studies, the Ethics Committee would normally give special attention to research that may exploit the unwary or disadvantaged. This includes research:
- (a) involving children, prisoners and adults not competent to give consent,
 - (b) involving the use of genetic material,
 - (c) that may impose an undue disadvantage upon participants.

7.6 Ethics Committee approval is not normally required for

- (a) research solely involving the use of educational tests (cognitive, diagnostic, aptitude, achievement),
- (b) survey procedures, interview procedures and data collection in the public domain, and
- (c) diagnostic and therapeutic procedures that are an accepted part of treatment and are recognized as a current practice by the medical profession.

8. SPECIFIC GUIDELINES FOR THE ETHICAL CONDUCT OF RESEARCH

8.1 Relevance of Proposed Study

A literature search should be made to verify if a similar study had been conducted in other centres and to determine if the method adopted had been fruitful.

It is important that the proposed study is kept relevant to, and focused on, the local scientific and population's needs.

Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and the society. A trial should be initiated and continued only if the anticipated benefits justify the risks posed to participants.

The study must employ scientifically valid design to answer the research question. It would be unethical to conduct human experiments that are inadequately designed (cannot answer the research question)

or address a question of no benefit to society. Such studies impose unnecessary expenditure and unnecessary nuisance or inconvenience to subjects to no benefit.

The study must be conducted honestly. It should be carried out as stated in the approved protocol, and the institution's Ethics Committee has an obligation to ensure that this is the case.

The systems and procedures that assure the quality of every aspect and stage of the trial should be carefully planned and rigorously implemented.

Risks should be reasonable in relation to anticipated benefits and there should be available credible scientific information (such as prior animal studies) to justify the benefits of the study.

8.2 Approval for the Trial.

This refers to the affirmative decision of the Ethics Committee that the clinical trial has been reviewed and may be conducted at the institution (investigational) site within the constraints set forth by the institution, GCP, and the applicable regulatory requirements.

8.3 Qualifications of investigator(s)

Researchers, one or collectively, should be capable and suitable to undertake the study. Studies beyond the capability of the investigators are not likely to be properly conducted or achieve credible results.

8.4 Recruitment of subjects

Consideration should be given to the characteristics of the study population drawn from, the means of contact and recruitment of

research subjects, the inclusion and exclusion criteria, the nature and content of information given to subjects, and any inducements given to subjects. The principles of respect for the person and equitable distribution of the burdens and benefits of research, should always be adhered to.

8.5 Care and protection of subjects (patients/healthy volunteers)

Risks to subjects should be minimized. There should be no unnecessary exposure to risk. There should be supervision and support for research subjects, available rescue mechanisms, and means for the research subjects to contact the investigator(s) whenever necessary. Patient/healthy volunteers taking part in a clinical trial should be satisfactorily insured against any possible injury caused by the trial.

The research plan documentation should also include provisions for privacy of subjects and confidentiality of data. Personal medical information must be respected and protected, in accordance with the MMC Code of Professional Conduct, Good Medical Practice and Confidentiality.

8.6 Insurance and Liability

The liability of the involved parties (i.e. Investigators, sponsors or manufacturer, hospital/clinic, etc) must be clearly explained and understood before the start of a trial of the medicinal product containing an active ingredient.

8.7 Safeguards for vulnerable subjects

When vulnerable groups, such as prisoners, pregnant mothers, mentally disabled, and the economically and educationally

disadvantaged are the participants selected for the research, particular cognisance should be taken of their rights and the safe-guarding of their rights. Special attention is given to situations where the consent from the next of kin, guardian or legal representatives, are sought. Ethical concerns should have priority over legality of such consent.

8.8 Informed consent process

This is a process by which a subject voluntarily confirms his willingness to participate in a particular trial/research, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate, including the purpose of the trial. It should be freely given and documented by means of a written, signed and dated and witnessed.

The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal.

A subject's treatment in a trial without consent may be grounds for legal action on the basis of "unauthorized touching", which is dealt with as assault in criminal law and battery in civil law.

The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.

Information given to potential research subjects should be adequate, complete and understandable. Such information should preferably be documented in a subject information sheet. There should be no coercion or inducements. Informed consent should be properly sought and documented. The person obtaining consent should be identified.

8.9 Cost considerations

Cognisance should be taken of the role of the sponsor, coverage of research costs, coverage for adverse reactions and injuries, and payment for inconvenience to research subjects. While there should be no financial coercion or undue influence on subjects to participate in the study, subjects should not have to bear financial loss or cost because of the research.

Funds provided by sponsor for research should be only utilized for that specific purpose and not diverted to other channels.

8.10 Community considerations

Any special sensitivities of the community towards the study should be considered.

8.11 Time Frame

The time frame, that is the time envisaged that would be taken from the commencement to the conclusion of the trial should be defined and stated, so that workers and participants can allocate their time fruitfully to the completion of the trial, and so that the trial can be monitored.

8.12 Documentation and Adverse Event Reporting

Proper documentation of research findings and monitoring are essential throughout the research period. An Adverse Event is any untoward medical occurrence in a patient or trial subject administered a pharmaceutical product and which does not necessarily have a causal relationship with his treatment. This should be documented and reported to the Ethics Committee, and approval obtained for any change in the protocol or design of the research.

9. THE USE OF PLACEBOS

A placebo is an inert substance without pharmacological action. The use of placebos is occasionally remarkably successful in therapeutics, but the practice is more difficult to justify morally in the experimental situation. The controlled use of a placebo necessarily involves the deception of patients and this raises some complex issues.

The extreme position is that placebos offend against the fundamental rightness of fidelity. When used as a substitute particularly for pain, it may never give the subject any benefit at all for his suffering.

The basic circumstances when placebo trials are ethical and perhaps necessary are:

- a. when there is no alternative to the experimental treatment available – for example it may be right to include a placebo control in the evaluation of a drug intended for the treatment of AIDS, for which there is no known cure, and
- b. when the effect of adding a new treatment to an established one is under study.

In the majority of instances, the purpose of using placebos is to analyse the effect of a treatment on subjective symptoms rather than on organic disease. In such instances, the use of placebos is acceptable.

10. PUBLICATION OF RESULTS

Recognising that publication is the endpoint of research, the Malaysian Medical Council views the following breaches of publication ethics as an extension of research misconduct:

- Publication of fraudulent or forged data
- Plagiarism
- Unjustified authorship
- Duplicate publication
- Copyright infringements

The following steps in the publication of results highlight the above and other important points:

- (a) Upon completion of the trial, the investigator, where required by the applicable regulatory requirements, should inform the institution, and the investigator/institution should provide the sponsor with all required reports, the IRB with a summary of the trial's outcome, and the regulatory authorities with any reports they require.
- (b) Publishing the results in a journal could be a pre-arrangement before the start of the trial with the sponsor and regulatory authorities.
- (c) Study findings must be reported accurately and promptly. Methods, results and conclusions must be recorded completely and without exaggeration to allow interested clinicians to draw reasonable conclusions.
- (d) Study results should be reported quickly to allow physicians timely access to potentially important clinical information.

- (e) In clinical trials involving pharmaceutical preparations, the results whether favourable or unfavourable, should be reported quickly. It is ethically imperative to report adverse or unfavourable results and outcomes, so that the information is available to clinicians using such preparations.
- (f) The temptation to forge data or falsify results or to suppress the truth must be aggressively curbed, as any such behaviour can lead to valueless or even dangerous treatment schedules, with disastrous consequences. When proven, such fraudulent behaviour by researchers may be grounds for disciplinary action.
- (g) When multiple authors are involved in preparing the final report, all authors must be involved in the preparation or revising of the manuscript before submission for publication. However, unjustified authorship may be grounds for disciplinary action.
- (h) All authors must take public responsibility for the research by certifying that the manuscripts represent valid work. Fraud and forgery are serious professional misconduct
- (i) All references to literature and the assistance of research workers should be acknowledged. Plagiarism, which is defined as an intentional verbatim copying of own or other's work without providing appropriate references, is also serious professional misconduct.
- (j) Any benefits or sponsorship received for the conduct of the trial should be stated.
- (k) The publication of research results in the lay media is prohibited, as also duplicate publications in different medical journals.

- (1) Copyright infringements in the publication of the results should be avoided.

11. THE POST TRIAL PERIOD

The investigator shall arrange for the retention of the patient identification codes for at least fifteen (15) years after the completion or discontinuation of the trial.

Patient files and other source data shall be kept for the maximum period of time permitted by the hospital, institution or private practice.

The sponsor or other owner(s) of the data shall retain all other documentation pertaining to the trial as long as the product is authorised (i.e. product's lifetime).

The final report shall be retained by the sponsor or subsequent owner for five (5) years after the product is no longer authorised. [Any change of ownership of the data shall be documented.]

All data and documents shall be made available if and when requested by relevant authorities.

REFERENCE:

1. International Conference on Harmonisation Expert Working Group, (1st May, 1996). ICH Harmonised Tripartite Guideline: Guideline for Good Clinical Practice. For adoption by the Regulatory Bodies of the European Union, Japan and USA.
2. CPMP Working Party on Efficacy of Medical Products, (11 July 1991). Good Clinical Practice for Trial on Medicinal Products in the European Community.
3. Royal College of Physicians London (1990) Research involving Patients
4. Medical Research Council (1992) Responsibility in Investigations on Human Participants and Material and on Personal Information
5. World Medical Association: Declaration of Helsinki, 1996
6. National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research. The Belmont Report (1979 Apr 18) 1-18
7. Malaysian Guidelines for Good Clinical Practice, MOH, 1999
8. Code of Professional Conduct of the Malaysian Medical Council.
9. Good Medical Practice, MMC
10. Confidentiality, MMC

ANNEXURES

EXCERPTS FROM THE DECLARATION OF HELSINKI (REVISED 1996)

1. Introduction

It is the mission of the physician to safeguard the health of the people. His or her knowledge and conscience are dedicated to the fulfillment of this mission.

The Declaration of Geneva of the World Medical Association binds the physician with the words: “The health of any patient will be my first consideration,” and the International Code of Medical Ethics declares that, “A physician shall act only in the patient’s interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient.”

The purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding of the aetiology and pathogenesis of disease.

In current medical practice most diagnostic, therapeutic or prophylactic procedures involve hazards. This applies especially to biomedical research.

Special caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

I. Basic Principles

- a. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific tradition.
- b. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted for consideration, comments and guidance to a specially appointed committee independent of the investigator and the sponsor, provided that this independent committee is in conformity with the laws and regulations of the country in which the research experiment is performed.
- c. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.
- d. Biomedical research involving human subjects cannot be legitimately carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

- e. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
- f. In publication of the results of his or her research, the physician is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principle laid down in this Declaration should not be accepted for publication.
- g. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

II. Medical Research Combined With Professional Care (Clinical Research)

- a. In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgement it offers hope of saving life, re-establishing health or alleviating suffering.
- b. The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.
- c. The refusal of a patient to participate in a study must never interfere with the physician-patient relationship.

- d. The physician can combine medical research with professional care, the objective being the acquisition of a new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

III. Non-therapeutic Biomedical Research Involving Human Subjects (Non-clinical biomedical research)

- a. In the purely scientific application of medical research carried out on a human being, it is the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.
- b. The subjects should be volunteers – either healthy persons or patients for whom the experimental design is not related to the patient's illness.
- c. The investigator or the investigating team should discontinue the research if in his/her judgment it may, if continued, be harmful to the individual.
- d. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject..

EXCERPTS FROM THE CODE OF PROFESSIONAL CONDUCT MMC

Medical Research

In the scientific application of medical research carried out on a human being, it is the duty of the practitioner to remain the protector of the life and health of that person on whom biomedical research is being carried out.

1.9.1 In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The practitioner should then obtain the subject's freely-given informed consent, preferably in writing.

1.9.2 The practitioner can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

1.9.3 A medical practitioner shall use great caution in divulging discoveries or new techniques or treatment through non-professional channels.

1.9.4 The results of any research on human subjects should not be suppressed whether adverse or favourable.

The initial draft of this Guideline on the *Clinical Trials and Biomedical Research* was prepared by Dr. Abdul Hamid Abdul Kadir, Dato MBBS (S'pore) FRCSEd., MChOrth (Liverpool) and Dr. Choy Yew Seng MBBS (Mal), M.Paed (Mal), MRCP (Paed)(Edin)

The members of the Ethics Committee of the Malaysian Medical Council, instrumental in preparing this Guideline, are:

Chairman :

Dr. Abdul Hamid Abdul Kadir, Dato
MBBS (S'pore), FRCSEd., MChOrth (Liverpool)

Members :

Professor Emeritus Datuk Dr. Alexius Delilkan
MBBS (S'pore), FRCA (England), FANZCA (Australia), FAMM

Prof. Dr. Mohd Nizam Isa
PhD (Australia)

Dato' Dr. Mohd Rani Jusoh
MBBS (Mal), FRCP (Edinburgh), FRCP (Ireland)

Dr. Raja Malek bin Raja Jallaludin
MBBS (Mal)

Dr. Ravindran Jegasothy
MBBS (Mal), FRCOG (London), FAMM

Dr. Choy Yew Seng
MBBS (Mal), M.Paed (Mal), MRCP (Paed)(Edin)

Ms. Sharon Kaur Gurmukh
LLB (Hons)(Cardiff), MA (Medical Law & Ethics)(London)