# Medical Research Council of Zimbabwe

Guidelines for Researchers

and

Ethics Review of Committees in Zimbabwe

March , 2004

# Medical Research Council of Zimbabwe

## Definition / Establishment

The Medical Research Council of Zimbabwe, which is the National Ethics Committee (NEC) was established in 1974 in terms of the Research Act of 1959 and Government Notice Number 225 of 1974 in order to provide health researchers and institutions which/in which health research is conducted, with independent ethical advice on research conducted by those researchers or by/within those institutions. The MRCZ is established and supported by the Government of Zimbabwe through the Ministry of Health and Child Welfare. The MRCZ is composed of scientists, medical experts, ethicists, patient representatives, and community representatives. It is independent in its reflection, advice, and decision.

## Objectives

The MRCZ is established in order to among other functions, provide independent guidance, advice, and decision on biomedical research conducted/carried out within Zimbabwe by all researchers and institutions, as well as ethical advice on issues presented to it by the Institutional Ethical Committees that exist within the various health institutions in Zimbabwe. The MRCZ functions similarly to an institutional review board (in USA). The Medical Research Council of Zimbabwe undertakes the following specific tasks:

- To provide guidance, advice, and decision (in the form of 'approval /disapproval') of specific research protocols intended to be conducted in Zimbabwe by all researchers and health institutions.
- To provide ethical guidance and advice on research programmes undertaken by within Zimbabwe.
- To provide ethical guidance and advice on specific ethical issues presented to it by the IERCs and any other interested parties.
- To develop and /or review, as requested, ethical guidelines for Zimbabwe.

The MRCZ is particularly concerned with research that addresses issues that are of relevance to Zimbabwe. The MRCZ presents the conclusions of its reflections to the applicants (Principal Investigators) in the form of an independent decision (approval/disapproval or positive/negative advice).

## Principles and Procedures

The MRCZ recognizes that the protocols it approves may also be reviewed by other ethics committees prior to their implementation in specific localities. In evaluating protocols and ethical issues, the MRCZ is mindful of the laws and practices governing research and medical practice in Zimbabwe as well as international guidelines. It keeps itself informed of the requirements and conditions of research in Zimbabwe regarding the research it considers. The MRCZ also seeks to be informed as appropriate, of the outcome of the research it has approved. The MRCZ is guided in its reflection, advice, and decision by the ethical principles expressed in the Declaration of Helsinki as well as the CIOMS guidelines. It makes further reference to other international and national research guidance documents. In providing assurances of the good functioning of its operations, the MRCZ refers to the Complementary Guidelines for Surveying and Evaluating Ethical Review Practices (WHO TDR) and other guidelines as appropriate. The MRCZ has obtained recognition from the US Office for Human Research Protections (OHRP) and is established and functions in accordance with Zimbabwean Laws.

The MRCZ has established guidelines for researchers and ethics committees based on the Declaration of Helsinki, CIOMS Guidelines and Zimbabwean laws governing the conduct of research. The following statements which may be collectively referred to as the MRCZ Guidelines for Researchers and Ethics Committees (March 2004) are offered as guidance to researchers and research teams engaged in the conduct of health research in Zimbabwe. They are also aimed at assisting ethics committees in Zimbabwe; to ensure that they maintain the highest level of ethical conduct in research conducted within their institutions. These guidelines will be reviewed from time to time as appropriate, as procedures and scientific information are developed in the future. As an aid to researchers and ethics committees, the Declaration of Helsinki and a summary of the CIOMS Guidelines are included at the end of this handbook. Researchers and ethics committees may consult the complete version of the CIOMS guidelines for the full commentaries. The various forms that are used by the MRCZ and affiliated ethics committees are also annexed. These include the following:

- Application to conduct health/medical research MRCZ FORM101
- Application for continuing annual review of research activity MRCZ FORM102
- Request for amendment/modification form MRCZ FORM103
- Adverse event reporting form MRCZ FORM104
- Final report/study termination form MRCZ FORM105
- Reviewers' evaluation form MRCZ FORM106
- Administrative review form MRCZ FORM107

**GENERAL ETHICAL PRINCIPLES**

All research involving human subjects should be conducted in accordance with three basic ethical principles, namely respect for persons, beneficence and justice. It is generally agreed that these principles, which in the abstract have equal moral force, guide the conscientious preparation of proposals for scientific studies. In varying circumstances they may be expressed differently and given different moral weight, and their application may lead to different decisions or courses of action. The present guidelines are directed at the application of these principles to research involving human subjects.

***Respect for persons*** incorporates at least two fundamental ethical considerations, namely:

a) respect for autonomy, which requires that those who are capable of deliberation about their personal choices should be treated with respect for their capacity for self-determination; and

b) protection of persons with impaired or diminished autonomy, which requires that those who are dependent or vulnerable be afforded security against harm or abuse.

***Beneficence*** refers to the ethical obligation to maximize benefits and to minimize harms. This principle gives rise to norms requiring that the risks of research be reasonable in the light of the expected benefits, that the research design be sound, and that the investigators be competent both to conduct the research and to safeguard the welfare of the research subjects. Beneficence further proscribes the deliberate infliction of harm on persons; this aspect of beneficence is sometimes expressed as a separate principle, *nonmaleficence* (do no harm).

***Justice*** refers to the ethical obligation to treat each person in accordance with what is morally right and proper, to give each person what is due to him or her. In the ethics of research involving human subjects the principle refers primarily to *distributive justice*, which requires the equitable distribution of both the burdens and the benefits of participation in research. Differences in distribution of burdens and benefits are justifiable only if they are based on morally relevant distinctions between persons; one such distinction is vulnerability. For the purpose of definition, vulnerability is operationally defined as 'the potential risks

associated with the physical and mental status of an individual which might reasonably be anticipated irrespective of the context in which care is provided'.

Increasingly, vulnerability is being described in terms of potential for exposure to deliberate maltreatment (active) and unintentional or thoughtless acts (passive). There are many risks involved, which mean that the potential for a breach of care is always present and is not restricted to specific care contexts.

All people are potentially vulnerable but, by concentrating on those groups considered to be most at risk of abuse and on raising awareness about vulnerability amongst all carers, it is anticipated that all population groups will benefit. Individuals in the following population groups are considered to be at greatest risk. They apply across all care settings, including the home, and are relevant irrespective of age and/or severity.

- people with limited physical mobility
- people with impaired mental function
- people with learning disabilities
- people with impaired communication
- people with reduced levels of consciousness
- people participating in research
- people with a heightened emotional state
- people caring for individuals in any of the above groups.

The above categories are not mutually exclusive and it is possible that an individual may belong to more than one grouping, even if only temporarily.

***Justice Considerations for research that is sponsored by developed countries*** -Sponsors of research or investigators cannot, in general, be held accountable for unjust conditions where the research is conducted, but they must refrain from practices that are likely to worsen unjust conditions or contribute to new inequities. Neither should they take advantage of the relative inability of low-resource countries such as Zimbabwe or vulnerable populations to protect their own interests, by conducting research inexpensively and avoiding complex regulatory systems of industrialized countries in order to develop products for the lucrative markets of those countries. In general, the research project should leave low-resource communities better off than previously or, at least, no worse off. It should be responsive to their health needs and priorities in that any product developed is made reasonably available to them, and as far as possible leave the population in a better position to obtain effective health care and protect its own health.

Justice requires also that the research be responsive to the health conditions or needs of vulnerable subjects. The subjects selected should be the least vulnerable necessary to accomplish the purposes of the research. Risk to vulnerable subjects is most easily justified when it arises from interventions or procedures that hold out for them the prospect of direct health-related benefit. Risk that does not hold out such prospect must be justified by the anticipated benefit to the population of which the individual research subject is representative.

**What is health research?**

The term "research" refers to a class of activity designed to develop or contribute to generalizable knowledge. Generalizable knowledge consists of theories, principles or relationships, or the accumulation of information on which they are based, that can be corroborated by accepted scientific methods of observation and inference. In the present context "research" includes both medical and behavioural studies pertaining to human health. Usually "research" is modified by the adjective "biomedical" to indicate its relation to health.

Progress in medical care and disease prevention depends upon an understanding of physiological and pathological processes or epidemiological findings, and requires at some time research involving human

subjects. The collection, analysis and interpretation of information obtained from research involving human beings contribute significantly to the improvement of human health.

Research involving human subjects includes:
- studies of a physiological, biochemical or pathological process, or of the response to a specific intervention – whether physical, chemical or psychological – in healthy subjects or patients;
- controlled trials of diagnostic, preventive or therapeutic measures in larger groups of persons, designed to demonstrate a specific generalizable response to these measures against a background of individual biological variation;
- studies designed to determine the consequences for individuals and communities of specific preventive or therapeutic measures; and
- studies concerning human health-related behaviour in a variety of circumstances and environments.

Research involving human subjects may employ either observation or physical, chemical or psychological intervention; it may also either generate records or make use of existing records containing biomedical or other information about individuals who may or may not be identifiable from the records or information. The research may be concerned with the social environment, manipulating environmental factors in a way that could affect incidentally-exposed individuals. It is defined in broad terms in order to embrace field studies of pathogenic organisms and toxic chemicals under investigation for health-related purposes.

Biomedical research with human subjects is to be distinguished from the practice of medicine, public health and other forms of health care, which is designed to contribute directly to the health of individuals or communities. Prospective subjects may find it confusing when research and practice are to be conducted simultaneously, as when research is designed to obtain new information about the efficacy of a drug or other therapeutic, diagnostic or preventive modality. Professionals whose roles combine investigation and treatment have a special obligation to protect the rights and welfare of the patient-subjects. An investigator who agrees to act as physician-investigator undertakes some or all of the legal and ethical responsibilities of the subject's primary-care physician. In such a case, if the subject withdraws from the research owing to complications related to the research or in the exercise of the right to withdraw without loss of benefit, the physician has an obligation to continue to provide medical care, or to see that the subject receives the necessary care in the health-care system, or to offer assistance in finding another physician.

Research with human subjects should be carried out only by, or strictly supervised by, suitably qualified and experienced investigators and in accordance with a protocol that clearly states: the aim of the research; the reasons for proposing that it involve human subjects; the nature and degree of any known risks to the subjects; the sources from which it is proposed to recruit subjects; and the means proposed for ensuring that subjects' consent will be adequately informed and voluntary. The protocol should be scientifically and ethically appraised by one or more suitably constituted review bodies, independent of the investigators.

New vaccines and medicinal drugs, before being approved for general use, must be tested on human subjects in clinical trials; such trials constitute a substantial part of all research involving human subjects. Protocols for such trials are supposed to be submitted for review to both the MRCZ and the Medicines Control Authority of Zimbabwe (MCAZ).

## GUIDELINES ON THE CONDUCT OF RESEARCH IN ZIMBABWE

1. All research projects involving human subjects, whether as individuals or communities, including the use of foetal material, embryos and tissues from the recently dead, supported and undertaken by any institution, researchers or student, wherever conducted within Zimbabwe, shall be reviewed by the Institutional Ethical Review Committee (IERC) at the institution in which it is to be conducted as well as the Medical Research Council of Zimbabwe (MRCZ) before the study begins. The basic responsibilities of ethical review committees are:

- to determine that all proposed interventions, particularly the administration of drugs and vaccines or the use of medical devices or procedures under development, are acceptably safe to be undertaken in humans or to verify that another competent expert body has done so;
- to determine that the proposed research is scientifically sound or to verify that another competent expert body has done so;
- to ensure that all other ethical concerns arising from a protocol are satisfactorily resolved both in principle and in practice;
- to consider the qualifications of the investigators, including education in the principles of research practice, and the conditions of the research site with a view to ensuring the safe conduct of the trial; and
- to keep records of decisions and to take measures to follow up on the conduct of ongoing research projects.

2. The informed consent of all the human subjects participating in your project must be sought before the research activities are initiated. Informed consent is a decision to participate in research, taken by a competent individual who has received the necessary information; who has adequately understood the information; and who, after considering the information, has arrived at a decision without having been subjected to coercion, undue influence or inducement, or intimidation.

   Informed consent is based on the principle that competent individuals are entitled to choose freely whether to participate in research. Informed consent protects the individual's freedom of choice and respects the individual's autonomy. As an additional safeguard, it must always be complemented by independent ethical review of research proposals. This safeguard of independent review is particularly important as many individuals are limited in their capacity to give adequate informed consent; they include young children, adults with severe mental or behavioural disorders, and persons who are unfamiliar with medical concepts and technology.

   *Process.* Obtaining informed consent is a process that is begun when initial contact is made with a prospective subject and continues throughout the course of the study. By informing the prospective subjects**,** by repetition and explanation, by answering their questions as they arise, and by ensuring that each individual understands each procedure, investigators elicit their informed consent and in so doing manifest respect for their dignity and autonomy. Each individual must be given as much time as is needed to reach a decision, including time for consultation with family members or others. Adequate time and resources should be set aside for informed-consent procedures.

   *Language.* Informing the individual subject must not be simply a ritual recitation of the contents of a written document. Rather, the investigator must convey the information, whether orally or in writing, in language that suits the individual's level of understanding. The investigator must bear in mind that the prospective subject`s ability to understand the information necessary to give informed consent depends on that individual's maturity, intelligence, education and belief system. It depends also on the investigator's ability and willingness to communicate with patience and sensitivity.

*Comprehension.* The investigator must then ensure that the prospective subject has adequately understood the information. The investigator should give each one full opportunity to ask questions and should answer them honestly, promptly and completely. In some instances the investigator may administer an oral or a written test or otherwise determine whether the information has been adequately understood.

*Documentation of consent.* Consent may be indicated in a number of ways. The subject may imply consent by voluntary actions, express consent orally, or sign a consent form. As a general rule, the subject should sign a consent form, or, in the case of incompetence, a legal guardian or other duly authorized representative should do so. The ethical review committee may approve waiver of the requirement of a signed consent form if the research carries no more than minimal risk – that is, risk that is no more likely and not greater than that attached to routine medical or psychological examination – and if the procedures to be used are only those for which signed consent forms are not customarily required outside the research context. Such waivers may also be approved when existence of a signed consent form would be an unjustified threat to the subject's confidentiality. In some cases, particularly when the information is complicated, it is advisable to give subjects information sheets to retain; these may resemble consent forms in all respects except that subjects are not required to sign them. Their wording should be cleared by the ethical review committee. When consent has been obtained orally, investigators are responsible for providing documentation or proof of consent.

*Waiver of the consent requirement.* Investigators should never initiate research involving human subjects without obtaining each subject's informed consent, unless they have received explicit approval to do so from an ethical review committee as well as the MRCZ. However, when the research design involves no more than minimal risk and a requirement of individual informed consent would make the conduct of the research impracticable (for example, where the research involves only excerpting data from subjects' records), the ethical review committee and the MRCZ may waive some or all of the elements of informed consent.

*Renewing consent.* When material changes occur in the conditions or the procedures of a study, and also periodically in long-term studies, the investigator should once again seek informed consent from the subjects. For example, new information may have come to light, either from the study or from other sources, about the risks or benefits of products being tested or about alternatives to them. Subjects should be given such information promptly. In many clinical trials, results are not disclosed to subjects and investigators until the study is concluded. This is ethically acceptable if an ethical review committee has approved their non-disclosure.

*Cultural considerations*. In some cultures an investigator may enter a community to conduct research or approach prospective subjects for their individual consent only after obtaining permission from a community leader, a council of elders, or another designated authority. Such customs must be respected. In no case, however, may the permission of a community leader or other authority substitute for individual informed consent. In some populations the use of a number of local languages may complicate the communication of information to potential subjects and the ability of an investigator to ensure that they truly understand it. Many people in all cultures are unfamiliar with, or do not readily understand, scientific concepts such as those of

placebo or randomization. Sponsors and investigators should develop culturally appropriate ways to communicate information that is necessary for adherence to the standard required in the informed consent process. Also, they should describe and justify in the research protocol the procedure they plan to use in communicating information to subjects. For collaborative research in developing countries the research project should, if necessary, include the provision of resources to ensure that informed consent can indeed be obtained legitimately within different linguistic and cultural settings.

*Consent to use for research purposes biological materials (including genetic material) from subjects in clinical trials.* Consent forms for the research protocol should include a separate section for clinical-trial subjects who are requested to provide their consent for the use of their biological specimens for research. Separate consent may be appropriate in some cases (e.g., if investigators are requesting permission to conduct basic research which is not a necessary part of the clinical trial), but not in others (e.g., the clinical trial requires the use of subjects' biological materials).

*Use of medical records and biological specimens.* Medical records and biological specimens taken in the course of clinical care may be used for research without the consent of the patients/subjects only if an ethical review committee and the MRCZ have determined that the research poses minimal risk, that the rights or interests of the patients will not be violated, that their privacy and confidentiality or anonymity are assured, and that the research is designed to answer an important question and would be impracticable if the requirement for informed consent were to be imposed. Patients have a right to know that their records or specimens may be used for research. Refusal or reluctance of individuals to agree to participate would not be evidence of impracticability sufficient to warrant waiving informed consent. Records and specimens of individuals who have specifically rejected such uses in the past may be used only in the case of public health emergencies**.**

*Secondary use of research records or biological specimens.* Investigators may want to use records or biological specimens that another investigator has used or collected for use, in another institution in the same or another country. This raises the issue of whether the records or specimens contain personal identifiers, or can be linked to such identifiers, and by whom. If informed consent or permission was required to authorize the original collection or use of such records or specimens for research purposes, secondary uses are generally constrained by the conditions specified in the original consent. Such specimens can only be used for further analysis after obtaining permission from the ethics committee and the MRCZ. Consequently, it is essential that the original consent process anticipate, to the extent that this is feasible, any foreseeable plans for future use of the records or specimens for research. Thus, in the original process of seeking informed consent a member of the research team should discuss with, and, when indicated, request the permission of, prospective subjects as to: i) whether there will or could be any secondary use and, if so, whether such secondary use will be limited with regard to the type of study that may be performed on such materials; ii) the conditions under which investigators will be required to contact the research subjects for additional authorization for secondary use; iii) the investigators' plans, if any, to destroy or to strip of personal identifiers the records or specimens; and iv) the rights of subjects to request destruction or anonymization of

biological specimens or of records or parts of records that they might consider particularly sensitive, such as photographs, videotapes or audiotapes.

**Essentials of informed consent are:**

3.1 **Comprehension** Investigator must ensure that the informed consent is clearly comprehended by the subject / guardian

**3.2 Purpose of research** must be clearly explained.

**3.3 Procedure** In simple word describe the procedure that the subjects would be expected to undergo. Identify any procedures that are experimental/ investigational/ non-therapeutic. Indicate type and frequency of monitoring during and after the study.

**3.4 Length of time** subject is expected to participate. If subject's participation is expected to continue over a long period of time, please indicate that any new information that develops during the study and may affect the subjects' willingness to continue participation will be communicated to them. This would apply even when the intervention/investigation phase of the study has ended but monitoring continues.

**3.5 Benefits** of the research must be shared with/communicated to:

a. Subjects
b. Other study participants
c. Society

In studies evaluating drugs or other products the subjects should be advised as to the availability of the product after discontinuation of the study. Please indicate whether drug would be available to the patients free of cost. If not, kindly specify expected local cost.

3.6 Please specify financial burden to be incurred by the research subject while participating in the study.

3.7 **Explain all foreseeable risks or discomforts** to the subjects. Note this not only includes physical injury, but also possible psychological, social, or economic harm, discomfort, or inconvenience. If risk is unknown, state so.

3.8 **Treatment for adverse experiences** Explain what therapeutic measures would be available to the subjects in case of adverse reactions or injury as a result of being a participant in the study. All research related adverse reactions are the financial responsibility of the researchers.

3.9 **Confidentiality** Describe the extent to which confidentiality of records identifying the subject will be maintained.

3.10 **Person to contact** for answers to questions, or in event of research related injury or emergency.

3.11 Statement that **participation is voluntary** and that refusal to participate will not result in any penalty or any loss of benefits that the person is otherwise entitled to receive.

3.12 Subjects **right to withdraw** from the study at any time.

3.13 How sharing of results with subjects will occur.

3.14 No abbreviations will be used.

Consent document must be clearly written and/or verbally explained so as to be understandable to subjects (local language wherever applicable). The language must

be non- technical (comparable to the language in a newspaper or general circulation magazine), and scientific, technical or medical terms must be plainly defined. It is PI's responsibility to ensure quality of consent procedure.

5 **Medical research** involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person.

**Non-medical research** should be conducted by suitably qualified persons.

6. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy and confidentiality of the patient's information. Minimize the impact of the study on the subject's physical, mental and social integrity.

7. In the conduct of research, the investigator must at all times respect the personality, rights, wishes, beliefs, consent and freedom of the individual subject.

8. Volunteers and patients should be reimbursed for travel and any out of pocket expenses e.g. any wage loss if applicable.

## APPLICATION FORMS

9. The researcher responsible for the ethical and scientific conduct of the research should submit **a typed** application for review of the ethics of proposed biomedical research. The procedure is as follows:

All information and application forms are available from:
Ms O. Zenda/Mr P. Ndebele
MRCZ Secretariat
C/o National Institute of Health (Formely Blair Research Institute)
Cnr Mazowe/J. Tongogara
P O Box Cy573
Causeway
Harare
Zimbabwe
Fax: (263) 4 253 979
Tel: (263) 4 791 792.
E-mail: pndebele@jhsph.edu

## DOCUMENTS FOR SUBMISSION

12. Five copies of the MRCZ/IERC application form (see annexure) should be submitted. Information in the form should be typed.

13. Five copies of full research protocol (clearly identified and dated), together with supporting documents and annexes. The protocol should include all the items relevant to the study/project in question as appropriate. These requirements are also listed in the Application Form [MRCZ Form 101].

- Title of the study;
  A summary of the proposed research in lay/non-technical language.

- A clear statement of the justification for the study, its significance in development and in meeting the needs of the country /population in which the research is carried out;
- The investigators` views of the ethical issues and considerations raised by the study and, if appropriate, how it is proposed to deal with them;
- Summary of all previous studies on the topic, including unpublished studies known to the investigators and sponsors, and information on previously published research on the topic, including the nature, extent and relevance of animal studies and other preclinical and clinical studies;
- A statement that the principles set out in these Guidelines will be implemented;
- An account of previous submissions of the protocol for ethical review and their outcome;
- A brief description of the site(s) where the research is to be conducted, including information about the adequacy of facilities for the safe and appropriate conduct of the research, and *relevant* demographic and epidemiological information about the country or region concerned;
- Name and address of the sponsor;
- Names, address*es*, institutional affiliations, qualifications and experience of the principal investigator and other investigators;
- The objectives of the trial or study, its hypotheses or research questions, its assumptions, and its variables;
- A detailed description of the design of the trial or study. In the case of controlled clinical trials the description should include, but not be limited to, whether assignment to treatment groups will be randomized (including the method of randomization), and whether the study will be blinded (single blind, double blind), or open;
- The number of research subjects needed to achieve the study objective, and how this was statistically determined;
- The criteria for inclusion or exclusion of potential subjects, and justification for the exclusion of any groups on the basis of age, sex, social or economic factors, or for other reasons;
- The justification for involving as research subjects any persons with limited capacity to consent or members of vulnerable social groups, and a description of special measures to minimize risks and discomfort to such subjects;
- The process of recruitment, e.g., advertisements, and the steps to be taken to protect privacy and confidentiality during recruitment;

- Description and explanation of all interventions (the method of treatment administration, including route of administration, dose, dose interval and treatment period for investigational and comparator products used);
- Plans and justification for withdrawing or withholding standard therapies in the course of the research, including any resulting risks to subjects;
- Any other treatment that may be given or permitted, or contraindicated, during the study;
- Clinical and laboratory tests and other tests that are to be carried out;
- Samples of the standardized case-report forms to be used, the methods of recording therapeutic response (description and evaluation of methods and frequency of measurement), the follow-up procedures, and, if applicable, the measures proposed to determine the extent of compliance of subjects with the treatment;
- Rules or criteria according to which subjects may be removed from the study or clinical trial, or (in a multi-centre study) a centre may be discontinued, or the study may be terminated;
- Methods of recording and reporting adverse events or reactions, and provisions for dealing with complications;
- The known or foreseen risks of adverse reactions, including the risks attached to each proposed intervention and to any drug, vaccine or procedure to be tested;
- For research carrying more than minimal risk of physical injury, details of plans, including insurance coverage, to provide treatment for such injury, including the funding of treatment, and to provide compensation for research-related disability or death;
- Provision for continuing access of subjects to the investigational treatment after the study, indicating its modalities, the individual or organization responsible for paying for it, and for how long it will continue;
- For research on pregnant women, a plan, if appropriate, for monitoring the outcome of the pregnancy with regard to both the health of the woman and the short-term and long-term health of the child.
- The potential benefits of the research to subjects and to others;
- The expected benefits of the research to the population, including new knowledge that the study might generate;
- The means proposed to obtain individual informed consent and the procedure planned to communicate information to prospective subjects, including the name and position of the person responsible for obtaining consent;

- When a prospective subject is not capable of informed consent, satisfactory assurance that permission will be obtained from a duly authorized person, or, in the case of a child who is sufficiently mature to understand the implications of informed consent but has not reached the legal age of consent, that knowing agreement, or assent, will be obtained, as well as the permission of a parent, or a legal guardian or other duly authorized representative*;*

- An account of any economic or other inducements or incentives to prospective subjects to participate, such as offers of cash payments, gifts, or free services or facilities, and of any financial obligations assumed by the subjects, such as payment for medical services;

- Plans and procedures, and the persons responsible, for communicating to subjects information arising from the study (on harm or benefit, for example), or from other research on the same topic, that could affect subjects' willingness to continue in the study;

- Plans to inform subjects about the results of the study;

- The provisions for protecting the confidentiality of personal data, and respecting the privacy of subjects, including the precautions that are in place to prevent disclosure of the results of a subject's genetic tests to immediate family relatives without the consent of the subject;

- Information about how the code, if any, for the subjects' identity is established, where it will be kept and when, how and by whom it can be broken in the event of an emergency;

- Any foreseen further uses of personal data or biological materials;

- A description of the plans for statistical analysis of the study, including plans for interim analyses, if any, and criteria for prematurely terminating the study as a whole if necessary;

- Plans for monitoring the continuing safety of drugs or other interventions administered for purposes of the study or trial and, if appropriate, the appointment for this purpose of an independent data-monitoring (data and safety monitoring) committee;

- A list of the references cited in the protocol;

- The source and amount of funding of the research: the organization that is sponsoring the research and a detailed account of the sponsor's financial commitments to the research institution, the investigators, the research subjects, and, when relevant, the community;

- The arrangements for dealing with financial or other conflicts of interest that might affect the judgement of investigators or other research personnel: informing the institutional conflict-of-interest committee of such conflicts of interest; the communication by that committee of the pertinent details of the information to the ethical review committee; and the transmission by that

committee to the research subjects of the parts of the information that it decides should be passed on to them;

- The time schedule for completion of the study;
- For research that is to be carried out in a developing country or community, the contribution that the sponsor will make to capacity-building for scientific and ethical review and for biomedical research in the host country, and an assurance that the capacity-building objectives are in keeping with the values and expectations of the subjects and their communities;
- Particularly in the case of an industrial sponsor, a contract stipulating who possesses the right to publish the results of the study, and a mandatory obligation to prepare with, and submit to, the principal investigators the draft of the text reporting the results;
- In the case of a negative outcome, an assurance that the results will be made available, as appropriate, through publication or by reporting to the drug registration authority;
- Circumstances in which it might be considered inappropriate to publish findings, such as when the findings of an epidemiological, sociological or genetics study may present risks to the interests of a community or population or of a racially or ethnically defined group of people;
- A statement that any proven evidence of falsification of data will be dealt with in accordance with the policy of the sponsor to take appropriate action against such unacceptable procedures.
- A statement of agreement to comply with ethical principles set out in relevant guidelines.
- All significant previous decisions (e.g., those leading to a negative decision or modified protocol) by other MRCZ/IERCs or regulatory authorities for the proposed study (whether in the same location or elsewhere) and an indication of modification(s) to the protocol made on that account. The reasons for previous negative decisions should be provided.
- Specify the cost of management directly related to the study and indicate what portion of the cost would be incurred by the study participants.
- The researcher should also declare any personal and institutional benefits (monitory or otherwise including travel) accrued through study participation.
- Please also specify benefits of the study to the funding agency or sponsors if any.
- The research protocol should indicate that there is compliance with the principles of Helsinki Declaration (Appended). In case of conflict kindly specify the particular clause, which is being contravened.

12. A registration fee is payable on submission of a research proposal for review. This can be paid in cash or cheques payable to the Medical Research Council of Zimbabwe (MRCZ).
13. Proposals by foreign-based researchers have to be submitted through the Research Council of Zimbabwe, including a registration fee of US$500,00 payable to the Research Council of Zimbabwe.
14. Documentary evidence of institutional support and clearance will help to expedite

approval of proposals.

15. For research involving the testing of drugs and medical devices, permission also has to be sought from the Medicines Control Authority of Zimbabwe.
16. A 1% research levy (administration and monitoring fee) based on overall research budget is payable to the MRCZ for approved projects.

**MRCZ decisions on submitted protocols**

10. The MRCZ meets every second Thursday of the month.

11. The deadline for submission of the application is one month prior to the next meeting.
14. Applications will be acknowledged and researchers shall be informed of the review date. The researchers shall also be communicated regarding the incompleteness of an application. This will obviously delay the review process.
15. The outcome of review shall be communicated to the researchers within a week after the MRCZ/IERC meeting.
16. In cases where the MRCZ/IERC requests supplementary information or changes to documents from the applicant, such information should be provided at least a week before the next meeting.
17. In cases where clarification is sought and researchers fail to respond within 3 months, MRCZ/IERC will send a reminder and allow a further 3 months period for response. Beyond these 6 months, the file will be closed.
18. Researcher may be asked to present their studies or respond to issues raised in the meeting if required.

## APPROVAL CONDITIONS

19. Approval is given for a specified period. If the project takes longer than the specified period to complete, a request for an extension of the ethics clearance should be sought. After this date, the project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the MRCZ Offices, should be submitted one month before the expiration date for continuing review.
20. Approval is given on condition that any alterations proposed to the approved protocol are submitted to the Committee for approval prior to the alterations being effected. Prior MRCZ and IERC approval using standard forms obtainable from the MRCZ Offices is required before implementing any changes in the Protocol (including changes in the consent documents).
21. Approval is given on condition that a copy of the research project final report is lodged with the Ethics Committee for its information.
22. Approval is given subject to researchers notifying the Ethics Committee if and when a project is curtailed, terminated or completed. On termination of a study, a report has to be submitted to the MRCZ using standard forms obtainable from the MRCZ Offices.
23. Approval is given for therapeutic trials subject to the principal investigator notifying the Ethics Committee within seven (7) days of any adverse event or occurrence that takes place during that trial. All serious problems having to do with subject safety must be reported to the Institutional Ethical Review Committee (IERC) as well as the MRCZ within 10 working days using standard forms obtainable from the MRCZ Offices.
24. Research could be audited by MRCZ/IERC during the research period to ensure compliance with guidelines.

**References:**

1. International Ethical Guidelines for Biomedical Research Involving Human Subjects Prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO), Geneva 1993.

2. Institutional Review Board Guidebook, National Institutes of Health, USA Year 2000.
3. Operational Guidelines for Ethics Committees that Review Biomedical Research, World Health Organization, Geneva 2000.

**Appendix 2**

Initiated: 1964

17.C
Original: English

# WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

## Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly
Helsinki, Finland, June 1964
and amended by the
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
and the
52nd WMA General Assembly, Edinburgh, Scotland, October 2000

## A. INTRODUCTION

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects**.** Medical research involving human subjects includes research on identifiable human material or identifiable data.

2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.

3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my 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."

4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.

6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.

7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.

8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

## B. BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH

10. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.

11. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.

12. Appropriate 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.

13. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

14. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.

15. Medical 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 consent.

16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

17. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.

18. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.

19. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.

20. The subjects must be volunteers and informed participants in the research project.

21. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient’s information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. 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. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

23. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or

may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.

24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.

25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.

26. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.

27. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

## C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE

28. The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.

29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.

30. At the conclusion of the study, every patient entered into the study should be assured of access to the best-proven prophylactic, diagnostic and therapeutic methods identified by the study.

31. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.

32. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

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## Council for International Organizations of Medical Sciences (CIOMS) 2002

*Guideline 1: Ethical justification and scientific validity of biomedical research involving human beings*

The ethical justification of biomedical research involving human subjects is the prospect of discovering new ways of benefiting people's health. Such research can be ethically justifiable only if it is carried out in ways that respect and protect, and are fair to, the subjects of that research and are morally acceptable within the communities in which the research is carried out. Moreover, because scientifically invalid research is unethical in that it exposes research subjects to risks without possible benefit, investigators and sponsors must ensure that proposed studies involving human subjects conform to generally accepted scientific principles and are based on adequate knowledge of the pertinent scientific literature.

*Guideline 2: Ethical review committees*

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.

*Guideline 3: Ethical review of externally sponsored research*

An external sponsoring organization and individual investigators should submit the research protocol for ethical and scientific review in the country of the sponsoring organization, and the ethical standards applied should be no less stringent than they would be for research carried out in that country. The health authorities of the host country, as well as a national or local ethical review committee, should ensure that the proposed research is responsive to the health needs and priorities of the host country and meets the requisite ethical standards.

*Guideline 4: Individual informed consent*

For all biomedical research involving humans the investigator must obtain the voluntary informed consent of the prospective subject or, in the case of an individual who is not capable of giving informed consent, the permission of a legally authorized representative in accordance with applicable law. Waiver of informed consent

is to be regarded as uncommon and exceptional, and must in all cases be approved by an ethical review committee.

*Guideline 5: Obtaining informed consent: Essential information for prospective research subjects*

Before requesting an individual's consent to participate in research, the investigator must provide the following information, in language or another form of communication that the individual can understand:

1. that the individual is invited to participate in research, the reasons for considering the individual suitable for the research, and that participation is voluntary;

2. that the individual is free to refuse to participate and will be free to withdraw from the research at any time without penalty or loss of benefits to which he or she would otherwise be entitled;

3. the purpose of the research, the procedures to be carried out by the investigator and the subject, and an explanation of how the research differs from routine medical care;

4. for controlled trials, an explanation of features of the research design (e.g., randomization, double-blinding), and that the subject will not be told of the assigned treatment until the study has been completed and the blind has been broken;

5. the expected duration of the individual's participation (including number and duration of visits to the research centre and the total time involved) and the possibility of early termination of the trial or of the individual's participation in it;

6. whether money or other forms of material goods will be provided in return for the individual's participation and, if so, the kind and amount;

7. that, after the completion of the study, subjects will be informed of the findings of the research in general, and individual subjects will be informed of any finding that relates to their particular health status;

8. that subjects have the right of access to their data on demand, even if these data lack immediate clinical utility (unless the ethical review committee has approved temporary or permanent non-disclosure of data, in which case the subject should be informed of, and given, the reasons for such non-disclosure);

9. any foreseeable risks, pain or discomfort, or inconvenience to the individual (or others) associated with participation in the research, including risks to the health or well-being of a subject's spouse or partner;

10. the direct benefits, if any, expected to result to subjects from participating in the research

11. the expected benefits of the research to the community or to society at large, or contributions to scientific knowledge;

12. whether, when and how any products or interventions proven by the research to be safe and effective will be made available to subjects after they have completed their participation in the research, and whether they will be expected to pay for them;

13. any currently available alternative interventions or courses of treatment;

14. the provisions that will be made to ensure respect for the privacy of subjects and for the confidentiality of records in which subjects are identified;

15. the limits, legal or other, to the investigators' ability to safeguard confidentiality, and the possible consequences of breaches of confidentiality;

16. policy with regard to the use of results of genetic tests and familial genetic information, and the precautions in place to prevent disclosure of the results of a subject's genetic tests to immediate family relatives or to others (e.g., insurance companies or employers) without the consent of the subject;

17. the sponsors of the research, the institutional affiliation of the investigators, and the nature and sources of funding for the research;

18. the possible research uses, direct or secondary, of the subject`s medical records and of biological specimens taken in the course of clinical care (See also Guidelines 4 and 18 Commentaries);

19. whether it is planned that biological specimens collected in the research will be destroyed at its conclusion, and, if not, details about their storage (where, how, for how long, and final disposition) and possible future use, and that subjects have the right to decide about such future use, to refuse storage, and to have the material destroyed (See Guideline 4 Commentary);

20. whether commercial products may be developed from biological specimens, and whether the participant will receive monetary or other benefits from the development of such products;

21. whether the investigator is serving only as an investigator or as both investigator and the subject`s physician;

22. the extent of the investigator's responsibility to provide medical services to the participant;

23. that treatment will be provided free of charge for specified types of research-related injury or for complications associated with the research, the nature and duration of such care, the name of the organization or individual that will provide the treatment, and whether there is any uncertainty regarding funding of such treatment.

24. in what way, and by what organization, the subject or the subject`s family or dependants will be compensated for disability or death resulting from such injury (or, when indicated, that there are no plans to provide such compensation);

25. whether or not, in the country in which the prospective subject is invited to participate in research, the right to compensation is legally guaranteed;

26. that an ethical review committee has approved or cleared the research protocol.

*Guideline 6: Obtaining informed consent: Obligations of sponsors and investigators*

Sponsors and investigators have a duty to:

- refrain from unjustified deception, undue influence, or intimidation;

- seek consent only after ascertaining that the prospective subject has adequate understanding of the relevant facts and of the consequences of participation and has had sufficient opportunity to consider whether to participate;

- as a general rule, obtain from each prospective subject a signed form as evidence of informed consent – investigators should justify any exceptions to this general rule and obtain the approval of the ethical review committee (See Guideline 4 Commentary, *Documentation of consent*);

- renew the informed consent of each subject if there are significant changes in the conditions or procedures of the research or if new information becomes available that could affect the willingness of subjects to continue to participate; and,
- renew the informed consent of each subject in long-term studies at pre-determined intervals, even if there are no changes in the design or objectives of the research.

*Guideline 7: Inducement to participate*

Subjects may be reimbursed for lost earnings, travel costs and other expenses incurred in taking part in a study; they may also receive free medical services. Subjects, particularly those who receive no direct benefit from research, may also be paid or otherwise compensated for inconvenience and time spent. The payments should

not be so large, however, or the medical services so extensive as to induce prospective subjects to consent to participate in the research against their better judgment ("undue inducement"). All payments, reimbursements and medical services provided to research subjects must have been approved by an ethical review committee.

*Guideline 8: Benefits and risks of study participation*

For all biomedical research involving human subjects, the investigator must ensure that potential benefits and risks are reasonably balanced and risks are minimized.

- Interventions or procedures that hold out the prospect of direct diagnostic, therapeutic or preventive benefit for the individual subject must be justified by the expectation that they will be at least as advantageous to the individual subject, in the light of foreseeable risks and benefits, as any available alternative. Risks of such 'beneficial' interventions or procedures must be justified in relation to expected benefits to the individual subject.

- Risks of interventions that do not hold out the prospect of direct diagnostic, therapeutic or preventive benefit for the individual must be justified in relation to the expected benefits to society (generalizable knowledge). The risks presented by such interventions must be reasonable in relation to the importance of the knowledge to be gained.

*Guideline 9*: *Special limitations on risk when research involves individuals who are not capable of giving informed consent*

When there is ethical and scientific justification to conduct research with individuals incapable of giving informed consent, the risk from research interventions that do not hold out the prospect of direct benefit for the individual subject should be no more likely and not greater than the risk attached to routine medical or psychological examination of such persons. Slight or minor increases above such risk may be permitted when there is an overriding scientific or medical rationale for such increases and when an ethical review committee has approved them.

*Guideline 10: Research in populations and communities with limited resources*

Before undertaking research in a population or community with limited resources, the sponsor and the investigator must make every effort to ensure that:

- the research is responsive to the health needs and the priorities of the population or community in which it is to be carried out; and

- any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community.

*Guideline 11: Choice of control in clinical trials*

As a general rule, research subjects in the control group of a trial of a diagnostic, therapeutic, or preventive intervention should receive an established effective intervention. In some circumstances it may be ethically acceptable to use an alternative comparator, such as placebo or "no treatment".

Placebo may be used:

- when there is no established effective intervention;

- when withholding an established effective intervention would expose subjects to, at most, temporary discomfort or delay in relief of symptoms;

- when use of an established effective intervention as comparator would not yield scientifically reliable results and use of placebo would not add any risk of serious or irreversible harm to the subjects.

*Guideline 12: Equitable distribution of burdens and benefits in the selection of groups of subjects in research*

Groups or communities to be invited to be subjects of research should be selected in such a way that the burdens and benefits of the research will be equitably distributed. The exclusion of groups or communities that might benefit from study participation must be justified.

*Guideline 13: Research involving vulnerable persons*

Special justification is required for inviting vulnerable individuals to serve as research subjects and, if they are selected, the means of protecting their rights and welfare must be strictly applied.

*Guideline 14: Research involving children*

Before undertaking research involving children, the investigator must ensure that:

- the research might not equally well be carried out with adults;
- the purpose of the research is to obtain knowledge relevant to the health needs of children;
- a parent or legal representative of each child has given permission;
- the agreement (assent) of each child has been obtained to the extent of the child`s capabilities; and,
- a child`s refusal to participate or continue in the research will be respected.

*Guideline 15: Research involving individuals who by reason of mental or behavioural disorders are not capable of giving adequately informed consent*

Before undertaking research involving individuals who by reason of mental or behavioural disorders are not capable of giving adequately informed consent, the investigator must ensure that:

- such persons will not be subjects of research that might equally well be carried out on persons whose capacity to give adequately informed consent is not impaired;
- the purpose of the research is to obtain knowledge relevant to the particular health needs of persons with mental or behavioural disorders;
- the consent of each subject has been obtained to the extent of that person's capabilities, and a prospective subject's refusal to participate in research is always respected, unless, in exceptional circumstances, there is no reasonable medical alternative and local law permits overriding the objection; and,
- in cases where prospective subjects lack capacity to consent, permission is obtained from a responsible family member or a legally authorized representative in accordance with applicable law.

*Guideline 16: Women as research subjects*

Investigators, sponsors or ethical review committees should not exclude women of reproductive age from biomedical research. The potential for becoming pregnant during a study should not, in itself, be used as a reason for precluding or limiting participation. However, a thorough discussion of risks to the pregnant woman and to her fetus is a prerequisite for the woman’s ability to make a rational decision to enrol in a clinical study. In this discussion, if participation in the research might be hazardous to a fetus or a woman if she becomes pregnant, the sponsors/ investigators should guarantee the prospective subject a pregnancy test and access to effective contraceptive methods before the research commences. Where such access is not possible, for legal or

religious reasons, investigators should not recruit for such possibly hazardous research women who might become pregnant.

Guideline 17: Pregnant women as research participants.

Pregnant women should be presumed to be eligible for participation in biomedical research. Investigators and ethical review committees should ensure that prospective subjects who are pregnant are adequately informed about the risks and benefits to themselves, their pregnancies, the fetus and their subsequent offspring, and to their fertility.

Research in this population should be performed only if it is relevant to the particular health needs of a pregnant woman or her fetus, or to the health needs of pregnant women in general, and, when appropriate, if it is supported by reliable evidence from animal experiments, particularly as to risks of teratogenicity and mutagenicity .

*Guideline 18: Safeguarding confidentiality*

The investigator must establish secure safeguards of the confidentiality of subjects' research data. Subjects should be told the limits, legal or other, to the investigators' ability to safeguard confidentiality and the possible consequences of breaches of confidentiality.

*Guideline 19: Right of injured subjects to treatment and compensation*

Investigators should ensure that research subjects who suffer injury as a result of their participation are entitled to free medical treatment for such injury and to such financial or other assistance as would compensate them equitably for any resultant impairment, disability or handicap. In the case of death as a result of their participation, their dependants are entitled to compensation. Subjects must not be asked to waive the right to compensation.

*Guideline 20: Strengthening capacity for ethical and scientific review and biomedical research*

Many countries lack the capacity to assess or ensure the scientific quality or ethical acceptability of biomedical research proposed or carried out in their jurisdictions. In externally sponsored collaborative research, sponsors and investigators have an ethical obligation to ensure that biomedical research projects for which they are responsible in such countries contribute effectively to national or local capacity to design and conduct biomedical research, and to provide scientific and ethical review and monitoring of such research.

Capacity-building may include, but is not limited to, the following activities:

- establishing and strengthening independent and competent ethical review processes/ committees
- strengthening research capacity
- developing technologies appropriate to health-care and biomedical research
- training of research and health-care staff
- educating the community from which research subjects will be drawn

*Guideline 21: Ethical obligation of external sponsors to provide health-care services*

External sponsors are ethically obliged to ensure the availability of;

- health-care services that are essential to the safe conduct of the research,
- treatment for subjects who suffer injury as a consequence of research interventions;

- and, services that are a necessary part of the commitment of a sponsor to make a beneficial intervention or product developed as a result of the research reasonably available to the population or community concerned.