Medical Research Council of Zimbabwe

Conducting Health Research In Zimbabwe: What researchers need to know

August, 2004

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Conducting health research in Zimbabwe

The Medical Research Council of Zimbabwe (MRCZ) regulates the conduct of health research in Zimbabwe. Trials, which involve drugs, biologics and medical devices, are also regulated by the Medicines Control Authority of Zimbabwe (MCAZ), which is a statutory body responsible for the registration of drugs, biologics and medical devices. For such trials, investigators may only proceed with the trial once they obtain approval from both the MRCZ and the MCAZ. The Medical Research Council of Zimbabwe, which also serves as 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 provides independent guidance, advice, and decisions on biomedical research conducted or carried out within Zimbabwe by all researchers and institutions They also provide ethical advice on issues presented to it by the Institutional Ethical Committees (IEC) that exist within the various health institutions in Zimbabwe. The MRCZ functions similar to an institutional review board in USA. The Medical Research Council of Zimbabwe provides the following specific tasks:

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

The MRCZ is particularly concerned with research issues relevant to Zimbabwe. The MRCZ presents the conclusions of its determinations to the applicants (i.e., Principal Investigators) in the form of an independent decision (approval/disapproval or 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. The MRCZ considers the requirements and conditions of research in Zimbabwe when evaluating research proposals. The MRCZ also seeks to be informed, as appropriate, of the outcome of the research it has approved. The MRCZ has established guidelines for the conduct of researchers and ethics

committees based on the Declaration of Helsinki, CIOMS Guidelines and Zimbabwean laws. 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 will assist Zimbabwean ethics committees ensure that they maintain the highest level of ethical conduct in research conducted within their institutions. These guidelines will be reviewed 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 available from the MRCZ Offices as well as on the MRCZ website (www.mrczimshared.co.zw or www.afronets.org/mrcz.php). 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

The MRCZ is guided by the ethical principles expressed in the Declaration of Helsinki as well as the Council for International Organisations of the Medical Sciences (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 (World Health Organisation Tropical Diseases Research) and other guidelines as appropriate. The MRCZ has obtained an assurance recognized by the US Office for Human Research Protections (OHRP) and is established and functions in accordance with Zimbabwean Laws.

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 serving 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;
    - determine that the proposed research is scientifically sound or to verify that another competent expert body has done so;
    - ensure that all other ethical concerns arising from a protocol are satisfactorily resolved both in principle and in practice;
    - 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
    - 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. The information should be approved 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 provided that confidentiality and privacy safeguards have been addressed), 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 an individual's provision of 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 the potential research participants truly understand the consent form information. 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 biological materials (including genetic material) from subjects in clinical trials for research purposes. Consent forms for the research protocol involving clinical-trial subjects should include a separate stand alone section where they may 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:

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

Purpose of research must be clearly explained.

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.

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.

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.

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

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.
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.
Confidentiality Describe the extent to which confidentiality of records identifying the subject will be maintained.
Person to contact for answers to questions, or in event of research related injury or emergency.
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.
Subjects **right to withdraw** from the study at any time.
How sharing of results with subjects will occur.
No abbreviations will be used.

Consent document(s) 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 the PI's responsibility to ensure quality of the consent procedure.

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 (determined by whom??).

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.

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

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

APPLICATION FORMS

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:
The Chairman
Medical Research Council of Zimbabwe
C/o National Institute of Health (Formerly 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: mrcz@mrczimshared.co.zw or mrczimbabwe@yahoo.com or
Website :www.mrczimshared.co.zw or www.afronets.org/mrcz.php

DOCUMENTS FOR SUBMISSION

12. The following documents make up the complete application package that should be submitted to the MRCZ Office. Information in the form should be typed.

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APPLICATION PACKAGE

The Ethical Review Committee presents this following checklist in order to aid investigators in preparing a complete application and to help expedite review. Your cooperation in complying will be greatly appreciated.

Twelve copies of application form duly completed.

Twelve copies of protocol summary (less than 3 pages in length).

Four copies of complete research protocol in general/funding agency format.

Four copies of consent forms in English and local language of the study population.

Four copies of Drug Brochure or any supplementary information (if applicable).

Four copies of Questionnaire being administered during the study (if applicable).

13. FOUR 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 the study participants would incur.
- 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. Contact Details for the Research Council of Zimbabwe are as follows:

The Secretary
Research Council of Zimbabwe
P O Box CY294
Causeway
Harare
Zimbabwe
Tel :+263 4 727562 /68/69
Telex :22141
Fax :+263 4 726860

14. Documentary evidence of local institutional support and clearance will help to expedite approval of proposals submitted by foreign researchers.
15. For research involving the testing of drugs and medical devices, permission also has to be sought from the Medicines Control Authority of Zimbabwe. The MCAZ is contactable on the following address:

The Director General
Medicines Control Authority of Zimbabwe
106 Baines Avenue
P O Box UA 559
Union Avenue
Harare
Zimbabwe
Tel : +263 4 736981-5/ 708255 / 792165
Fax : +263 4 736 980
E-mail :mcaz@africaonline.co.zw

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
The MRCZ meets every second Thursday of the month.

The deadline for submission of the application is one month prior to the next meeting.
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.
The outcome of review shall be communicated to the researchers within a week after the MRCZ/IERC meeting.
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.
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.
Researcher may be asked to present their studies or respond to issues raised in the meeting if required.

APPROVAL CONDITIONS

Approval is given for a specified period of one year or six months depending on the amount of risks involved. 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.

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).

Approval is given on condition that a copy of the research project final report is lodged with the Ethics Committee for its information.

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.

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.

Research could be audited by MRCZ/IERC during the research period to ensure compliance with guidelines.

GUIDELINES FOR INVESTIGATORS CONDUCTING RESEARCH WITH CHILDREN

In general, all children who are asked to participate in research studies are expected to give their assent. The following statements and definitions need to be kept in mind:

(1) "Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

(2) "Therapeutic Research" refers to research that holds out the prospect of direct benefit to the individual subject that in only available through participation in the research study.

(3) "Non-therapeutic Research" refers to research that offers no benefit or only indirect benefit to the individual subject; and

(4) "When a community mental health board or agency conducts, participates in, or is the site of research activity with human subjects, this research activity shall comply with the following requirements: An overt refusal to participate by either the adult or child subject or the parent or guardian is to be taken as final."

For non-psychosocial research, the investigators should take into account the ages, maturity, and psychological state of the children involved when the parents or guardians consent and the child dissents. Greater weight should be given to the child's dissent when the research is non-therapeutic.

SPECIFIC REQUIREMENTS

For children 13 years old to 17 years old

For both therapeutic and non-therapeutic research involving children 13 years old to 17 years old, the investigator can use the Informed Parental Consent Form that the parents or guardians are signing. Following the parent's signature portion, a separate paragraph should be added which includes at least the following statement.

> My participation in this research study is voluntary. I have read and understood the above information, asked any questions which I may have and have agreed to participate. I will be given a copy of this form to keep.

_____

Name of Subject Ages 13 to 17

_____

Signature of Subject Ages 13 to 17

For children between the ages of 7-12 a distinction is made between therapeutic and non-therapeutic research.

Non-therapeutic Research:

In addition to the consent form which the parents sign, a separate assent form is needed. This form should be brief. Depending on the research study, it will probably be between one paragraph and one page. It should be in simplified language, appropriate for the 7-12 age group; it should sketch what is involved for the child/subject; and, it should emphasize the voluntary nature of the study.

Therapeutic Research:

In addition to the consent form which the parents sign, the child's assent should be obtained in one of two ways.

1. As above, the investigator may have the child sign a separate assent form. This form should be brief. Depending on the research study, it will probably be between one paragraph and one page. It should be in simplified language, appropriate for the 7-12 age group, and it should sketch what is involved for the child/subject.
2. The alternate procedure will involve a single paragraph following the consent form and the signature of the parent. It should read as follows: "I have discussed this clinical research study with the child using language which is understandable and appropriate. I believe I have fully informed this participant of the nature of the study and its possible risks and benefits. I believe the participant understood this explanation and assented to participate in this study."

   This statement should be signed by the physician/investigator and by a witness.

In circumstances when a specific child is not capable of providing assent and the prospect of therapeutic benefit is great, a request may be made to the IRB to waive consent.

Requirements for Permission by Parents or Guardians:

Unless the MRCZ determines otherwise, the permission of one parent is sufficient when:

1) the MRCZ finds that no more than minimal risk is present; or,
2) the MRCZ finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit to the individual subject.

Both parents must give their permission when:

1) research involves greater than minimal risk and no prospect of direct benefit to individual subject, but likely to yield general knowledge about the subject's disorder or condition; or,

2) research that is not otherwise approvable but which presents an opportunity to understand, prevent or alleviate a series of problems affecting the health or welfare or children, UNLESS one parent is deceased, unknown, incompetent or not reasonably available or when only one parent has responsibility for the care and custody of the child.

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.

Operational Guidelines for Ethics Committees that Review Biomedical Research, World Health Organization, Geneva 2000.