

**South African
Medical Research Council
Ethics Committee**

**STANDARD OPERATING
PROCEDURES**

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1. THE MRC ETHICS COMMITTEE

1.1 MRC RESEARCH

The MRC subscribes to the values enshrined in the Constitution of the Republic of South Africa, Act No 108 of 1996: human dignity, the achievement of equality and the advancement of human rights and freedoms.

All research sponsored by the MRC must be of the highest ethics standard. No research will be sponsored without approval from the MRC Ethics Committee.

1.2 THE ROLE OF THE MRC ETHICS COMMITTEE

The MRC Ethics Committee functions as the official Ethics Committee of the MRC. It is registered with the National Health Research Ethics Council (NHREC) in South Africa and in the USA with the Office for Human Research Protections (OHRP) as follows:

NHREC: registration number **REC-050809-22**

OHRP: Federalwide Assurance number **FWA00002753**, expires 27 April 2013 and institutional review board **IRB00001569**, expires 12 July 2013.

The objective of the Committee in reviewing biomedical research is to contribute to safeguarding the dignity, rights, safety and well-being of all actual or potential research participants and to ensure that the goals of research do not override the health, well-being, and care of research participants.

The Committee aims to provide independent, competent, and timely review of the ethics of proposed studies.

The Committee is multi-disciplinary and multi-sectorial in composition, with relevant scientific expertise, balanced age and gender distribution, and laypersons representing the interests and the concerns of the community. The Committee functions according to *Ethics in health research: principles, structures and processes*, Department of Health, 2004.

1.3 THE FUNCTIONS OF THE MRC ETHICS COMMITTEE

- Reviewing all intramural and extramural research proposals and protocols to ensure that research conducted will be to promote health, and/or prevent disease and/or disability and cure disease.
- Ensuring that humans involved in research are treated with respect and dignity and that their well-being is not compromised.
- Ensuring that the research has value and that it is scientifically sound.

- Ensuring that informed consent is obtained.
- Granting approval where research proposals and protocols meet ethics standards.

No participant may be enrolled on a study before the Committee issues its written approval.

No deviations from, or changes to the protocol, increasing risk to participants and/or affecting significantly the conduct of the research, should be initiated without prior written approval from the Committee, except when necessary to eliminate immediate hazards to participants or when the change(s) involves only logistical or administrative aspects of the research. The Committee must be informed immediately of any new information that may adversely affect the safety of the participants or the conduct of the research.

1.4 MEMBERSHIP OF THE MRC ETHICS COMMITTEE

The Committee consists of members who, collectively, have the qualifications and experience to review and evaluate the science, health aspects and ethics of the proposed research.

1.4.1 Composition

Committee members include (according to *Ethics in health research: principles, structures and processes*, Department of Health, 2004):

- A chairperson
- at least nine members, with five members constituting a quorum
- at least one member whose primary area or interest is in a non-scientific area
- members of both genders and not more than 70% either male or female
- at least two lay members not currently involved in medical, scientific or legal work and who are preferably from the community
- at least one member with knowledge of and experience in the areas of research that are regularly considered by the Ethics Committee
- at least one member with knowledge and experience in professional care or treatment of people
- at least one member who has professional training in both qualitative and quantitative research methodologies

- at least one member who is legally trained

1.4.2 Appointment of new members

(CVs of the Committee members are available on request.)

- The Board of the MRC appoints the members of the Committee for a term of 5 years.
- Only members who participate in the review and discussion will vote/provide their opinion and/or advice.
- The Ethics Committee may invite non-members with expertise in special areas for assistance.
- The investigator may provide information on any aspect of the protocol, but will not participate in the deliberations of the Ethics Committee or in the vote/opinion of the Ethics Committee.

1.4.3 Quorum requirements

- At least **50%+1** members are required to compose a **quorum**.
- No **quorum** will consist entirely of members of **1 (ONE)** profession or **1 (ONE)** gender.
- A **quorum** will include at least **1 (ONE)** member whose primary of expertise is in a non-scientific area.
- All members must be independent of the institution.

The Committee will ensure that their members receive initial and continued education in research ethics and science, and are kept aware of current issues and developments in the broad area of ethics and science.

1.4.4 Conflict of interest

Committee members may have no undisclosed conflict of interest with sponsors and must disclose actual, apparent or potential conflicts of interest to the Committee. Each member will be required to sign a *conflict of interest agreement*.

1.4.5 Confidentiality

All matters pertaining to the documents reviewed will be kept confidential by all members of the Committee and will not be distributed to a third party, unless required by law.

All members will sign a confidentiality agreement regarding meeting deliberations, applications, and information on research and related matters.

1.5 MEETINGS

- Meetings will be held every last Monday of the month from February to November.
- The meetings for the months of February, May, August, and November will be held in Cape Town at the MRC offices at 10:00.
- The meetings in March, April, June, July, September, and October will be held as teleconferences at 14:00.
- All documentation must be submitted **NO LATER** than **AT LEAST 15 (fifteen) working days** before the scheduled date of the meeting.

1.6 AGENDA

The agenda will list the protocols, major amendments, annual status reports, serious adverse event reports and responses to queries to be discussed, and will be sent to the members, together with the study documents. The final agenda will be sent to members approximately **5 (five)** working days before the meeting.

1.7 REVIEW AND APPROVAL PROCEDURES

The Ethics Committee will consider all aspects of the design of the protocol and must be satisfied that the research is scientifically sound, that it has value, that there is a favourable risk-benefit ratio and that the research participants will be treated with respect.

All Committee members will participate on an equal basis in a democratic open deliberation process regarding the science of the protocol, the risks and benefits, the value of the research, the fair participant selection and the informed consent document and any other ethical issues.

The Ethics Committee may approve, require amendment to, or reject a research proposal on ethics grounds.

Decisions are recorded in writing and will include reasons for rejection.

In considering a research protocol, the Committee may seek assistance from experts, but the Committee must be satisfied that such experts have no conflicts of interest in relation to the research project under consideration.

No member of the Committee will be allowed to adjudicate on research in which that member has any conflict of interest in relation to the research project under consideration.

A research proposal must include a statement of the ethics considerations involved in the proposed research. The Committee must be satisfied that the research protocol gives adequate consideration to participants' welfare, rights, beliefs, perceptions, customs and cultural heritage.

Research proposals for health research to be conducted in community settings must include a clear plan on how the communities will be consulted or involved in the research process, and how in general they are to be kept informed.

The process of how informed consent will be obtained should be included in the protocol. Special attention should be paid on how it will be ensured that the participants understand and appreciate the information provided.

Communication between the Ethics Committee and the investigators committees should be directed through the Principal Investigator.

All PhD and Masters degrees that are sponsored in full or in part by the MRC should first obtain approval from the Research Ethics Committee where the degree will be obtained, before the application is sent to the Ethics Committee for approval.

All documents and other material used to inform potential research participants must be approved by the Committee, including plain-language information sheets, consent forms, questionnaires, advertisements and letters.

The applicant will be informed of the approval, conditional approval or disapproval via letter, or in some cases email, within **15 (fifteen)** working days after the meeting. No verbal feedback will be given.

1.8 EXPEDITED REVIEW PROCEDURES

The Committee will review certain categories of research through an expedited procedure if the research involves not **more than minimal risk to the participants**, and for final approval of **minor changes to research**. The expedited review may be carried out by the chairperson of the Committee or by one or more designated, experienced reviewers from among the Committee members. The decisions will be ratified by the full Committee during the next meeting.

In general, research with potential to cause physical or psychological harm will not be considered for expedited review. This includes research with medications, research involving invasive procedures and research involving sensitive personal or cultural issues.

1.9 RECORDING OF DECISIONS

The Committee maintains a record of all research protocols received and reviewed.

The Committee will retain on file a copy of each research protocol and application submitted for approval. The file will include information sheets, consent forms and relevant correspondence, all in the form in which they were approved. A list will be kept of the Committee members who were present during discussion of the application and when the final decision of the Committee was reached.

1.10 MONITORING

The Committee has the responsibility to ensure that the conduct of all research approved by them is monitored. The Committee requires annual reports from the Principal Investigator after which annual re-approval will be given for the study to continue.

All monitoring reports must be submitted to the Committee.

The Committee will adopt any additional appropriate mechanisms for monitoring, including random inspection of research sites, data and signed consent forms and records of interviews, with the prior consent of research participants, where indicated.

It is required that researchers immediately report anything that might warrant a review of ethics approval of the protocol such as: SAEs, proposed changes in the protocol or unforeseen events that might affect continued ethical acceptability of the project.

Researchers must inform the Committee, giving reasons, if the research project is discontinued before the expected date of completion.

The Committee may ask to review site monitoring reports on an ad hoc basis as part of the monitoring process. The Committee can also monitor high-risk studies on an ad hoc basis.

1.11 COMPLAINTS AND SUSPENSION OR DISCONTINUATION OF RESEARCH

The contact details of the Committee must be available to all research participants and researchers in the event that they wish to forward a complaint. All complaints will be investigated and parties will receive a response from the Committee.

Where the Committee is satisfied that circumstances have arisen that a research project is not being conducted in accordance with the approved protocol and that the welfare and rights of participants are compromised, the Committee may withdraw approval.

The Committee will inform the researcher or sponsor of its action and shall recommend discontinuation or suspension. In such instances, the researcher must discontinue the research and comply with any special conditions required by the Committee.

1.12 ARCHIVING

The Committee will retain **1 (ONE)** set of all submitted documents for a period of at least **15 (FIFTEEN)** years, following the completion of a study.

2. PROTOCOL APPLICATION FOR APPROVAL BY THE MRC ETHICS COMMITTEE

2.1 PRINCIPAL INVESTIGATOR

The Principal Investigator (PI) must be a South African citizen.

The PI must submit an application to the Committee and the Medicines Control Council where applicable. Both of these reviewing institutions must approve the project before the study may commence. PIs bear full responsibility for the scientific and ethics aspects of their study, and are the means of communication with the Ethics Committee while obtaining approval. Once a study is in progress all reports of adverse events and management issues dealt with by the sponsoring company should be transmitted to the Ethics Committee, ideally through the PI, who should be fully informed of these issues.

Researchers in South Africa have the ethical responsibility to ensure that their research is relevant both to the broad health and development needs of the country and to the individual needs of those who suffer from the diseases and concerns under study. The findings of the research must be translatable into mechanisms for improving health status of South Africans.

2.1.1 Clinical trials

A clinical trial may not commence before receiving a national study number from the Department of Health's National Clinical Trials Register.

The information in the South African National Clinical Trials Register should be available publicly, with the reservation that it be limited to information that would not jeopardise commercial interests. It will include:

- Title of research project.
- Duration of the project.
- PI name and affiliation.

A regular update of an anonymised research profile from the database may be placed on the Department of Health's website with information such as:

- The number and proportion of studies by type (for example, trials or non-trials) proportions by study site.
- Total sponsorship by type of study and study site.

The CVs of the PI and co-investigators must be submitted for consideration by the MRC Ethics Committee.

2.2 **NEW PROTOCOL**

An application for review of the ethics of proposed biomedical research should be submitted by a qualified researcher responsible for the ethical and scientific conduct of research.

The following documentation should be submitted to the Ethics Office 15 (fifteen) working days before the next meeting (one unbound hard copy plus an electronic copy emailed to adri.labuschagne@mrc.ac.za):

1. Signed and dated checklist or application form for clinical trials (**see Appendix 1**)
(The clinical trial application form must be signed by ALL applying principal investigators)
2. Letter from the Scientific Review Committee stating that the science of protocol has been reviewed and approved.
3. Protocol of the proposed research (*clearly identified & dated*), together with supporting documents and annexes.
(Provision must be made for a protocol signature page signed by all local principal investigators)
4. A summary, synopsis, or diagrammatic representation (*flowchart*) of the protocol.
5. Diary cards and other questionnaires intended for research participants.
6. Proposed **English** written informed consent form & consent form updates. (*Clearly identified and dated.*)

(Final informed consent document translated in other languages accompanied by a letter from an official translator.)

7. Participant recruitment procedures (e.g. *advertisements*) and any other written information to be provided to participants.
8. Information about payments and compensation available to participants (*including costs to participants for study participation*).
9. The process for obtaining informed consent at the various sites.
10. Details of financial agreements/study budget with investigators **signed and dated**.
11. A motivation for the use of a placebo control (*where applicable*).
12. Post-research treatment explanatory document (*where applicable*).
13. A list of site details including the site address and names of the PI, sub-investigators, study coordinators, registered pharmacists.
14. Investigator's brochure/registered package insert/available safety information.
15. Principal and co-/sub-investigator's current *Curriculum Vitae* in the required format and/or other documentation evidencing qualifications (*updated, signed and dated*) including the signed and dated MCC Declaration by PI.
16. A copy of the insurance certificate covering the protocol. (1 copy)
17. MCC application/approval letter (*if applicable*). (1 copy)
18. South African National Clinical Trials Registration Forms (*if applicable*)

2.3 PROTOCOL AMENDMENT

- All protocol amendments received will be reviewed by the amendment subcommittee and will be tabled as part of the agenda at the next Committee meeting for ratification by the full Committee.
- An amendment is a change that is administrative in nature or has an impact on the safety or integrity of the participants, alters scientific value of the research or interpretation of the results, affects validity of data, the design of the study, planned statistical analyses or significantly alters other aspects of the research. Changes in clinicians or pharmacists on a clinical trial also constitute an amendment, and applications for such amendment should include information on the role and tasks of the persons involved.

The following documentation should be submitted to the Ethics Office **15 (fifteen)** working days before the next meeting:

- i. Application form
- ii. Covering letter
- iii. Synopsis of the approved protocol
- iv. Major protocol amendment
- v. Rationale for the amendment
- vi. Summary of changes made to the protocol
- vii. The English version of the revised informed consent document (incorporating **highlighted** changes made to it) where applicable – all files

2.4 CONTINUING REVIEW / ANNUAL RE-APPROVAL

- Continuing review of research will be conducted at appropriate intervals but **not less than once per year**. Continuing review can be done more frequently if the Committee requests it.
- The Committee must receive an application for annual re-approval at the latest **ONE YEAR after approval by them**.
- For research that will be completed within a year, no continuing review is necessary, but the Committee must be supplied with the **FINAL STATUS REPORT** for each site.
- In conducting continuing review all members will receive and review a protocol summary and a status report on the progress of the research at the sites approved by the Committee.
- Status reports must be completed **per site** and must be signed and dated by the Principal Investigator. The status report should include the following information:
 - i) The number of participants entered **per site**
 - ii) A summary of serious adverse events and unanticipated problems **per site**, including the outcome of the SAEs and their relationship to the study medication
 - iii) The number of withdrawals and the reason for the withdrawals per site
 - iv) Any relevant new information

2.4.1 Submission requirements

The following documentation should be submitted to the Ethics Office 15 (fifteen) working days before the next meeting:

- i. The application form
- ii. Covering letter
- iii. The protocol summary
- iv. The **status report per site**
- iv. All relevant line listings

2.5 RESUBMISSIONS

- i) Major deficiencies will usually result in a refusal to approve the protocol or amendment. A new submission will have to be made.
- ii) Minor deficiencies in the submission of protocol/amendment will result in **conditional approval** with a request for changes or additional information.

2.6. SERIOUS ADVERSE EVENTS AND ADVERSE DRUG REACTION REPORTING

2.6.1 Serious adverse events (SAEs)

- All serious adverse events (all deaths or serious, unexpected, adverse drug reactions which are fatal or life threatening) should be reported electronically and in hard copy to the Committee within **48 (forty eight) hours of becoming aware of the event**. This includes related and unrelated SAEs.
 - All **supporting information related to the SAE** (i.e. follow-up reports, CIOMS reports, etc.) must be forwarded in writing to the Committee within **48 (forty eight) hours** of the sponsor receiving this information. When general abnormalities in participants are reported in SAEs, information on whether they had been exposed to drugs should be included.
- i) A designated SAE Committee consisting of the chairperson and three members of the Committee will review all SAEs.
 - ii) All decisions will be ratified by the full Committee.
 - iii) The Committee will acknowledge receipt of all SAEs in writing.

- Every 3 months a line listing of all SAEs must be submitted to the Committee in the required format, available on the Internet at <http://www.sahealthinfo.org/ethics/c.htm>

At least the following information should be included when an SAE is reported:

- Protocol number
- Protocol title
- Research participant number
- Date of birth of participant
- Event onset date – time of onset
- Diagnosis (most significant SAE being reported)
- Investigator's name
- Study product
- Description of event
- Event outcome
- Action taken with regard to study product
- Treatment
- Causality with study product

2.6.2 Adverse event (AE) reporting

- All adverse events must be reported to the Committee in **line listing** format on an **annual basis** in conjunction with the application for **annual re-approval** (see under SAEs).
- Pertinent safety information must be reported in writing to the Committee as soon as possible.
- **All suspected serious, unexpected adverse drug reaction reports** originating from worldwide clinical sites **outside South Africa** should be reported to the Committee in line listing format on an **annual basis in conjunction with application for annual re-approval.**
 - i) A designated SAE Committee consisting of the chairperson and three members of the Committee will review all AEs.
 - ii) All decisions will be ratified by the full Committee.
 - iii) Line listings will **only** be reviewed during the annual re-approval process and not on a bi-annual basis, unless otherwise specified by the Committee.
 - iv) The Committee will acknowledge receipt of all AEs in writing.

2.7 DOCUMENTS ACKNOWLEDGED BY ETHICS COMMITTEE

The following documents will only be acknowledged by the Committee:

- **Translated** patient information sheets and informed consent forms (certificate of translation must be included)
- **Translated** questionnaires and patient diary cards (certificate of translation must be included)
- **Updated** investigator's brochures (a summary of the changes must be included)

2.8 **PATIENT INFORMATION AND INFORMED CONSENT REQUIREMENTS**

Separate patient information and informed consent documents must be submitted for:

- The main study
- HIV testing
- Pharmacogenetic research
- Tape recording
- Consent for minors between 7 and 18 years

The *Ethics in health research: principles, structures and processes*, Department of Health, 2004 stipulates as follows: "In South Africa, researchers must be particularly aware of the vulnerability of prospective participants in terms of access to health services and education levels. Research details must be provided in a clear, simple and culturally appropriate manner. If a participant lacks capacity to exercise an informed choice to participate, an appropriate person to make the choice for them must be identified by the investigator. A participant is free at any time to withdraw consent to further involvement in the research, without having to face any unfair negative consequence or disadvantage. The following essential elements must be understood and appreciated before a participant is capable of giving informed consent.

- That consent is being given to participate in research.
- The purpose of the research.
- The expected duration of the participant's involvement.
- A description of the procedures to which the participant will be subjected, including any experimental procedures that are innovative and have not been used in medical practice.

Prospective participants should be helped to arrive at an informed decision by, for instance, use of appropriate language, selection of a non-threatening environment for interaction and the availability of peer counselling. Participants may find information about the following points useful:

- The investigators' qualifications.
- Explanation of participants' responsibilities.
- Description of foreseeable risks or discomforts.
- Description of benefits to the participants or to others, both during and after the research.
- Disclosure of alternative procedures or courses of treatment.
- Description of the extent to which confidentiality will be maintained.
- Statement that sponsors of the study may be able to inspect research records.
- Statement that the research has been approved by an accredited research ethics committee.
- Contact details of research ethics committee representatives.
- Explanation as to whether compensation will be given for research-related injuries.
- Explanation as to the consequences of injury, including medical treatments.
- Explanation of who to contact in the event of research-related injury.

Investigators must assure potential participants that participation is voluntary, and that refusal to participate, or a decision to discontinue participation, will not involve any form of penalty. The approximate number of participants should be disclosed. Details of treatment must be supplied and, where appropriate, the possibility of random assignment to various treatments or procedures must be made clear. The nature of experimental and control groups must be explained, as well as circumstances that might lead to the termination of participation. Unforeseeable risks obviously cannot be foreseen, but participants must be told the nature and extent of risks – including financial risks – attendant on participation. Participants must be made aware of their right to be informed of relevant new findings, and of the consequences of their withdrawal from research. They should know, too, whether the investigator might terminate participation.

The above points may be regarded as essential elements of informed consent, and all should be incorporated in an informed consent form or document. Informed consent is a vital requirement in ethical conduct, and is valid only when it is obtained without deceit or misrepresentation. The informed consent requirements are not intended to pre-empt the laws of the country, which may require that additional information be provided to the participants. The moral duties of the medical practitioner or other investigator are in no way limited by these requirements”.

The Committee requires the following information on the **informed consent process with each new application**:

- i. A description of the process for obtaining informed consent, including the process for ascertaining understanding and appreciation of the information provided.
- ii. The adequacy, completeness, and understandability of written and oral information to be given to the research participants, and when appropriate, e.g. for unconscious participants, or participants with Alzheimer, and any other condition where it may be applicable, their

legally acceptable representatives. Clear justification for the intention to include in the research individuals who cannot consent, and a full account of the arrangements for obtaining consent for such individuals.

- iii. Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation.
- iv. The provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project.
- v. In all instances **verbal and written** informed consent should be obtained, unless there are good reasons to the contrary, such as a situation of coma, emergency, or mental incapacity.
- vi. Verbal consent, **where the participant is illiterate**, should be obtained in the presence of and countersigned by a literate, independent **witness confirming that all the relevant information was provided to the research participant in an understandable manner.**
- vii. For **minor participants under the age of 18 years**, consent from the **parent or legal guardian** must be sought.
- viii. Adequate steps should be outlined to obtain the child's **consent**, when the child is judged to be capable of providing such consent. Assent should be sought when in the judgment of the parents and investigator the child is capable of providing their consent (**±7 years**). Maturity, psychological state of mind and age should be taken into account. Special care should be taken to create an informed consent document that will be understandable to minors.

For more information, refer to the Department of Health: 'Ethics in Health Research Principle, Structures and Processes' 2004

2.9 PLACEBO-CONTROLLED STUDIES

As a general rule placebo control will not be allowed by the Committee as research participants in the control group of a research study of a diagnostic, therapeutic, or preventative intervention should receive an **established effective intervention**. However, the Committee will consider placebo-controlled application in the following circumstances:

- i) Where there is no **established effective intervention**.
- ii) When withholding an established effective intervention would expose participants to, at most, **temporary discomfort or delay in relief of symptoms**.

- iii) Use of an established effective intervention as comparator would **not yield scientifically reliable results** and use of placebo would **not add any risk or serious irreversible harm to the participants**.

In all instances where placebo control is suggested, the Committee must receive a separate **motivation for the use of placebo for the submitted application**.

2.10 GENETIC RESEARCH

In the case of human genetic research, the Committee requires a sub-protocol or Appendix to the main protocol, outlining the objectives and procedures to be followed.

The Committee will only allow genetic research within the scope of the protocol (study medication toxicity, metabolism and efficacy and specific disease entity studied within the protocol), i.e. pharmacogenetic research. **No open-ended genetic research will be approved.**

The following will be considered:

- Social and cultural significance of the research.
- The balance between the contribution of knowledge and the potential for harm to individuals or collectives.
- The confidentiality and privacy of stored genetic information or research results relating to identified or potentially identified participants.

The samples should be stored in South Africa. Clear information regarding place and length of storage of samples should be included.

If that is not the case a separate motivation is needed explaining the reasons why it is not possible.

2.10.1 Informed consent

- A separate informed consent for the specific collection of a blood sample for pharmacogenetic research must be submitted.
- This document must contain at least the following information:
 - i) The genetic research will be limited to the medication (specify name) and disease/condition (specify name) under investigation.
 - ii) No unspecified open-ended research will be conducted without prior consent from the participant and approval from the Committee.
 - iii) The costs of the research will be covered by the sponsor.
 - iv) Information on privacy and confidentiality.
 - v) Information on compensation in the event of a study-related injury.
 - vi) If samples are to be exported to a central laboratory outside South Africa, the physical address of this laboratory must be specified.

- vii) The period for which the samples will be stored (maximum 15 years).
- viii) In the consent statement, participants must consent to their samples being shipped to a secure laboratory outside South Africa.

2.10.2 Genetic counselling

- If it is anticipated that participants will receive results from the genetic testing, they should be counselled about the possible consequences of doing so. Reference must be made to the counselling in the consent document.
- Counselling can be provided at the time of obtaining consent or in the future, prior to the provision of feedback, where applicable.

2.11 USE OF HUMAN TISSUE SAMPLES

Where human tissue is to be used in research, researchers and Research Ethics Committees must be satisfied that the research proposal conforms to the principles of ethical conduct and the prescribed regulations of the National Health Act, 61 of 2003:

- Approval must be obtained from the Committee for collecting samples of human material for research.
- New approval must be obtained for all research projects not specifically mentioned when consent was originally obtained

The samples should be stored in South Africa. Clear information regarding place and length of storage of samples should be included.

If samples will not be stored in South Africa, a separate motivation is needed explaining the reasons why it is not possible.

2.12 PUBLICATION OF RESULTS

Investigators have an obligation to disseminate research results, whether positive or negative, in a timely and competent manner. This is particularly important in clinical trials, where investigators are duty bound to ensure that findings are made public for all outcomes assessed. It is, however, important that the release of research findings be done in an ethical manner, to ensure that false expectations are not raised in a vulnerable population. Research results should not be prematurely released or published, or unreasonably delayed. It is advisable that the main results should be disseminated, using appropriate communication formats, to the participants and other interested members of the communities in which the study was conducted.

Results of a study, whether sponsored by government or industry, should be the intellectual property of the investigators, not the sponsor, and all results that have

scientific merit should be published. Requests to withhold findings, to change or tone down the content of a report are not acceptable in good ethics practice. However, sponsors or stakeholders should be afforded the opportunity to comment on research findings prior to publication, without any entitlement to veto, change the conclusions, or unreasonably delay publication of results. In collaborative research with pharmaceutical or other companies, the conditions of publication should be spelt out clearly in the protocol. Research ethics committees should be satisfied that there is no interference with the right to publish results.

2.13 PRESS RELEASES

Investigators have an obligation to communicate research results during press releases in an ethically responsible manner. Press releases of clinical trials approved by the Committee should be submitted to the Committee for approval before it is released.

2.14 ADVERTISEMENTS

Advertisements for recruitment purposes must be submitted to the Committee for review and approval and should comply with the following guidelines:

- The advertisement should be in line with the NHREC template for advertisements.
- The name of the medical practitioner should not appear in the advertisement for study participants, but the particulars of an independent contact person should be given.
- The advertisement may be published in any medium, printed or electronic, including the internet and television, provided all the rules pertaining to advertisements as laid down in this document are adhered to.
- There are no limitations on the size or number of times a notice may be published.
- Details of the clinical research may be published e.g. "A phase II clinical trial in hypertension".
- Purpose of the research and a summary of eligibility criteria.
- Straightforward and truthful description of the benefits to the subject, if any.
- Direct mailing of advertisements is permissible.
- Bulk distribution is not permissible.
- Advertisements may be made available for issue individually to existing patients at the rooms of health care professionals and also at local information centres.

2.15. SPECIAL CLASSES OF PARTICIPANTS

Special consideration will be given to protecting the welfare of special classes of participants, such as children and adolescents, pregnant women, prisoners, people with mental disabilities, people with life-threatening illness, people whose first language is not English, or people from vulnerable communities. Certain types of research will also require special attention and the Committee may impose additional measures to protect the welfare of participants.

The Committee must pay special attention to protecting the welfare of certain classes of participants:

- Minors – children and adolescents
- Persons with intellectual or mental impairment
- Disabled persons
- Persons in dependent relationships
- Persons participating in research as groups (referred to as collectivities)
- Pregnant women
- Prisoners
- People whose first language is not English
- Traumatized and comatose patients
- Terminally ill patients
- Elderly or aged patients
- Minorities
- Students
- Employees

The Committee may impose additional measures to protect the welfare of participants, especially with regard to informed consent.

The Committee may make it mandatory to conduct post-research investigations to review whether there was compliance with the additional measures imposed. If compliance was defective, the Committee may withdraw approval for the research investigation concerned.

Types of research that need additional attention include:

- Research involving indigenous medical systems
- Emergency care research
- Innovative therapy or interventions
- Research necessitating ambiguity of information for participants

Types of research that need additional attention include:

- Research involving indigenous medical systems
- Emergency Care Research
- Innovative Therapy or interventions
- Research necessitating ambiguity of information for participants

For more information, refer to the Department of Health: 'Ethics in Health Research Principle, Structures and Processes' – 2004

2.16 EPIDEMIOLOGICAL RESEARCH

All epidemiological research must be approved by a research ethics committee and should be conducted according to written protocols that state the aims of the study, the data that is required and how the data will be collected, used and protected.

When the Committee considers a protocol for epidemiological research it must be satisfied that:

- The research complies with relevant South Africa legislation or approved policies dealing with the privacy and confidentiality of data.
- Researchers have the necessary facilities and skills in epidemiology to conduct the research.
- Permission should be obtained from principal investigators or custodians of primary data if further research is to be conducted on that data.
- Access to medical or other records for research should be obtained from the custodian of the data according to Access to Information Act - Act 2 of 2000.
- There is a scientifically acceptable process for the disclosure of information and dissemination of research results and, where there is to be selective disclosure of information, that there are scientifically justifiable reasons for doing so.

Informed consent of participants should generally be obtained for the use of identified or potentially identifiable data for all epidemiological research.

3 SUPPORTING DOCUMENTS

The Committee in granting its approval is in compliance with, and must be satisfied that the protocol conforms to the spirit of the following guidelines:

- The World Medical Association Declaration of Helsinki, 2008
- South African Constitution, 1996 (Act No.108 of 1996)
- National Health Act, 2003 (act 61 of 2003)
- Department of Health: *Ethics in Health Research: Principles, Structures and Processes*, 2004
- Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa, 2006
- MRC South Africa: Guidelines on Ethics for Medical Research, 2002
- ICH GCP Harmonised Tripartite Guideline E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95)

- Council for International Organisations of Medical Sciences (CIOMS): International Ethical Guidelines for Biomedical Research Involving Human Participants, 1993
- The Association of the British Pharmaceutical Industry (ABPI) Compensation Guidelines
- FDA Code of Federal Regulations Parts 50, 56 & 312

APPENDIX 1

MRC ETHICS COMMITTEE**New clinical trial application checklist (tick appropriate boxes)**

<input type="checkbox"/>	Covering letter	
<input type="checkbox"/>	Letter of approval from the MRC Scientific Committee	
<input type="checkbox"/>	Completed application form signed by all participating Principal Investigators	
<input type="checkbox"/>	Protocol	Version: Date:
<input type="checkbox"/>	Protocol synopsis (as a separate document)	
<input type="checkbox"/>	Patient information and informed consent document <input type="checkbox"/> Not applicable	Version: Date: Language:
<input type="checkbox"/>	Patient information and informed consent document for collection and storage of genetic material for future use <input type="checkbox"/> Not applicable	Version Date: Language:
<input type="checkbox"/>	Patient information and informed consent document for blood or tissue collection and storage for future use <input type="checkbox"/> Not applicable	Version: Date: Language:
<input type="checkbox"/>	Assent form for minors between 9 and 18 years <input type="checkbox"/> Not applicable	Version: Date: Language:
<input type="checkbox"/>	Consent to perform HIV testing <input type="checkbox"/> Not applicable	Version: Date: Language:
<input type="checkbox"/>	The process for obtaining informed consent at the various sites	
<input type="checkbox"/>	A list of site details, including the site address, names of principal investigators, sub-investigators, study co-ordinators, registered pharmacists and dispensers	
<input type="checkbox"/>	Trial payment schedule per site/ draft financial contract	
<input type="checkbox"/>	Justification document for trial items and procedures that are not financed by the sponsor. Please include costs per item and total out of pocket costs to participant or medical aid/ <input type="checkbox"/> Not applicable	
<input type="checkbox"/>	Post-trial treatment explanatory document <input type="checkbox"/> Not applicable	
<input type="checkbox"/>	Advertisement (s): please submit mediums to be used <input type="checkbox"/> Not applicable	Version: Date:
<input type="checkbox"/>	Justification document for placebo arm <input type="checkbox"/> Not applicable	
<input type="checkbox"/>	Patient questionnaire(s) and/or diary cards; <input type="checkbox"/> Not applicable	Version: Date:

<input type="checkbox"/>	Investigator's brochure(s) <input type="checkbox"/> Not applicable	Drug name(s): Version: Date:
<input type="checkbox"/>	Package inserts(s) <input type="checkbox"/> Not applicable	Drug name(s): Version: Date:
<input type="checkbox"/>	MCC approval letter <input type="checkbox"/> / letter of application <input type="checkbox"/> /Not applicable <input type="checkbox"/>	Date of letter:
<input type="checkbox"/>	NHREC Trial Registration Form	NHREC Reference No:
<input type="checkbox"/>	Curricula Vitae of all investigators (MCC Format)	
<input type="checkbox"/>	Declaration of trialists in MCC format (PI and all sub-investigators)	
<input type="checkbox"/>	Delegation letter from all principal investigators, delegating their responsibility to obtain Committee approval to the sponsor/CRO, where applicable	
<input type="checkbox"/>	Insurance certificate	Valid from: to:

APPLICATION FORM

Applicant details

Applicant name.....

Applicant VAT number:.....

Applicant role: Principal investigator Co-investigator Sub-investigator Sub-investigator Site coordinator Sponsor CRO

Contact person or responsible individual to whom all correspondence to be addressed

.....

Physical Address

.....

Postal Address

.....

Contact details : Telephone Fax

Cell E mail

.....

Have any regulatory responsibilities been delegated to a CRO? No Yes

If yes, provide details below.

Investigator and site details (this information can be supplied in a table format)

To add additional investigators and collaborators, please copy.

Principal investigator name

.....

Sub-investigator name

.....

Site name for conduct of study

.....

Investigator physical address

.....

.....
Investigator postal address

.....
.....
.....

Investigator contact details : TelephoneFax
CellEmail.....

Site physical address
.....
.....
.....

Site postal address
.....
.....
.....

Site contact details : Telephone Fax
.....
Cell
Email.....

If site is within a hospital, provide hospital name
.....

Will any aspect of the study be conducted by the investigator at any locations (sites) other than the above?
 No Yes If yes, complete section "Additional research sites under supervision of Principal Investigator" below

General regulatory information (applicant to complete)

Other ethics committees and regulatory offices to which this specific application is being made:

- Cape Town Free State KwaZulu-Natal MCC Pretoria SAMA
 Stellenbosch Wits
 Other (specify)
.....

For

Submission type: Initial Review Continuing Review Amendment

For amendment, please state prior ethics number assigned by each committee

.....

Committee name

Prior ethics reference number assigned

.....

.....

.....

.....

MCC

An independent MCC submission has been made for:

notification expedited review (bioequivalence) full review (phase 1-3 clinical trials)

No MCC application required:- Registered medications are being used for registered indications

Has this study been denied national regulatory approval in any other country? No

Yes

If yes, list country(ies) and reason provided for denial

.....
.....

Has this study been denied approval by any other ethics committee in South Africa?

No Yes Unknown

If yes, list committee(s) if known and reason provided for denial

.....
.....

Anticipated start date (enrolment of first patient)

.....

Anticipated end date

.....

Anticipated recruitment end date:

.....

Total number of participants to be enrolled for entire study

.....

Total number of study sites for entire study

Trial-specific general details required

Protocol number (sponsor's reference)Version number

MCC approval reference number (if available)..... Not applicable

Version Version date

Protocol title

.....

.....

Brief title

.....

Major disease

Condition

Total number of patients to be enrolled at the site(s)

.....

Trial scope: Single site Multiple site, RSA only Multiple site, multi-national

Trial type: Tick all relevant boxes Randomised Non-randomised

Masking type:- double blind single blind open label

Controls type: Active ingredient standard care placebo

Group assignment: Parallel Cross-over Factorial

Trial phase: Phase 1 Phase 1 & 2 Phase 2 Phase 2 & 3 Phase 3

Phase 4

Intervention type: Unregistered drug Registered drug, new application

Registered drug Device Gene transfer Stem cell Vaccine

Procedure Behavioural

Does the trial involve hospitalisation of patients? No Yes

Recruitment status as at date

Not yet recruiting Recruiting No longer recruiting Completed

Suspended Terminated

Material collected for storage

Will genetic material be collected & stored as part of the protocol? No

Yes

If yes, requires submission of separate informed consent (see checklist)

Will blood or tissues be stored for future use or future testing as part of this trial?

No Yes

If yes, requires submission of separate informed consent (see checklist)

If yes, provide location of storage facility

Name type of specimen to be retained

Placebo arm

Will a placebo be used in this study?: No Yes

If yes, submit justification for placebo use document (see checklist)

Product or procedures not financially covered by the study

Will patients or their medical aids be expected to pay for anything? No

Yes

Is this stated in the informed consent document? No Yes

If patients/medical aids do have to pay for anything, please submit a summary procedure, fee structure and explanation / justification document (see checklist)

Language translations

Additional languages (in addition to English) that subject-related materials will be translated into:

- Afrikaans Zulu Xhosa South Sotho
- Venda Ndebele Pedi Swazi
- Tsonga Tswana

NB: Following approval of original English versions, all translations with authenticity certificates (or other method used to confirm accuracy) must be submitted to the committee for information & filing.

Study-related invasive procedures:

Procedure

- Venipuncture blood sampling
- Arterial blood sampling.
- Biopsy
- Endoscopy
- Radiology procedures
- Radioisotope administration (specify)
 - Does it require radiation control committee approval? Yes No
 - If yes, submit approval document (see checklist)
- Lumber puncture
- Use of bio-hazardous material, please specify
- Other, please specify

Declaration by applicant:

We, the undersigned, have submitted all requested and required documentation, and have disclosed all information which may influence the approval of this application.

We, the undersigned, agree to ensure that if the above-said clinical trial is approved, it will be conducted according to the submitted protocol and South African legal, ethics and regulatory requirements.

Applicant (local contact)

Date

Principal Investigator

Date

Principal Investigator

Date

Ethics Committee secretariat to complete
Assigned Ethics Committee reference number: