University of Zululand Research Ethics Committee (UZREC)

Standard Operating Procedures

1. Terms of ReferenceThe University of Zululand Research Ethics Committees (UZREC) is mandated to fulfil its function by the Senate of the University of Zululand (UNIZULU)
2. The essential purpose of UZREC is to protect the dignity, rights, safety, and well-being of all research participants (human and animal). UZREC will do this through independent, prospective and ongoing ethics review of all research projects undertaken by members of staff, registered students, and affiliates.
3. The definition of health research used by UZREC is in accordance with the SA National Health Act No 61. 2003.
4. UZREC may accept for review research protocols involving participants submitted to it by researchers from other institutions who are not UNIZULU staff members, students, or affiliates.
5. UZREC functions in compliance with, but is not limited to the DoH 2015 guidelines. The guidelines draw on prevailing international, foreign, and national codes of conduct declarations and other documents which are relevant to humans to strengthen processes of transnational research collaboration while taking into account the socioeconomic, ethnic and cultural diversity in South Africa. The guidelines also draw on and refer to international and national standards and guidelines for research using animals. The principal documents which UZREC functions in compliance with are:

- The SA National Health Act. No. 61 of 2003.
- The SA Department of Health (2004) Ethics in health research: Principles, structures and processes and (2006) South African good clinical practice guidelines.

Check other references from policy

B. Appointment and Membership

Appointment

- Members of the University of Zululand Research Ethics Committee (UZREC) are appointed for a period of two years, with a letter of appointment, by the Chairperson of UZREC.
- Members may serve more than one term.
- All members will be asked to sign a non-disclosure agreement.
- UNIZULU will obtain professional liability insurance to cover both affiliated and non-affiliated persons carrying out any professional duties under the auspices of UZREC.

Membership

The composition of UZREC will be in accordance with the provisions of the Department of Health (2015), Ethics in Health Research: Principles, structures and processes (2006) and South African Good Clinical Practice Guidelines. These include:

1. Members of UZREC should collectively have the qualifications, experience and expertise to review and evaluate the scientific, medical, legal, psychosocial and ethical aspects of research proposals.
2. Appointment to the committee will be by nomination and co-option. The total number of committee members must be no less than nine (9.). Members serve on the committee for a period of two years. Membership is renewable for a consecutive period of two years after which a replacement member must be appointed.
3. All members are expected to provide the UZREC administrative office with an abbreviated CV at the beginning of their term.
4. A quorum will be considered present if 50%+1 of the members are present. Alternate members will only count towards a quorum if they are present as a replacement for the main member, and provided that they have produced evidence of research ethics training.
5. Members will be persons of good standing who have a working knowledge of the ethical codes and guidelines mentioned previously.
6. Be representative of the communities it serves and, increasingly, reflect the demographic profile of the population of South Africa; Include members of both genders, although not more than 70% should be either male or female;
7. Include at least one lay person who have no affiliation to the institution, are not currently involved in medical, scientific or legal work and are preferably from the community in which the research is to take place;
8. Include at least one member with knowledge of, and current experience in, areas of research that are likely to be regularly considered by UZREC

9. Include at least one member with knowledge of, and current experience in, the professional care, counselling or treatment of people. Such a member might be, for example, a medical practitioner, psychologist, social worker or nurse);
10. Include at least one member who has professional training in both qualitative and quantitative research methodologies;
11. Include at least one member who is legally trained.
12. Ensure that the membership is equipped to address all relevant considerations arising from the categories of research likely to be submitted to it.
13. Ensure that it is adequately informed on all aspects of a research protocol, including its scientific and statistical validity, that are relevant to deciding whether the protocol is both acceptable on ethical grounds and conforms to the principles of this document.
14. Members not attending 2 consecutive meetings without a valid written reason, and without submitting their reviews, risk termination of their membership of UZREC
15. UZREC members will be required to have continuous personal development in research ethics.
16. UZREC may co-opt expert members and other representatives as voting members as required by particular protocols. Voting status is to be confirmed by the UZREC in advance on a case by case basis.
17. On invitation or request, UZREC meetings may be attended by bona fide students, researchers and other interested parties as non-voting observers, subject to the signing of confidentiality undertaking and subject also to being excluded from certain agenda items as determined by the Chair.
18. **Resignation Process**

19. The member that is resigning will send a letter of resignation to the Chair of UZREC. A new member will be appointed based on the type of membership that is vacant.

C. Ethical Research Application Procedure

- Application forms and guidelines for submission are available on the Research office website. Submissions will be made with the approval of the Deputy dean on the Higher Degrees management system.
- The following documents should be submitted to UZREC

1. Standard Application Form
2. Covering letter (optional, unless an expedited review is requested)
3. Checklist
4. Proposal with:
   4.5.1 Literature review and rationale of the research
   4.5.1 Research Protocol including the approved research instrument such as a questionnaire, question schedule, etc
   4.5.3 Budget
5. Declaration on conflict of interest
6. Signed confidentiality form

Please note:

1. Applications can be submitted on a rolling basis, but must be received a minimum of 2 weeks prior to any specific meeting date to appear in the Agenda of that meeting if this can be accommodated. If not, the application will appear at the next meeting.
2. The supervisor of undergraduate projects will be regarded as the Principal Investigator and the project will be registered under his/her name.
3. The dates of meetings are published in the University of Zululand Calendar.
4. The application will be checked for completeness by the relevant Faculty administrative team. Incomplete applications will be returned to the applicant.

D. Review Process

According to the DoH 2015 guidelines, the review process should entail an independent and objective assessment of the potential effect of the proposed research on potential participants and on the general day-to-day functioning of the infrastructure that provides the site or context for the research.

The review process must ensure that ethical and scientific standards are maintained in order to:
1. Protect participants from harm by weighing the risk of harm against likelihood of benefit by minimising risks of harm to the extent possible and then by balancing the risk of harm relative to the likelihood of benefit
2.Protect the safety and welfare of animals used in research by ensuring close adherence to the expected benchmark.3. Hold researchers accountable for the research activities4.Promote important social and ethical values.

Criteria:
Research studies will be reviewed within the context of aforementioned regulations and guidelines. UZREC, in reviewing a protocol, must consider any and all factors that may influence the scientific validity and ethical acceptability of the protocol.

The following criteria will be used to review projects:

1. **Social and scientific value of project**

UZREC must consider the project to have relevance to the community involved and/or the greater South African and African community.

2. **Scientific validity**

UZREC must ensure that the proposed research is scientifically valid. (Research subjects and volunteers may not, ethically, be exposed to potential risks and burdens where the

project will not generate the intended knowledge). This requirement includes ensuring that the researchers are appropriately qualified to undertake the research.

3. Risk-benefit ratio of project

In order to approve research covered by this policy, UZREC shall determine that all of the following requirements are satisfied:

Risks to participants are minimised:

1. Using procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk, and
2. Whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.

Risks to participants must be reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, UZREC shall consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies participants would receive even if not participating in the research). UZREC shall not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among the research risks that fall within the purview of its responsibility.

When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants.

4. Fair selection of research subjects

1) Selection of participants is equitable. In making this assessment UZREC shall take into account the purposes of the research and the setting in which the research will be conducted and shall be particularly cognisant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, women, mentally disabled persons, or economically or educationally disadvantaged persons.

2) When some or all of the participants are likely to be vulnerable to undue influence or coercion, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these participants.

5. Informed consent process

The DoH guidelines 2015 (section 3 (3.1.9) describes the informed consent process as the process of providing the necessary information and of engaging with the person before a decision is reached.

UZREC assesses the proposed process for informed consent as well as the information that the potential participants will be given and the measures to facilitate understanding.

1) Informed consent will be sought from each prospective participant or the participant's legally authorised representative, in accordance with, and as required by Section E of this document.

2) Informed consent will be appropriately documented, in accordance with, and as required by UZREC policy.

6. Respect for participants

The research protocol demonstrates respect for participants throughout the course of the project e.g. there are adequate provisions to protect the privacy of participants and to maintain the confidentiality and security of data. Participants may withdraw from the study at any time without prejudice etc.

7. Respect for communities

The proposed research demonstrates respect for communities by appropriate community interaction andfeedback of results or findings and how they impact the community..

8. Independent ethics review

UZREC will ensure that all studies adhere to acceptable ethical standards. Independent reviewer(s) will confirm that scientific rigour and principles are not clouded by researchers' interests.

Additional points of note:

1) All health workers submitting protocols for ethics review should be registered with the Health Professions Council of South Africa (HPCSA) or other South African statutory body as appropriate. If not registered with HPCSA or other statutory body, the committee shall, based on the applicant's CV and other documentary submissions, satisfy itself that the applicant is competent to undertake the roles described in the protocol, subject to legal requirements. For non-South African citizens, proof of registration with an equivalent body in their home country and in South Africa will be necessary. Where this is not available, then a motivation and/or other supporting documents from a locally registered person or appropriate authority should accompany the application as evidence of competence.

2) All international collaborative research will have a local principal Investigator.

3) Studies that have a substantial clinical component, where the principal Investigator is not a clinician, s/he should appoint an HPCSA-registered clinician as a co-Investigator to the study.

9. Expedited Review

A new research study may be considered suitable for a "fast track" ethical review process only if it involves "minimal risk" (low or medium) research:

> ***Minimal risk means the probability and magnitude of harm or discomfort anticipated in the research, is not greater in and of themselves than those ordinarily encountered in daily life, or during the performance of routine physical or psychological examinations or tests.***

The following projects are considered by UZREC to be not suitable for fast track review and should (except in exceptional circumstances) be reviewed by a full committee.

- All clinical trials involving drugs/medical devices or other therapeutic interventions.
- Multi-institutional collaborative research projects.
- International grant- funded research.
- Animal research.

A **"fast track"** (expedited review) procedure for minimal risk research may be used, at the discretion of the UZREC chairperson, or any other person delegated this responsibility by the chairperson, under the following circumstances:

- All minimal risk research, for the purposes of a degree or diploma (under or post graduate).
- When an investigator specifically motivates for and justifies a "fast track" approval process.
- Any minimal risk project identified as suitable by the chairperson or any other person delegated by the chairperson for this purpose.

Expediting Postgraduate research for degree and diploma purposes

1. The investigator should submit all necessary documentation for a new application as well as a covering letter motivating for a "fast track" review process. If the study is being done for the purposes of a degree or diploma, the covering letter should be written and signed by the student's supervisor. A signed supervisor declaration and CV is required for all Doctoral, Master's and undergraduate research projects.
2. The administrative team will ensure all documents are in order and complete and contact the researcher to request missing information if necessary.

3. The chairperson, or UZREC member appointed by the chairperson, will review the research study and provide the chairperson with a written report. The chairperson will at her/his discretion:

    1) Approve the study.
    2) Request modifications prior to approval.
    3) Defer approval - i.e. refer the study to a full sitting of UZREC for consideration.

4. If modifications are requested then all requested changes must be made before a final letter of approval will be issued. The member delegated to do the original review will check that the changes are acceptable.
5. The investigator may start the project only once an approval letter has been received.
6. The approval will be considered for ratification by UZREC, at the following meeting.
7. Reports of reviewers and all written comments by the chairperson will be made available to all committee members in the printed agenda at this meeting.
8. UZREC has the authority to suspend the approval of any project approved via an expedited process and request further changes or additional information. All research activities must cease until this process is concluded.

PhD projects

- PhD projects will usually be reviewed by a full UZREC. However, if there is a good reason why expedited review is required, then a covering letter of motivation requesting expedited review should be submitted with the project.
- NB: All PhD projects must have undergone a scientific review process first before being submitted for ethics review and approval. The final version of the protocol should be submitted, not the first version.

Undergraduate student projects

Many undergraduate students are required to complete small research projects during the course of their studies. Supervisors of undergraduate research projects should note the following points:

- The scope and ethical sensitivity of the project should be carefully chosen and considered. Students are often inclined to choose projects which interest them, but which may well involve sensitive or ethically challenging issues and with which they are often poorly equipped to deal e.g. HIV/Aids.
- It is the supervisor's responsibility to decide whether or not the project requires formal ethical clearance. Are the students actually conducting a research project, i.e. a systematic investigation that will lead to generalisable knowledge? If the results of the project will be kept entirely internal i.e. there is no intention to present or publish in any forum external to the student's own classroom environment then the exercise is an educational exercise rather than a research project and may well not require ethics approval. Supervisors are advised to seek confirmation on this issue from the UZREC Chairperson or a delegated member.

- A research project conducted by students in the public domain e.g. in a school or hospital environment, using scholars or patients as participants, should be submitted for ethics approval.
- If the intention from the outset is to conduct health research with a view to presentation of results external to the classroom environment e.g. at a conference, or possible publication in a journal, then ethics approval is required.
- Many undergraduate research projects do in fact provide interesting and valuable results that may be worthy of publication. Proof of ethical clearance will be required for publication and this cannot be given retrospectively.

Application Procedure for Undergraduate Projects

1. Students should submit the written protocol they have developed as part of their course requirements as well as an application form and a checklist.
2. UZREC will regard the supervisor as the Principal Investigator or Applicant, who assumes ultimate responsibility for the project. The project will be registered under the name of the supervisor and all correspondence will be addressed directly to him/her, not to the student. The supervisor's CV and supervisor declaration must accompany the submission.
3. The chairperson will appoint a suitable member to review the project and if necessary, discuss the project with the supervisor and request corrections or changes.
4. The same expedited approval procedures as described above will be followed.
5. The UZREC administrative office will attempt to ensure that this process is completed in a maximum of 10 working days. However, this is subject to capacity, and the timing of the application.
6. If modifications are required, then all requested changes must be made before a final letter of approval is issued.
7. The approval will be considered for ratification by UZREC at its next meeting.

Convened (Full) Meeting Review

UZREC will convene on a quarterly basis unless when necessary a special meeting is held to review and consider:

- New research proposals and all supporting documentation such as participant information sheets, consent documents, advertising and recruitment material, and questionnaires. .
- New proposals approved via an expedited review mechanism, for ratification of approval.
- Major protocol amendments.
- Adverse events reported in previously approved studies.
- Continuing Review Reports (both progress and final) on research projects.
- General and policy matters.
- Allegations of misconduct in research or other complaints.

Pre-meeting processes

- New applications must be received at least 12 working days before a meeting. (Agenda closure dates are published in conjunction with meeting dates but do not guarantee that applications will be on a specific agenda.)
- An administrative review will be completed by the administrative staff who may request additional information.
- Projects are distributed to two members of the committee, at least one week prior to the meeting for evaluation and review.
- The chairperson may, at his/her discretion, co-opt an external consultant for a particular protocol if he/she feels the committee does not have the necessary expertise to adequately evaluate all aspects of a particular protocol.
- Reviewers will make written comments available to the chairperson, prior to each meeting if they are unable to attend the meeting.

The Meeting

The meeting proceeds as follows:

1. The chairperson opens the meeting.
2. A quorum, as described earlier must be present for all decision-making.
3. Members of UZREC declare any conflict of interest before the beginning of meeting
4. The secretary records those present and also notes apologies.
5. The minutes of the previous meeting are corrected and accepted.
6. New Agenda Items are generally discussed in the following order, but this may be subject to change depending on the volume and type of items received at each meeting:

    - Matters arising from the previous meeting.
    - Project progress reports/re-approvals.
    - New applications.
    - Other new applications.
    - Resubmission of “referred back” projects.
    - Ratification of projects approved by expedited review.
    - Substantial amendments for discussion. (A substantial amendment is one that may alter the risk benefit assessment of the study or result in a significant change in study procedures)
    - Ratification of substantial amendments approved via an expedited review process. NB Minor amendments such as minor changes to administrative protocol changes do not need to be ratified by the committee. (See section J for further details)
    - Serious adverse events (SAEs).
    - Other documents for noting/approval.
    - General items.

7. New applications are introduced by the chairperson. The primary reviewer presents a review of the study to the committee. The second reviewer adds comments. Discussion is then opened to the full committee.
8. If the investigator is a member of the committee, he/she may answer any specific queries that members wish to address but should voluntarily recuse him/herself prior to discussion and decision-making. This recusal should be recorded in the minutes.
9. Investigators will not attend the meeting routinely unless requested to do so by the chairperson, or unless they request to present information to the committee that will assist with decision making.
10. The chairperson facilitates discussion and summarises the perceived viewpoints of the committee.
11. The committee attempts to reach a decision by consensus.
    One of the following decisions must be made:
    - Approval with no changes.
    - Modifications required. (The project has no major ethical concerns but a number of clarifications or methodological changes are required that can be finalised by an expedited review process i.e. without having to serve before UZREC again).
    - Deferred. (The project has major ethical concerns and requires considerable revision. It will need to be reconsidered after changes, at a full UZREC sitting).
    - Rejected.
12. If a consensus is not reached, because of disagreement, then UZREC will vote on a proposal as summarised by the chair.
13. Voting will be recorded as numbers for, against and abstaining.
14. The secretariat records all decisions in the minutes and the method by which they were made. All discussion points, issues of controversy and reasons for decisions will be documented in the minutes. The secretariat also documents any member leaving or entering the room during the meeting, in order to record and ensure that a quorum is always present.
15. A protocol that is scientifically and ethically sound will have an average review time (from submission to approval) of 30 days. It may take considerably longer to finalise approval with respect to protocols that are scientifically and ethically flawed .

Communication of Review decisions

Decisions taken at UZREC meetings, or via an expedited review process, are communicated in writing to the applicant five days after the decision was made. It is not unusual for the committee to request some changes to the project, information and consent form, or clarification of certain issues. Only once these requirements are satisfactorily fulfilled, will a formal letter of approval be issued. On occasion, a research study may be rejected completely.

1. Investigators can address any queries to the UZREC secretary via the research office
2. It is the responsibility of the investigator to comply with all requests and return the requested documentation with a covering letter responding to the points raised, to

UZREC as soon as possible but not later than 6 months from the date of issue. The application will be cancelled if no feedback is received by 6 months.

3. All requested protocol and relevant changes must be clearly marked. The tracked changes facility on the word processor should be used.
4. The primary reviewer (or another UZREC member, if requested to do so by the primary reviewer or chairperson) will carefully check all amended documentation, including patient information and consent forms.
5. If correct, the said documentation will be forwarded to the chairperson for final approval.
6. If not correct a second letter will be sent to the investigator clarifying what aspects of the project still need to be addressed or changed. If the committee did not give a conditional approval ("modifications required" decision) to the protocol, but requested major alterations to the protocol i.e. DEFERRED or "Referred Back" the protocol must be resubmitted to a full sitting of the committee.
7. The initial period of approval is one year from the date of final approval. A progress report and request for re-approval should be submitted at least 2 months before expiry of approval.
8. The final approval date will be recorded as the start date and approval will expire one year from this date. However, if the project is funded by a US federal agency then the date the project was reviewed at a full meeting and given conditional approval will be considered the starting date of the project. Project re-approval occurs within 1 year of this date.
9. Approval letters are signed by the Deputy Vice-Chancellor for Research and Innovation, who is the chairperson of the UZREC.

E. Informed Consent

Except, as provided elsewhere in this document, no investigator may involve a human being as a participant in research covered by this policy unless the investigator has obtained the legally effective informed consent of the participant or the participant's legally authorised representative, where appropriate.

An investigator shall seek such consent only under circumstances that provide the prospective participant or their representative with sufficient opportunity to consider whether or not to participate and that minimise the possibility of undue influence or coercion. The information that is given to the participant or the representative shall be in language understandable to the participant or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the participant or their representative is made to waive or appear to waive any of the participant's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

- One of the primary justifications for a local review process with respect to multisite/multinational clinical trials is to ensure that the participant information is adapted to the requirements of the local community and potential participants.

- Written informed consent should always be obtained unless an alternative process is clearly justifiable.
- The process of recruitment and documentation of informed consent must be clearly described in the study protocol.

1. Basic Elements of Informed Consent

In seeking informed consent, the following information shall be provided to each participant:

1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the participant's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
2) A description of any reasonably foreseeable risks or discomforts to the participant.
3) A description of any benefits to the participant or to others which may reasonably be expected from the research.
4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant.
5) A statement describing the extent to which confidentiality of records identifying the participant will be maintained
6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
7) An explanation of whom to contact for answers to pertinent questions about the research and research participants' rights.
8) A statement that participation is voluntary and that refusal to participate will involve no penalty or loss of benefits or reduction in the level of care to which the participant is otherwise entitled.
9) A statement that the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.

2. Additional Elements of Informed Consent

When appropriate, one or more of the following elements of information shall also be provided to each participant:

1) A statement that the particular treatment or procedure may involve risks to the participant which are currently unforeseeable.
2) Anticipated circumstances under which the participant's participation may be terminated by the investigator without regard to the participant's consent.
3) Any additional costs to the participant that may result from participation in the research.
4) The consequences of a participant’s decision to withdraw from the research and procedures for orderly termination of participation by the participant.

5) A statement that significant new findings developed during the course of the research which may relate to the participant's willingness to continue participation will be provided to the participant.
6) The approximate number of participants involved in the study.

3. Variations of Consent procedures (including waiver of informed consent)

UZREC may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided UZREC finds and documents that:

1) the research involves no more than minimal risk to the participants.
2) the waiver or alteration will not adversely affect the rights and welfare of the participants.
3) the research could not practicably be carried out without the waiver or alteration.
4) Whenever appropriate, the participants will be provided with additional pertinent information after participation.

- Informed consent is not required for use of information in the public domain, although guidance may be needed concerning definition of what type of information about citizens is regarded as public.
- The informed consent requirements in this SOP are not intended to pre-empt any applicable governmental or local laws which require additional information to be disclosed in order for informed consent to be legally effective.
- Nothing in this policy is intended to limit the authority of for example, a registered health professional to provide emergency medical care, to the extent the registered health professional is permitted, under applicable governmental or local law.
- The participant must, having been fully informed, be asked to give his/her free and voluntary consent to inclusion in the study. Where a relationship of dependence exists between participant and researcher (e.g., service provider/service recipient), consent should ideally be obtained by an independent person.

4. Documentation of Informed Consent

1. Informed consent shall be documented by the use of a written consent form approved by UZREC and signed by the participant or the participant's legally authorised representative. A copy shall be given to the person signing the form.
2. The written consent document must include the elements of informed consent required by this policy. This form may be read to the participant or the participant's legally authorised representative, but in any event, the investigator shall give either the participant or the representative adequate opportunity to read it before it is signed. If the participant is unable to read or write there shall be an independent witness to the oral presentation who must verify in writing that the

informed consent process was valid and in accordance with the requirements of this SOP document.

3. UZREC may waive the requirement for the investigator to obtain a signed consent form for some or all participants if it finds either:
   a. That the only record linking the participant and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.
   b. That the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context. In cases in which the written documentation requirement is waived, UZREC may require the investigator to provide participants with a written statement regarding the research.
4. Once the participant has agreed to participate, at least 2 copies of the signed form will be made. The original is to be kept by the principal investigator. One copy will be given to the participant.

Translation of Patient Information and Consent

Multi-linguicism is a challenge to any research within a South African context. In a country that has 11 official languages, the task of translating and effectively communicating Information to, and obtaining consent from patients in several languages is daunting and costly.

The principle of justice requires that potential research participants of all local language groups should be afforded the opportunity to participate in research.

1. In the Eastern Cape information and consent documents should be available in three languages i.e. Xhosa, English and Afrikaans. An exemption of this requirement must be specifically requested and justified and approved by UZREC.
2. Documents may be submitted for UZREC approval, in English. Once the original document is approved it is the responsibility of the investigator to arrange for translations of the forms, if appropriate.
3. Once completed, the translations must be returned to the UZREC office accompanied by either a certificate of translation or letter from the PI declaring that the translation is an accurate reflection of the approved English version.
4. The committee will acknowledge receipt of translations. However only the original English version will be officially approved.
5. The committee reserves the right to check translations and delay approval of the study, if the translations are deemed to be of poor quality.
6. Investigators and sponsors are encouraged to ensure that Information and Consent documents are translated where appropriate.

F. Research Involving Children

1. A “Child” is defined in the Bill of Rights of the Constitution of South Africa as someone younger than 18 years.
2. Research with children should comply with the South African DoH (2015) Ethics Guidelines(Section 3.2.2) and be undertaken only when the research cannot be carried out equally well with adults, and the research question will not be answered using adult participants. The purpose of the research must be to obtain knowledge relevant to socio economic or health needs of children.
3. Research involving children must conform to ethical guidelines and the law.
4. Unless contrary to South African laws and regulations, research involving children should be determined by UZREC as falling into one of the following categories:
    a. Research not involving greater than minimal risk to the children.
    b. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child participants involved in the research.
    c. Research involving greater than minimal risk and with no prospect of direct benefit to the individual child participants involved in the research, but likely to yield generalisable knowledge about the participant’s disorder or condition provided that the risk represents a minor increase over minimal risk.
    d. Research that UZREC believes does not meet the conditions above but finds that it presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.
5. Adequate provision should be made for obtaining the assent of the children and consent from their parents or legal guardians.
6. Where parents and legal guardians are not available, UZREC shall be guided by applicable laws and guidelines, the merits of the study, and expert opinion on legal and technical points concerning the proposed study.
7. US DHHS funded research with children must comply with US 45 CFR 46.404-407 in addition to relevant South African legislation and regulations.

G. Community and Prison based Studies

UZREC must ensure that, particularly with regard to research involving communities, those communities’ traditions and values are respected. This applies particularly with regard to obtaining consent to participate in the research. However, permission given by a community’s leader does not absolve the researcher from also obtaining the fully informed consent of each individual participant.

When reviewing non-expedited studies involving prisoners, UZREC must ensure that:

1. At least one member of UZREC shall be a prisoners’ representative (e.g., prisoner, ex prisoner, prisoner or ex-prisoner service provider, or member of an NGO representing prisoners) with appropriate background or experience and be a voting member of UZREC, unless the study has also been reviewed by another accredited REC on which a prisoner representative was present.
2. At least one-member present shall be a community member not involved in research.
3. The majority UZREC members, other than the member described above, shall have no association with the prison(s) involved, apart from their membership of UZREC.

4. The Investigator has complied with the conditions specified in the South African DoH Ethical Guidelines (2015) (Section. 3.2.8).
5. Studies on prisoners should only be conducted on prisoners if the researcher satisfies UZREC that the research cannot be carried out equally well on non-prisoners and the research question cannot be answered with input from non-prisoners. The purpose of the research must be to obtain knowledge relevant to the health socio-economic or health needs of prisoners.
6. Studies with prisoners must comply with relevant South African legislation and regulations.

H. Genetic Research

UZREC requirements for a research protocol that includes genetic analysis

1. Steps to protect the privacy and confidentiality of potentially identifiable genetic information must be specifically outlined in the protocol and must not be released to others, including family members without written consent.
2. The protocol must state if information and samples will be identifiable, coded or de-identified. Consequences of storing either de-identified information or coded information must be carefully considered within the context of each protocol and justified.
3. The protocol must state if samples will be stored, for how long and where, and must describe the procedure that will be followed if a participant withdraws consent.
4. A researcher must not transfer genetic material and related information to another research group unless:
    a. There is a formal collaboration that has been approved by UZREC and a Material Transfer Agreement has been signed by the appropriate authorities.
    b. The genetic material and information are transferred in a form that ensures participants cannot be identified. (Prima facie principle)

Informed Consent

Written informed consent is required prior to removal of biological material from a living donor (NHA ss 56 and 62). The Participant Information and consent document for genetic research must be separate from the main consent form. Participants must be informed of the following:

1. They are free to refuse consent without giving reasons and still take part in the main trial.
2. An explanation of the genetic research study in simple layman's terms, including justification for the study must be given.
3. Arrangements to protect their privacy and confidentiality and whether or not specimens will be identifiable, coded but linked to identifiers or completely anonymous. The advantages and disadvantages of the chosen option should also be spelt out.

4. They are free to withdraw consent for the research without explanation or prejudice and if their specimen has remained linked and is identifiable, it will be destroyed.
5. They will be told whether or not feedback or results will be available and if not, an explanation must be given.
6. They will be asked whether or not they wish to be told of research results that could be of relevance to them as individuals.
7. They will be given details about involvement of other family members, if applicable and must give consent for researchers to approach other family members.
8. They must be assured that material and information will not be released for other uses without their consent.
9. Consent for storage should be requested. Information as to where and for how long the data will be stored should be provided.
10. When researchers propose to collect genetic material and information from individuals chosen by virtue of their membership of a particular collective, consent should be sought from appropriate collective representatives as well as from the individuals concerned.

Request for Waiver of Individual Consent for genetic analysis

UZREC adheres to the prima facie principle that if a researcher wishes to conduct research on stored genetic material, consent is required from the person from whom the material was derived or to whom the information relates. Before granting a waiver of consent UZREC must determine:

1. The nature of any existing consent, by reviewing the original consent documents.
2. Acceptance or not of the justification presented for the waiver, including how difficult it would be to obtain consent.
3. Arrangements with respect to protecting privacy and confidentiality, including de-identifying the information.
4. The extent to which the proposed research poses a risk to the privacy and well-being of the participant.
5. Whether the research proposal is an extension of or closely related to the original research.
6. The possibility of commercial exploitation of derivatives of the sample and relevant statutory provisions.

I. Stored Tissue

1. If blood or tissue specimens are to be stored for future analysis and such analysis is planned to take place outside UNIZULU, the specimens must be stored in a repository located within Kwa-Zulu-Natal (or as otherwise specified and approved by UZREC) and released only with UZREC approval and approval from a local Research Ethics Committee at the proposed site of the analysis (unless otherwise specified and approved by UZREC).
2. Only UZREC approved analyses may be done.

3. UZREC must be provided with details of provisions made to protect the privacy of the donors and the maintenance of the confidentiality of the data.
4. Specimens may not be shared with any party unless approved by UZREC in advance.
5. Where tissue samples are to be exported, a valid current export permit is required.
6. A separate consent form or section of the informed consent form for storage of additional or residual samples is required.
7. A separate consent form for genetic testing is required.
8. A signed Material Transfer Agreement (MTA) must be in place before samples are transferred to other sites. A copy must be submitted to UZREC for record purposes.

J. Amendments and Protocol deviations

All research should be conducted according to an ethically approved, written protocol.

The difference between a protocol deviation and a protocol amendment:

1. A protocol deviation is a “once off” instance when, for some reason, the protocol is not followed e.g. the protocol states that only people over the age of 18 will be enrolled. However, a participant, aged 17 years and 6 months meets all admission criteria and is deliberately enrolled in this study. Protocol deviations can also occur when mistakes are made e.g. the wrong follow- up date is given and thus follow- up occurs outside of a specified time frame.
2. Protocol amendments, sub-studies or addendums to studies are planned changes to a study protocol, made in advance. These changes should be submitted to UZREC as a requested “study amendment” using the application form for substantial/major amendments, and not implemented prior to UZREC approval. An exception to this would be where it is necessary to eliminate an immediate hazard to, for example, trial participants or when the change involves only administrative or logistical elements e.g. change of telephone number.
3. Minor amendments do not change the risk benefit profile of the study in any way. Examples of typical minor amendments are:
    - Additional Investigators or study sites
    - Small changes in the Informed Consent
    - Change in background information or update of literature review
    - Extension of period of study
    - Other changes that do not affect study design and will not affect study outcomes or results
    - Administrative changes
    - Stricter inclusion or exclusion criteria
4. Major or substantive amendments require a change(s) to the study methodology or procedure that may result in an alteration of the risk benefit profile of the study. Examples:
    - Change in study aims, objectives or design
    - Resulting changes to consent documents
    - Additional study procedures

- Easing of inclusion or exclusion criteria

5. The final decision as to whether an amendment is minor or major and whether it requires expedited or full committee review rests with the UZREC chairperson or a person delegated this authority by the UZREC chairperson. The same criteria for expedited review of new applications apply to amendments.

Protocol deviations:

Significant protocol deviations that are likely to adversely affect participant well-being or data integrity should be reported to UZREC within a maximum of 15 days. Minor protocol deviations can be listed with the annual progress report.

K. SERIOUS ADVERSE EVENT REPORTING

The term Serious Adverse Event (SAE) is usually used within the context of clinical or drug trials, but can occur in non-pharmaceutical research as well.
Any event that can affect research participants or data integrity negatively, or that has the potential to impact negatively on members of the research team, or on the project as a whole, and that is deemed significant by the investigator should be reported to UZREC. Adverse events can include a wide range of events such as breach of confidentiality, injury sustained during a procedure e.g. exercise programme, assault or robbery of staff members, needle stick injuries etc. Adverse events may in certain studies also include adverse drug events.

SERIOUS ADVERSE DRUG EVENT (FDA TITLE 21 PART 312, 32Any adverse drug experience, occurring at any dose that results in any of the following outcomes:

- Death
- A life-threatening incident
- Inpatient hospitalisation or prolongation of existing hospitalisation
- Significant or persistent disability/incapacity
- Congenital abnormality/birth defect
- Important medical events that may not result in death, be life threatening, or
- Require hospitalization, may be considered a SAE when based on appropriate medical judgment; they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition e.g. allergic bronchospasm, blood dyscrasias.

Any other serious study related event, which in the opinion of the investigator is significant with respect to study participants, staff or data integrity, should also be reported to UZREC

1. All significant adverse events occurring at the investigator's site must be reported to the UZREC, by the investigator within a maximum of 21 days. However, any event which in the opinion of a reasonable and competent investigator, could have serious negative consequences for research participants, research team members, the project as a whole, or the University, should be reported to UZREC within 48 hours of the investigator becoming aware of the event.

2. All significant or unexpected SAEs occurring at other sites should be reported to UZREC if deemed necessary by the investigator.
3. A standard reporting form for drug related SAEs must be completed and submitted. This should be attached to a more detailed narrative if the event occurred at the Investigator's site. Other adverse events can be briefly summarised in a letter.
4. A summary of all submitted SAE reports will be compiled each month and distributed to all UZREC committee members, for review and discussion at the monthly meeting.
5. SAEs that are unexpected or repeated will be investigated further and appropriate action taken, if deemed to be necessary by UZREC.

L. Guidelines for Routine Continued Review (progress Reports)

International and local guidelines and regulations (Dept of Health, ICH GCP, SA GCP, MCC and 45 CFR 46,) require that ethics committees conduct substantive and meaningful continuing review of all approved research at least annually and more frequently if the level of risk warrants this.

1. Ethics approval is valid for one year only. A progress report is an application for renewal of ethics approval and must be submitted annually, at least 2 months before the ethics approval expiry date, so that the progress report can be reviewed and the project re-approved prior to the expiry date. No research may continue without this process and re-approval. Six monthly progress reports may occasionally be requested if UZREC deems the project to be of particularly high risk.
2. The progress report must be submitted on the UZREC progress report form.
3. The progress report should contain sufficient information to allow the reviewer to conduct a substantive and meaningful review of the progress of the project, including any challenges or problems encountered.
4. For multi-centre studies the information in the progress report must pertain specifically to UNIZULU sites. All clinical trials falling under the jurisdiction of the MCC must submit a progress report to the MCC six monthly and should provide UZREC with a copy of this report. However, a site-specific progress report must be submitted annually, for ethics re-approval, preferably using the UZREC progress report form.
5. An updated complete protocol, incorporating all approved amendments should be submitted approximately every three years unless there have been no, or minimal changes to the project.
6. Copies of published abstracts may be submitted as attachments, and may replace text required in Section G of the report form, if appropriate and self-explanatory.
7. The Serious Adverse Event (SAE) Summary and Protocol Noncompliance Summary are applicable primarily to clinical research studies with an experimental design. If not applicable, then these pages need not be included and can be deleted.
8. All investigators whose projects are funded by US government federal funds (NIH, CDC etc) must comply fully with OHRP requirements for continuing review. These can be found at http://www.hhs.gov/ohrp/humansubjects/guidance/contrev0107.htm

- Main points to be included are:

- the number of participants recruited
- a summary of any unanticipated problems and available information regarding adverse events; (in many cases, such a summary could be a simple brief statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document and any investigator brochure)
- a summary of any withdrawal of participants from the research since the last UZREC review
- a summary of any complaints about the research since the last UZREC review; a summary of any recent literature that may be relevant to the research and any amendments or modifications to the research since the last UZREC review; any relevant multi-Centre trial reports
- any other relevant information, especially information about risks associated with the research; a copy of the current informed consent document and any newly proposed consent document

9. The above information will be distributed to all UZREC members prior to each meeting for discussion and renewal of approval.
10. The minutes of the UZREC meeting will document separate deliberations for each protocol undergoing continued review by the convened UZREC meeting.
11. OHRP requirements stipulate that continuing review and subsequent re-approval of federally funded or supported research must occur within one year of the approval date that correlates with a meeting i.e. the START DATE would be the Approval or Conditional Approval date, if the protocol was reviewed by the full UZREC, or the ratification date if the protocol was reviewed via an expedited review.
12. The UZREC has the authority to place restrictions on, suspend, or terminate any study in which the investigator fails to comply with the review process.
13. If a project was eligible for expedited review when initially approved, the continuing review may occur via an expedited process. However, if the project was not eligible for expedited review e.g. Phase III clinical trial, then the continuing review must occur at a convened and quorate meeting.
14. A study is considered active while analysis of any data collected or resulting from the study is ongoing.
15. Progress reports are required annually until such time as the investigator submits a final study report or notice of termination of the study.

M. Conflict of Interest Policy for Investigators

A conflict of interest (COI) occurs when professional judgement regarding an interest e.g. research, or patient care, is unduly influenced by another interest e.g. financial gain or gain in personal status. Admitting to a conflict of interest is not an indication of moral failure but an honest appraisal of the potential influence of secondary interests on one's judgement and actions. Conflicts of interests are an inherent and unavoidable part of the academic research environment and can be effectively managed by disclosure and transparency.

Investigator conflicts of interests are of particular importance when an unacknowledged or undisclosed interest, financial or otherwise, may negatively affect the well-being of research participants. It is this aspect of COIs that is of concern and relevance to UZREC.

1. Investigators must consider the potential effects that a financial relationship of any kind may have on the research or on interactions with research participants.
2. All investigators are obligated to sign the Conflict of Interest Declaration that is part of the Investigator declaration.
3. In particular, investigators should disclose the following potential conflict of interests to UZREC:
    - Equity or stock holding in a sponsor company
    - Proprietary interests in product-patent holding, intellectual property rights, trademark, and licensing agreements
    - Grants paid speaking arrangements, retainers for ongoing consultations, sitting on Pharmaceutical Advisory Boards and the like
    - Travel/conference sponsorship
    - Recruitment fees or other personal payments that are linked to study outcome, in any way
    - Co-authorship of articles, where the co-author's input has been minimal
    - Funding for additional staff and facilities, especially if not directly linked to the research project
    - Equipment for use in a study that will then belong to the department
    - Donation of equipment unrelated to study
    - Contributions to a departmental budget not directly related to project expenses

Please not that all of the above may well be potential but not actual conflict of interests after particular set of circumstances.

N. Conflict of Interest Policy for UZREC Members

Members of UZREC are expected to make decisions and conduct their oversight responsibilities in an independent manner, free from bias and undue influence. UZREC members (and members of their immediate families) may be involved in activities that could be perceived as conflicting with their UZREC responsibility.

The integrity of the REC review process can be compromised if such conflicts of interest are not disclosed and where necessary, avoided. 45 CFR Section 46.107 (e) states…" no IRB may have a member participate in the IRB's initial and continuing review of any project in which the member has a conflicting interest except to provide information requested by the IRB"

UZREC members must disclose any relationship, interest or other circumstances, which could reasonably be perceived as creating a conflict of interest – including the following:

1) Personal Relationship: The UZREC member has a personal relationship with the principal investigator or key personnel of a research protocol under review by UZREC
2) Relationship to the research study: The UZREC member (his/her spouse or immediate family member) is the principal investigator or co-investigator of the research protocol under review by UZREC.
3) Business relationship or Affiliation: The UZREC member serves as a trustee, director, officer, owner or partner of a for-profit entity that could be affected by the outcome of the research protocol under review by UZREC,
4) Financial Interest: The UZREC member has a financial interest that could be affected by the outcome of the research protocol under review by UZREC. Included in the definition of financial interest are equity interests e.g. stock, stock options or other ownership interests, payment or expectation of payment derived from intellectual property rights (e.g. patent royalties), and payments received from a for-profit entity for consulting or other services.

UZREC members are required to disclose only those interests that may be affected by the research, which is the subject of the research proposal and that might otherwise reasonably be perceived to affect their independent unbiased judgment with respect to the NHRECs review of the protocol or related matters.

UZREC members should make disclosures to the chairperson. The chairperson and committee shall determine whether a conflict exists. The determination of whether or not a conflict exists shall be reflected in the minutes.

The chairperson may similarly become involved in a situation of potential conflict of interest. In this case he/she should discuss the matter with the Committee.

Recusal

1) UZREC members who have a conflict of interest related to any research protocols that UZREC is about to consider will refrain from participating in any discussion of the protocol or related matters, except to the ext ent necessary to provide relevant factual information requested by the chair. Unless requested by the chair to provide such information to UZREC, the UZREC member with a conflict of interest will leave the meeting during the discussion and voting process. The outcome of the committee decision in the absence of the recused member will NOT be discussed upon return of the member concerned but may be conveyed after closure of the meeting.
2) All reviewers will sign a COI declaration which is part of the protocol review form. UZREC members assigned as a primary or secondary reviewer for a protocol or related matters, with respect to which a conflict of interest has been identified, will notify the chair so that the protocol can be reassigned.
3) In the event that the conflict of interest involves the chairperson, he or she will appoint the vice-chairperson, or another member as acting chairperson (with

approval of the committee). The acting chairperson will conduct the meeting, for the remainder of the discussion, of the item in question.

O. Record Keeping

Legal and ethical requirements regarding human and animal research participant protection require that records be retained in an orderly and easily accessible manner for future reference and for audit purposes. South African Good Clinical Practices (SAGCP) requires retention of records for a minimum of 5 years post-clinical trial. UZREC retains all research study records for 15 years in accordance with GCP requirements.

i. UZREC has the right to monitor the research they approve (Declaration of Helsinki 2013 para 23). Researchers should provide appropriate information to the UZREC to facilitate monitoring, including alerts and investigator brochures. The frequency and type of monitoring should reflect the degree and extent of risk of harm to participants or animals.
ii. UZREC may recommend and adopt any additional appropriate mechanism for monitoring, including random inspection of research sites, welfare monitoring sheets, data and signed consent forms, and records of interviews. Information and consent materials should indicate that such monitoring may take place.
iii. UZREC should request regular, at least annual, reports from principal investigators on matters including but not limited to
    - progress to date, or outcome in the case of completed research
    - current enrolment status (numbers, active or closed)
    - whether participant follow-up is still active or completed
    - information concerning maintenance and security of records
    - evidence of compliance with the approved protocol
    - evidence of compliance with any conditions of approval
    - negative reports from monitors or GCP inspectors
    - list of all adverse events in the past 12 months
    - list of all amendments made in the past 12 months.
iv. UZREC should inform principal investigators in writing of concerns arising from such monitoring activities.

Post passive and Post Active monitoring

UZREC does have a post- approval passive monitoring system of using annually written reports by the principal investigator about the progress of the research involving human participants, and problems or challenges met when undertaking the study. The post active monitoring system applies to animal research.

i) Principal investigators and supervisors shall in the first instance be responsible for monitoring compliance with research ethics obligation

ii) Generally, as well as any specific obligations that the UZREC may impose in a particular instance.

iii) Principal Investigators shall keep full records of all steps taken to comply with ethical obligations. In particular, monitoring of projects involving animals shall include keeping records of acquisition, breeding, health, care, housing, use and disposal of animals.

iv) UZREC may specify additional monitoring requirement and/or specific methods of monitoring a research project, the nature and the frequency of such monitoring being dependent upon the risk factors related to the research.

v) UZREC will require the principal investigator to do random monitoring of ethical compliance in high-risk research and submit a report to the committee after data has been collected.

vi UZREC retains the right to monitor or investigate any research project falling within this policy at any time, and to inspect any facility, equipment or process associated with such research.

vii) Inspections may occur on notice or randomly, and in the presence of a person involved in the research, preferably the Principal Investigator. Only in most exceptional and urgent instances shall inspections be conducted without a researcher being present; and in such instances the inspector shall inform the Principal Investigator, failing which another person involved in the research, immediately upon completion of the investigation or, if where attempts to contact them have been unsuccessful, within a reasonable period.

viii) Duration of the certificates is in accordance with NHREC guidelines of 1-year. The committee issues a 1-year ethical clearance certificate. When the certification reaches its expiry date, the researcher is required to submit an annual progress report stating all activities carried out during data collection. Researchers are allowed to request an extension via the recertification process if more time is required for continuity of data collection.

viii) The veterinary doctor (and member of UZREC) make regular site visits where animal research is conducted at UNIZULU..

Suspension or termination of ethical certificate

According to the NHREC 2015 guidelines:

i) Where circumstances indicate that a project is non-compliant with the approved protocol and the interests of participants are at risk of harm, the Research Ethics Committee may withdraw approval, after due process has been followed.

ii) A clear process should be followed that permits swift but proper investigation and decision-making to ensure protection of participants. The investigation should include interaction with the researchers and other interested parties to ensure a fair and transparent process.

iii) If the decision is to withdraw approval, UZREC should inform the principal investigator and other interested parties, including the institutional authorities, and recommend suspension (temporary stoppage) or termination (permanent stoppage) of the project. It should also recommend remedial action where appropriate.

iv) In the case of suspension, the principal investigator should comply with the

recommendations and any special conditions imposed by UZREC.

Research projects

1) A UZREC reference number is allocated to all new applications. This number is recorded on all correspondence and additional attachments/amendments.
2) A research ethics data base is used to capture project information such as name of department, investigators, title of project ,degree of study,
3) Hard copies of all research study related documents and correspondence are filed according to their reference number.
4) Hard copy records of all communication reports from UZREC between investigators and the UZREC office are recorded and filed using this reference number.

Meetings

Written minutes of UZREC meetings will be recorded in sufficient detail to:

1) Show attendance at the meetings
2) Indicate all actions taken by the UZREC
3) Indicate whether or not decisions were reached by consensus or voting,
4) If by vote, then the number voting for, against and abstaining.
5) The basis for requiring changes to, or disapproval of research.
6) A written summary of the discussion of controversial issues and their resolution.

Record of membership

An up-to-date list of UZREC members identified by name, earned degrees, representative capacity, indication of experience sufficient to describe chief anticipated contributions to UZREC deliberations, and any employment or other relationship between the member and the institution will be retained at the UZREC office and be publicly available.

P. Guidelines for Conducting Site Audits

According to the Department of Health's Ethics Guidelines for Research "an REC has the responsibility to ensure that the conduct of all research approved by an ethics committee is monitored on an ongoing basis. The frequency and type of monitoring should reflect the degree of risk to participants in the research project."

Monitoring routinely involves the regular review of study progress reports, but sometimes more in - depth monitoring of a project in the form of a site audit may be necessary. The main objective of a site audit is to ensure compliance with both the protocol and GCP guidelines, where applicable. UZREC has the authority to, from time to time, conduct audits on any active research activities involving human subjects.

- The UZREC chairperson or a person appointed by UZREC assumes responsibility for the conduct of an audit, directs the process, and acts as a facilitator.

- Parties generally involved in the process include the investigator, the research team, UZREC member, the UZREC chairperson, the auditor/audit team and the Deputy Dean of Research.
- The UZREC has the authority to audit any research site. However as site audits are costly and time consuming the following sites will be prioritised:

A. Routine

1) Inexperienced sites
2) High-recruiting sites
3) Sites recruiting vulnerable patients
4) Research that is more "risky"
5) Animal Research

B. For Cause

1. Sites from which complaints have been received (whether by a participant, sponsor or some other 3rd party).
2. Sites, at which it is suspected that the procedures approved by UZREC are not being followed, based on evidence provided in progress reports or in sponsor monitoring notes.

   An independent, suitably qualified auditor will usually be appointed to act on behalf of UZREC, on a per project contract basis to conduct the site audit.

Implementation of an Audit and Notification

1) Sites from Group A will be selected randomly by UZREC.
2) Sites from group B will be selected on an ad-hoc basis as necessary, either after discussion by UZREC, or on the specific instructions of Senate, for example.
3) A notification of Sites for proposed audits will be tabled at the next UZREC meeting.
4) The PIs will be given at least two weeks' notice that an audit will be performed, so as to ensure their active participation and to protect their right to due process.

The Audit

1) The audit team will examine the structure of the PI's research organisation and their standard operating procedures to determine whether he/she complies with the ethical standards and regulatory requirements governing research involving human subjects.
2) In the case of audits in response to a complaint, the audit team will be supplied with an Audit Brief, which will outline the complaint and indicate specific focus areas for the audit.
3) In the case of random audits, the audit team reviews records maintained by the PI, including site-monitoring notes where applicable, for the duration of the study.
4) The main focus of the audit team is to ensure that the research is being conducted in an ethical manner and that participants' interests are fully recognised, represented and protected.

Some or all of the following documents may be examined by the audit team during the audit process, depending on the nature of the audit and the nature of the study. **(NB: Some of the documents listed here may not be applicable)**

Investigator's Study File

a) Confirmation of Regulatory Approval
b) Signed funding agreement and copies of receipts or financial correspondence (where applicable)
c) Signed copy of the final protocol and any amendments
d) Specimen diary card, questionnaires,
e) Dated, signed CVs of all study site personnel
f) Specimen of signatures of site staff
g) Responsibilities list
h) Correspondence and communication with funders, and other authorities e.g. Provincial government authority
i) Record relating to equipment loan during the study
j) Equipment calibration logs
k) Laboratory certification (including updates)
l) Laboratory normal reference ranges (including updates)

UZREC Compliance

a) Any correspondence with UZREC
b) List of Committee members
c) Letter of UZREC approval and approval of any protocol amendments or other changes
d) annual progress report to UZREC
e) Annual re-certification from UZREC
f) Notification of end of study
g) Insurance statement (if applicable)
h) Signed indemnity letter (if applicable)
i) Any advertisement used for subject recruitment (if applicable)
j) Specimen subject information consent forms
k) Signed consent forms
l) Participant screening list (if applicable)
m) Participant recruitment log (if applicable)
n) Participant identification record
o) Copies of serious adverse events (if applicable)

Pharmacy and Drug Records (If Applicable)

a) Dispensing dates match up with visit date

b) Drug logs are complete
c) Tablet counts are recorded
d) All drug returns are counted
e) Boxes containing drugs for return are labelled ‘for return’
f) Drug storage is appropriately recorded

Case Record Forms

a) All CRFs are as complete as possible
b) All amendments are made correctly
c) Date of patient visits match recruitment logs
d) Laboratory result, x-ray results, etc.
e) All trial details filed in appropriate place

Additional Points of Note

- Interviews may be conducted with the PI and site personnel.
- Depending on the nature and timing of the audit, the audit team may contact research participants, observe the informed consent process or require a third party to observe the informed consent process or research procedures.

Reporting of Audit and Follow-up

a) The audit team will compile an audit report, which is submitted to the Chairperson of UZREC and/or to the PI.
b) The PI will be requested to respond formally in writing to the audit report and address each point. The PI’s report should also include a corrective action plan, if appropriate.
c) The audit team or UZREC then reviews the report, identifying irregularities in the statements and/or documents, summarising the issues that justify or refute the reasons for the initial complaint, where applicable and proposing a plan or corrective action if appropriate.
d) The auditor/team may arrange a formal meeting between the PI, audit team, and representatives from UZREC where appropriate, to discuss any findings of the audit, including any findings of non-compliance. This meeting is formal and should be minuted in detail.
e) The Audit Report, PI’s written response and minutes of the follow up meeting are confidential and will usually be tabled at a forthcoming UZREC meeting.

UZREC Deliberations and Decisions

The full UZREC reviews the audit team’s summary report, the PI’s written response and the minutes of the follow- up meeting report, where applicable.
UZREC will decide either by consensus or by vote to:

1) Accept the audit findings and PI's written response as acceptable with no cause for further action. A final letter will be sent to the PI, briefly summarising the outcome and declaring the matter satisfactorily resolved.
2) Request the PI to provide additional information, or take some other form of corrective action, which may even, involve a suspension of approval of the research study involved until proof of corrective action has been provided.
3) Withdraw study approval AND/OR
4) Refer the matter to line management for further investigation and action where appropriate.

- All correspondence between UZREC, auditor and PI will remain confidential except in cases of serious research non-compliance, in which instance the report may be forwarded to external regulatory bodies or funders as deemed appropriate after discussion with the Chairperson of the UZREC and other relevant stakeholders.

NB. When an audit is initiated in response to a 3rd party complaint about a researcher or research study, deviations from the above procedure may occur. This will depend on the nature, seriousness and context of the complaint.

University Research Ethics Committee: Appeals and Complaints
Generic Standard Operating Procedure

Appeals arise because UZREC rejects a research proposal, adjudges a protocol deviation or violation to be sufficiently serious to merit calling a halt to the research, or requires additional protections or conditions before approving a protocol and the Principal Investigator (PI) objects to the decision of UZREC and wishes to appeal.

An appeal must be directed to the chairperson of UZREC. A researcher may not appeal directly to other members of UZREC.

Complaints arise because of alleged UZREC procedural irregularities, breach of researcher confidentiality, unacceptable delays or conflict of interest.

Complaints should be directed, in the first instance, to the chair of UZREC.

The researcher retains the right to appeal or complain to the National Health Research Ethics Council, if the research falls under the jurisdiction of this council i.e. fulfils the definition of Health Research as defined in the National health Act No.61.2003.

1. Appeal Process (UZREC Level)

1. Where a PI is dissatisfied with a UZREC decision, he or she has the right to obtain from UZREC written reasons for its decision and should exercise this right before launching an appeal.
2. UZREC is expected to have a mechanism whereby a PI may appeal UZREC's decision. The chairperson of UZREC must appoint a subcommittee to revisit the substance of the application together with any additional information put forward by the PI. The subcommittee must obtain at least one independent, external, expert review of the research project and the substance of the appeal. Additional reviews should be obtained if deemed appropriate. The subcommittee may have the same powers as the UZREC, if so, constituted by the UZREC concerned.
3. The appeal is usually considered on the grounds of written submission only. However, the chairperson of the appeal subcommittee may invite the PI to provide an additional oral submission to the subcommittee and answer questions.
4. After deliberation of all the information placed before it, the subcommittee must either
   a) Uphold the appeal
   b) Reject the appeal
5. In any event, the decision of UZREC is final.
6. Researchers conducting "health research" retain the right to complain or appeal to the National Health Research Ethics Council in the event that they remain dissatisfied with the outcome of the appeal.

C. Complaints Process

1. All complaints against UZREC, for matters as described above, should be submitted directly to the UZREC chairperson, who should make every effort to investigate the complaint thoroughly, resolve the issue and communicate the outcome of the investigation to the complainant.
2. The chairperson of UZREC shall notify a committee member that a complaint has been made against that member, inform him/her of the nature and substance of the complaint and request that he/she responds in writing to the complaint, providing sufficient detail.
3. The chairperson of UZREC shall appoint an ad-hoc committee to investigate the complaint and report back to the full UZREC at a forthcoming meeting. Where necessary the subcommittee may need to interview the complainant, the chairperson and/or other persons.
4. UZREC shall compile a report of its findings and recommended action. The report shall be submitted to the Deputy Vice Chancellor: Research and Innovation, the chairperson of UZREC.
5. DVC (R&I) shall direct the report finding to UZREC and/ or relevant structures.
6. The PI shall be notified of the outcome of the UZREC investigation.

7. Whistle Blowing

7.1 Any individual who has a reasonable belief that there is serious misconduct relating to any of the protected matters specified in the Whistle blowing policy ("the Reporter"), may raise a concern or make a disclosure under the procedure set out in the policy.

7.2 The decision of the Responsible Person as to whether there is a *prima facie* case to respond to and, if so, what the nature of the investigation will be or whether the matter should be dealt with as envisaged in paragraph 7.4 of the Whistle blower policy, will be communicated to the Reporter in such manner as the Responsible Person deems appropriate.

1. Definition: Vulnerable Communities – UNAIDS (2000; 2007) and DoH, (2004)

- Vulnerable communities are defined as having some or all of the following characteristics:
- Limited economic development;
- Inadequate protection of human rights and discrimination on the basis of health status;
- Inadequate community or cultural experience with the understanding of scientific research;
- Limited availability of health care and treatment options;
- Limited ability of individuals in the community to provide informed consent;
- Culturally marginal groups
- Persons involved in illegal activities or livelihoods

2. Research Requiring Additional Attention: (SA GCP Guidance, DoH, 2006)

- Minors: Children and adolescents
- Women: Women and Pregnancy
- Foetuses in-utero
- Foetuses ex-utero
- Persons with mental disabilities
- Persons with substance abuse related disorders
- Persons in dependent or subservient relationships (e.g., students where the investigator is directly involved in their training; employees where the investigator has line authority over them).
- Prisoners
- Persons highly dependent on medical care
  Intensive care
  - Neonatal intensive care
  - Terminal care
- Persons with impaired capacity to communicate
- Unconscious persons
- Specific social collectives
- Persons in indigenous medical systems
- Emergency care research
- Innovative therapy or intervention

HIV/AIDS clinical and epidemiological research

(US Federal Government-Office for Human Research Protections (OHRP) guideline document available at: http://www.hhs.gov/ohrp/humansubjects/guidance/63fr60364.htm accessed 12.04.2010)
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Review of SOP-
On the recommendation of UZREC, Senate may review and amend sections of the Standard operation procedures, in which event the amendments take effect on the date of Senate approval.

Reference and Source Documents

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6. ICH Guidelines 1996.
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Department of Health, Pretoria. Guidelines for good practice in the conduct of clinical trials in human participants in South Africa. 2nd ed. 2006. http://www.doh.gov.za/nhrec
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16. Fred Hutchinson Cancer Research Centre /University of Washington. Institutional Review Board” IRB “Conflict of Interest Procedure.

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17. Prof Jacqui Greenberg, Div Human Genetics, UCT. IRENSA Lecture Series. 2003.
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21. Merz J et al “Protecting subjects’ interest in genetic research.” American Journal Human Genetics.2002.70: 965-971.
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