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Department:
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PROVINCE OF KWAZULU-NATAL

KWAZULU-NATAL DEPARTMENT OF HEALTH

UMGUNGUNDLOVU HEALTH ETHICS REVIEW BOARD (UHERB)

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STANDARD OPERATING PROCEDURES (SOP)

VERSION	5
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Contents

UMGUNGUNDLOVU HEALTH ETHICS REVIEW BOARD (UHERB)

STANDARD OPERATING PROCEDURE (SOP)

1. ACKNOWLEDGEMENT

The following documents were used to guide the development of these SOPs:

Department of Health (2015). Ethics in Health Research: Principles, Processes and Structures. Second Edition. Department of Health, Pretoria, South Africa.

Durban University of Technology (DuT) Institutional Research Ethics Committee. (2017). Standard Operating Procedures. Durban University of Technology, Durban, South Africa.

Biomedical Research Ethics Committee (BREC). (2010). Terms of reference and standard operating procedures. University of KwaZulu-Natal, Durban, South Africa.

Humanities and Social Science Research Ethics Committee (HSSREC). (2014). Terms Of Reference And Standard Operating Procedures. University of KwaZulu-Natal, Durban, South Africa.

2. PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to set out in systematic detail the review process of proposals, procedures and considerations that should be taken into account and adhered to when reviewing proposals, and to provide information or references to additional materials that would assist with the process of review and application for ethics approval by the Umgungundlovu Health Ethics Review Board (UHERB). The aim of the SOP is to provide clear, unambiguous instructions so that the related activities of the committee are conducted in accordance with the relevant national and international regulations and ethical guidelines.

3. SCOPE

This SOP covers the operational processes and procedures that UHERB is expected to adhere to when reviewing and engaging in decision-making about the ethics of research proposals that have been submitted to the Committee.

4. INTRODUCTION:

The Umgungundlovu Health Ethics Review Board (UHERB) has the responsibility of evaluating, approving and monitoring health research involving humans. UHERB shall use the principles outlined by the Department of Health (2015) in "Ethics in Health Research: Principles, Processes and Structures, Second Edition" and the Declaration of Helsinki as the basis for evaluating research proposals. UHERB aims to protect the rights and welfare of research participants by adhering to the principles of beneficence, justice and respect for people, especially vulnerable populations.

5. ETHICAL AND REGULATORY REQUIREMENTS FOR RESEARCH WITH HUMANS

UHERB will endeavour to align itself with, inter-alia the following guidelines:

- The SA National Health Act No. 61. (2003)
- The SA Department of Health (2015) Ethics in health research: Principles, structures and processes, 2nd Edition
- The SA Department of Health's Guideline for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa (2006)
- Declaration of Helsinki (2013)
- The Belmont Report
- Medical Research Council: Guidelines on Ethics for Medical Research: HIV Preventive Vaccine Research
- The Singapore Statement on Research Integrity
- Human Heredity and Health in Africa (H3Africa) Initiative

6. INSTITUTIONAL LINES OF AUTHORITY AND RESPONSIBILITY

UHERB falls directly under the Provincial Health Research & Ethics Committee (PHREC), and reports to the Chairperson of this Committee, who in turn is appointed by the Head of Health, KwaZulu-Natal.

7. REC ACTIVITIES AND PROCESSES

UHERB MEETINGS

Meetings will be held once a month, on the first Thursday of every month for 11 months of the year (February to December). Members will be notified annually of the scheduled dates no later than the fourth week of January. The minutes of meetings and the agenda will be circulated to members at least 7 days prior to the meeting. A schedule of meeting dates and deadlines for submission for any given year will be placed on the UHERB web page by the fourth week of January each year. The Chairperson of UHERB may call a special meeting if and when the need arises.

PREPARATION OF AGENDA AND MINUTES

The minutes of meetings and the agenda will be circulated to members at least 7 days prior to the meeting. The Agenda shall be determined by the Chairperson of UHERB.

Agenda

The Agenda of the monthly UHERB meeting will document the following:

- Date
- Time
- Venue
- Welcome
- Apologies
- Quorum
- Confirmation of previous minutes
- Protocol reviews: KZNCN, Other
- Matters arising
- Date of next meeting
- Closure

Minutes

The recording and circulation of the minutes of each meeting is the responsibility of the Administrator of UHERB. Minutes should be filed accordingly. Minutes on file should be signed. Final minutes must be signed at the next meeting and placed in the record of agendas and minutes to ensure an appropriate record of proceedings of the Committee. Final approved minutes should be signed by the Chairperson.

The minutes of meetings must document the proceedings of the monthly meetings according to the Agenda for that month.

Minutes should record attendance from the signed attendance registers and indicate whether the meeting was quorate.

The minutes should include a clear record of the follow-up of matters that were discussed in previous meetings. This includes review comments from previous meetings, whether the Principal Investigators (PI's) response was accepted and the protocol approved. Final decisions of review of proposals must be documented.

All decisions regarding the outcome of ethics review of a proposal will be recorded in the UHERB minutes including the status, outcome and other decisions regarding the proposal.

For meetings that are not quorate, the minutes should indicate that the meeting outcomes will be circulated for ratification by committee members via email, within a time period of 10 working days. Responses within this time period will be required by members. Support of decisions made via email correspondence will be recorded and will be ratified or acted upon at the next quorate meeting.

The minutes of the meeting should indicate if there were any conflict of interest declared and if the member was recused in that instance.

REGISTERS FOR MEETINGS

Each meeting must have a register, signed by all attendees, in order to record attendance. The register must be filed with the minutes of the meeting. The responsibility of the register for meetings is of the Administrator of UHERB. The following must be recorded on the register:

- Name of the meeting
- Date
- Time
- Venue

- Name of person attending, their institution and contact details (if it has changed from what has been recorded) and attendee's signature.

8. QUORUM REQUIREMENTS

The Committee will make its decisions at scheduled or extraordinary meetings at which a quorum of members is present.

In accordance to the DOH 2015 Ethics in health research: Principles, structures and processes, a quorum is defined as simple majority when UHERB membership is made up of a minimum of nine members. If UHERB has more than 15, the quorum may be 33%.

As per the "Minutes" section above, if the meeting is not quorate, decisions will be circulated to members by email, and ratified at the following quorate meeting.

Decisions will be determined by consensus (general agreement). In situations where consensus cannot be achieved, the decision will be arrived at by vote, where the decision will be taken by a simple majority. The Chair will vote as an ordinary member.

Minutes taken at UHERB meetings will be of sufficient detail to show attendance at the meetings; actions taken by UHERB; if applicable, the vote on these actions including the number of members voting for, against and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of disputed issues and their resolutions.

9. CONFLICT OF INTEREST

Members of UHERB are expected to make decisions and conduct their oversight responsibilities in an independent manner that is free from bias and undue influence. The integrity of the UHERB review process may be compromised if such conflicts of interests are not avoided; where impossible to avoid, such conflicts of interest must be disclosed.

UHERB members shall declare any prior interest and/or involvement in any matter being discussed by UHERB to avoid conflict of interest in UHERB decision-making, including reviewing of protocols. UHERB members should not review or make decisions about research proposals in which they are involved personally or financially. When such a proposal is to be discussed, the member concerned should declare the potential conflict and offer to recuse themselves from the meeting for that time. In convened UHERB meetings, the Chair shall determine whether the member should be recused for items of discussion, or be allowed to remain and address questions when asked to do so, but this member may not vote or participate in final decision-making on the matter in question. The minutes of the meeting should indicate if any conflict of interests was declared and whether the member was recused or not.

Conflict of interest must also be declared when UHERB reviewers are assigned to review a protocol or related matter.

10. THE PROTOCOL REVIEW PROCESS

THE APPLICATION PROCESS

All documentation for submission should be made available on the UHERB webpage, http://portal.kznhealth.gov.za/components/sps/hrkm/umgungundlovuhealthethicsreviewboard/Home.aspx or can be obtained from the UHERB Administrator via email.

UHERB will undertake to review observational studies that involve human participants which are "minimal risk" or "medium risk" in nature. UHERB will also endeavour to review "high risk" studies should it have the capacity to do so at the time of receiving an application.

Below is the different classification of risk levels for the review of study applications.

Minimal risk	"The probability and magnitude of harm or discomfort anticipated in the research are 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" (45CFR 46.101).
Medium Risk	Studies that have an increase over minimal risk (HSSREC, 2014).
High Risk	Research which may involve risk to participants and/or researchers above the everyday norm during which real and anticipatable harm or discomfort is identified that may lead to serious adverse consequences if not appropriately managed (RMIT HREC, 2005).

The following documents are required by applicants for submission to UHERB for ethical review:

1) Completed UHERB application form for full ethical review or for expedited review
2) Copy of research proposal
3) Copy of applicant's current CV(s) in abbreviated format
4) Copy of evidence of research ethics training /GCP in the last three years
5) Copies of all questionnaires to be used in the study
6) Copies of the participant information leaflet (Appendix A), translated into local language if necessary by an accredited translator
7) Copies of informed consent forms (Appendix B), translated into local language if necessary by an accredited translator

8) Information about payments to participants, if applicable.
9) Information on compensation for research related injury (insurance) for participants, if applicable.
10) Other documentation necessary for UHERB to make an informed decision regarding the research proposal.
11) Approval of proposal by a scientific/proposal committee, if applicable
12) Advertisements or recruitment materials
13) Institutional support letters

The above documents together with a cover letter should be submitted electronically to the UHERB Administrator by the applicant. The above will also serve as a checklist for the administrator when receiving applications for UHERB approval.

The UHERB Administrator will accept applications for ethical clearance from applicants on a rolling basis. The UHERB Administrator will check the application ensuring that all relevant documentation has been submitted by the use of a submission/application checklist (Appendix C). If there are any outstanding documents by the applicants, the UHERB administrator will contact the applicant directly via email.

If the application was submitted within the UHERB submission deadline, then the application will be added to the Agenda of the next month's meeting.

If the applicant does not possess approval from a scientific committee, the study application will first be reviewed by UHERB's Scientific Review Working Group. This will be communicated to the applicant. Once UHERB's working group has reviewed the application and is satisfied that the applicant's proposal is scientifically valid, it will continue to process the application for ethics review.

APPLICATIONS FOR ETHICS REVIEW

I. Each application should include whether the application is:
    a. exempted from ethical review
    b. for expedited review or
    c. full ethical review
II. Each research proposal should include a description of the ethical considerations implicated in the research.

III. The protocol should reflect adequate consideration of participants' welfare, rights, beliefs, perceptions, customs and cultural heritage.

IV. All documents and other material to be used to inform potential participants should be included in the ethics review application, such as information sheets, consent forms, questionnaires, etc.

V. Researchers should ensure that plain language adapted to anticipated literacy levels is used in the participant documentation.

VI. If research is going to be conducted in community settings, evidence of consultation and plans for ongoing involvement should be included.

VII. All researchers 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.

VIII. 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.

IX. 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.

X. All international collaborative research should have a local Principal Investigator (PI).

XI. Studies that have a substantial clinical component, where the Principal Investigator is not a clinician, should appoint an HPCSA-registered clinician as a Co-Investigator to the study.

THE REVIEW PROCESS

The review process involves an independent and objective evaluation of the effects of possible risk and harm of the proposed research on potential participants and on the general daily functioning of the organization that provides the site or context for the research.

When reviewing a proposal, UHERB must ensure that the rights, safety and well-being of the research participants and their communities are upheld. This will be done by evaluating all factors that may influence the scientific validity and ethical acceptability of the proposal by applying the

various ethical benchmarks. UHERB in its review also aims to hold researchers accountable for their research actions and to stimulate important social and ethical values.

UHERB will not provide retrospective review if a study has already been completed, nor will it provide approval or ethics clearance once a study has started.

The UHERB Administrator in conjunction with the Chairperson will determine whether the application falls into one of three mutually exclusive categories as follows:

I. *EXEMPTION FROM ETHICAL REVIEW*

UHERB may grant exemption from ethical review for research which

(1) *Does not involve human participants and carries no risk for the well-being of individuals or groups of individuals (e.g. research which is restricted to the secondary analysis of data sources which are in the public domain or observations of behaviour which is in the public domain).*

(2) Research that relies exclusively on secondary use of anonymous information or anonymous human biological materials usually need not undergo formal ethics review, provided that no identifiable information is generated.

(3) Quality assurance and quality improvement studies (audits), programme evaluation activities and performance reviews which are not for publication purposes do not constitute research and thus do not undergo formal ethics review.

It should be noted, however, that if publication of such studies in a peer reviewed journal or presentation at a conference or seminar outside of Government is desirable, ethics approval must be obtained before the study/evaluation begins.

An indication for exemption from ethical review must be received or must be determined by the Chair and reviewer when completing the Protocol Review Proforma (Appendix D).

The review of ethics applications to UHERB will be recorded by the designated reviewers on the Protocol Review Performa.

II. EXPEDITED REVIEW PROCESS

An expedited review process consists of a faster review (two weeks) of a research-related request through the process of the Chairperson of the REC allocating two REC members for this fast track review. The request is approved and only ratified during the next REC meeting.

UHERB may use the expedited review procedure in the following circumstances:

(1) The research is deemed to involve no more than minimal risk;

(2) To approve minor changes in previously approved research during the period for which approval is authorised;

(3) UHERB will consider "Class approvals" for expedited review in circumstances where the usual criteria for expedited approval are met, in addition to the following:

(a) Where an investigator wishes to do exploratory research involving several lines of inquiry on retrospectively collected data, or

(b) Where an investigator needs to repeat a specified and previously approved research exercise, for teaching or training purposes.

Expedited Review Process

Under an expedited review procedure, the review may be carried out by the UHERB Chair and by one or more experienced reviewers designated by the Chair from among members of UHERB.

An indication for expedited review must be received or must be determined by the Chair and reviewer when completing the Protocol Review Proforma (Appendix D).

In reviewing the research, the reviewers will exercise all the authority of UHERB.

A research activity may be disapproved only after review in accordance with the non-expedited procedures set out below.

Members of UHERB will be informed at committee meetings of all protocols that have been approved using the expedited review process since the last committee meeting.

III. FULL COMMITTEE REVIEW

Research which is deemed to constitute a minor increase over minimal risk will be reviewed by the full UHERB Committee. Full Committee review will also take place when applicants apply for full ethical review in their application.

Full Ethical Review Process

A full review process consists of a more extensive, time consuming review done before a REC meeting by a minimum of two REC members allocated to this task by the chairperson of the REC, but deliberated on in a face-to-face manner during a full sitting of a REC meeting.

The review process for protocols categorized for full Committee review will be as follows:

Protocols received at least 10 days prior to a scheduled UHERB committee meeting will be tabled at the next committee meeting, with feedback on the committee's conclusions being provided to the Principle Investigator within five working days of the committee meeting.

Each protocol will be discussed at a convened UHERB meeting with an at least simple majority of the members of the UHERB are present, including at least one member whose primary concerns are in non-scientific areas.

For all non-expedited reviews, all committee members will receive copies of the UHERB application form and the protocol including information sheet, informed consent, questionnaires, PI' CV and Ethics Training Certificate.

Each non-expedited/full ethical review application and protocol will be reviewed in advance of a convened UHERB meeting by all UHERB members. A primary and secondary reviewer, and where necessary, an expert reviewer will be allocated to review each full ethical review application.

At the UHERB meeting, the primary and secondary reviewer (and expert reviewer, where applicable) will initially provide a brief background of the application, the scientific validity and ethical issues arising, an evaluation of the positive and negative aspects of the proposed research, their determined level of risk of the study and their recommendation. Thereafter, other committee members present at the meeting will engage in discussions regarding the reviewer's queries as well as their own assessment of the study protocol.

Apart from the scientific input, opinions from members representing the community must also be taken into account.

Decisions for full ethical review applications are reached either by consensus or by a vote.

The review process must take into consideration the following:

Each application under review must have a completed Protocol Review Proforma (Appendix D)

The level of risk of each application must be documented by the Reviewer on the appropriate Protocol Review Proforma.

The time for screening applications undergoing reviews is five days.

A protocol that is ethically and scientifically sound will have a review time of 30 days.

UHERB's review of a protocol will lead to written confirmation to the applicant of either:

Final approval

I. Provisional approval conditional to modifications required by the Committee
II. Rejection

(1) Reasons for provisional approval and rejection will be furnished to the researcher in writing.
(2) Outright rejection should be avoided if a researcher can be advised to improve the proposal.
(3) UHERB must document its views in writing to the applicant and reflect in the minutes of the meeting accordingly, clearly identifying the study, the documents reviewed, and the dates for the following:
    I. Approval;
    II. Modifications required prior to resubmission for approval;
    III. Rejection; and
    IV. Termination or suspension of any prior approval.
(4) The Chair will inform the researcher in writing of the UHERB decision. Feedback should be sufficiently detailed so that the concerns of UHERB are understandable to the researchers.
(5) If a proposal is approved, the approval letter should clearly outline the requirements of the researcher in an event that might warrant reconsideration of ethical approval of the protocol, including but not limited to the following:
    I. Report immediately anything serious or unexpected adverse effects on participants
    II. Proposed changes in the protocol
    III. Unforeseen events that might affect continued ethical acceptability of the project

(6) UHERB require researchers to report immediately if a project is terminated or suspended before the anticipated date of completion.

11. CONTINUING REVIEW AND RE-CERTIFICATION PROCEDURES

UHERB will review each ongoing study at intervals appropriate to the degree of risk to human participants, but at least once per year. In special circumstances, such as heightened risk or participant vulnerability as determined by UHERB as a condition of approval, more frequent reports may be called for. These maybe tri annual or bi annual reports.

Approval granted by UHERB for a research study is valid for one year unless otherwise stipulated. In order to ensure that an approved study has uninterrupted ethical clearance beyond the expiry date, the applicant should ensure that they apply for recertification from UHERB at least 2 – 3months before the expiry date on the appropriate UHERB Recertification Application Form (Appendix E).

The UHERB Chairperson should receive and review a UHERB recertification application form containing essential study information including a protocol summary and status report on the progress of the research. A primary reviewer will be nominated by the chair to review the recertification application. Should changes in circumstances make it necessary, UHERB may at any time withdraw approval of a protocol previously approved.

12. PROTOCOL AMENDMENT PROCEDURES

Any proposed amendment of an approved study must be submitted to UHERB for further approval using the current UHERB Amendment Application Form with supporting documents, e.g., change in protocol, key personnel/senior investigators and research site/s. A clarification memo is to be submitted for other minor notifications. UHERB approval must be received prior to implementation of the modifications/changes.

13. COMPLETION OF STUDY

A study is considered active or on-going until all data is collected, follow up at all research sites is complete and participant participation is no longer needed. The principal investigator must submit a letter to UHERB informing them that the study is completed along with the final study report or a copy of the study abstract (in the case of student research). This should be done after the comments from the examiner's report have been addressed successfully. If a study is not closed but is allowed

to expire (a lapse in approval) an administrative suspension letter may be sent to the principal investigator.

14. ADVERSE EVENTS AND UNANTICIPATED PROBLEMS

Reports on adverse events and serious adverse events (AEs and SAEs) should be reported in writing to UHERB, the study sponsors, and any regulatory authority (where appropriate), within 7 working days of the occurrence for local sites and one month for all other South African sites. Protocol violations and deviations shall also be reported in the same manner. A record of the reported events must also be filed by the UHERB Administrator.

15. PROTOCOL DEVIATIONS AND PROTOCOL VIOLATIONS

Protocol deviations are defined as a “once off” instance where the research protocol is not followed either deliberately or by mistake, the deviation will fall into one of two categories: major or minor. If minor, the deviation must be reported to UHERB in the annual progress report. If the deviation is major, it will need to be reported to UHERB within 15 days. The Chairperson will then decide the action to be taken.

16. NON-COMPLIANCE CONSEQUENCES

SUSPENSION AND TERMINATION

UHERB may suspend or terminate approval of a study that is not being conducted in accordance with prevailing UHERB or South African Department of Health Ethical requirements. The primary justification for suspension or termination of approval should be the safety of participants or others), or that there has been associated unexpected serious harm to participants or others. Such suspension or termination of approval must be authorised by the UHERB Chair in minuted consultation with a UHERB subcommittee and/or other co-opted parties as soon as possible but not more than seven days after receipt of relevant information by the chair. Such action must be reported to UHERB at the next quorate meeting.

UHERB shall also inform the researcher and the institution or organisation of its action, and shall recommend that the research project be discontinued or suspended, or that other appropriate steps be taken.

Where ethical approval has been withdrawn, a researcher must discontinue the research and comply with any special conditions required by UHERB. A report to this effect has to be submitted to UHERB within 2 weeks of suspension/ discontinuation of the project.

When the safety of participants is at risk, the Chairperson of UHERB in consultation with the subcommittee and/or other co-opted parties will call a meeting as soon as possible but not more than seven days after receipt of such information. The outcome of such a meeting will be reported to all UHERB members via email and at the next meeting. UHERB will give a detailed written reason for suspending or terminating the study to the relevant parties e.g. the principal investigator, the study sponsor or agency, the investigator's departmental head, the South African National Health Research Ethics Council and the South African Health Products Regulatory Authority (SAHPRA) (if applicable).

In the case where a research project is prematurely suspended/ terminated, the principal investigator must notify UHERB in writing of the reasons for suspension/termination and give a summary of the results obtained in a study thus far.

17. COMPLIANCE CHECKS AND AUDITS

UHERB may be audited by the National Health Research Ethics Committee (NHREC). UHERB will comply with NHREC audits by making the relevant records available for inspection upon request. UHERB will report annually to NHREC the following:

(1) Membership and membership changes

(2) The number of meetings held

(3) Confirmation of participation by required categories of members

(4) The number of protocols presented, approved and rejected

(5) Any changes to its Terms of Reference or Standard Operating Procedures.

18. INFORMED CONSENT

All applications to UHERB to conduct studies that involve human participants are required to have a letter of information and consent compiled according to the guidelines in Appendix B & C.

"Informed consent" refers to the ability of a person to choose voluntarily whether to participate in research on the basis of information provided by the researcher in order to make an informed choice. This process during which there is a dialogue between the prospective participant and the researcher whereby the researcher provides the information and the prospective participant reaches a decision regarding participation in the study is known as the informed consent process. Even though informed consent is critical for the conduct of a study it is not the sole basis for determining whether the research is ethical.

The following are considerations for informed consent:

I. Adults, i.e. persons over the age of 18 years, may make independent decisions

II. Each participant or, where necessary, the participant's legally authorised representative, must be given sufficient time to read the letter of information and consent and have the opportunity to ask questions.

III. There should be no coercion or undue influence.

IV. No person should be required to make an immediate decision.

V. The letter of information and consent should be in a language understandable to the participant or representative, allowing them to make an informed decision to participate in

the research. Only then may the participant or representative sign the letter of information and consent.

VI. In the case where the participant is illiterate, verbal consent may be given in the presence of a literate witness who will verify and sign the letter of information and consent on behalf of the participant, indicating that informed verbal consent was given.

It is necessary for UHERB to assess the proposed process for informed consent by the research applicant as well as the information that potential participants will be given and the measures to facilitate understanding. (DoH, 2015)

Considerations for assessment include whether:

• The setting will minimise the possibility of undue influence and be sufficiently private and appropriate

• The person obtaining informed consent for the study will be appropriately trained, independent and bias-free

• The text will be

- in plain language and appropriate to the participants' level of understanding17
- free of jargon and unexplained acronyms
- clear and explains technical terminology e.g. randomisation
- translated into language(s) appropriate to the context
- explicit in providing participants with UHERB contact details if they have queries or complaints about their rights and welfare as research participants
- able to encourage participants to contact the researcher at the contact details provided if they have queries about the research project
- confined to that stated in the proposal

• The information explains

- that the person is being asked to participate in research
- that the choice whether to participate is voluntary
- that refusal to participate will not be penalised

- that choosing to participate can be reversed, i.e. the person may decide to terminate participation at any time without explanation or prejudice
- the purpose and nature of the research procedures and components
- the research-related activities and procedures that the participant is being asked to consent to
- the expected duration of participation
- the nature of the participant's responsibilities
- the nature of the researcher's responsibilities
- the anticipated risks of harm or discomfort
- the measures to minimise risk of harm
- the extent to which confidentiality is possible
- whether reimbursement for expenses is available
- that sponsors of the research and regulatory authorities may inspect research records
- who the researchers are and the nature of their expertise
- the potential benefits, if any, for participants both during and after the research
- that the research may be terminated early in particular circumstances
- that the research has been approved by UHERB (include identifying details)

(DoH, 2015)

• A measure to probe understanding and comprehension of the information is planned and how it proposes to do so especially for very vulnerable potential participants

The letter of information and consent must include the following:

- The qualification/s and contact details of the researcher/s
- Participants' responsibilities
- Purpose of the research
- Any risks and benefits to participants
- Outline study procedure e.g. placebo or control groups if necessary
- Duration of study
- Alternative procedures or treatments

- Contact Details of UHERB's administrator

- Confidentiality
  - A statement that participation is voluntary and that non-participation will not result in any penalty
  - A statement that ethical approval for the study was obtained
  - A statement that sponsors or the ethics committee may inspect research records
  - Compensation for research related injury
  - Contact details of UHERB
  - Contact details of the person to contact should there be research related injury

The letter of information and consent must be written in simple language.

19. PRIVACY AND CONFIDENTIALITY REGARDING PARTICIPANTS AND THEIR HEALTH CARE INFORMATION

Due to the major ethical principle of respects for persons, it is vital that aspects of privacy and confidentiality are well determined in the review of ethical applications.

Privacy in research is defined as having control over the extent, timing and circumstances of sharing oneself – physically, behaviourally or intellectually – with others. This means respecting an individuals' right to be free from unauthorised or unreasonable intrusion relating to the individual's private information, including control over the extent, timing and circumstances of obtaining such information. Privacy is concerned with participants or potential participants as 'people' in terms of access to personal information from or about them.

Confidentiality refers to the use of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways inconsistent with the original intent of the disclosure, without that individual's permission.

Protocols must describe provisions to protect participants' privacy and to respect their right to be free from unauthorised intrusion. Investigators must be particularly vigilant when accessing personal or sensitive information without participants' knowledge or consent, for instance when reviewing medical records or databases solely for research purposes (UCT, 2018).

All information relating to human participants in research studies must be kept secure and confidential to the extent permitted by law. This is to protect participants from potential harms,

including stigmatisation, embarrassment and loss of insurance or employment. Researchers must provide a detailed plan of how participants' private and personal information will be collected, stored and shared with others (UCT, 2018).

20. RESEARCH INVOLVING MINORS

Minors are persons under the age of 18. Minors are not usually participants of research. Minors are only considered as participants if it is absolutely required. The premise under which minors are allowed to participate in health research is only when they are able to benefit from health related advances (DoH, 2015).

UHERB must determine that research involving minors is scientifically necessary and ethically sound; for instance, research-related risks to minors must be minimised and within permissible levels, parental permission and assent must be appropriate and privacy and confidentiality protections adequate. UHERB should include members with sufficient expertise and experience to evaluate the distinctive features of neonatal, child and adolescent research (UCT, 2018).

UHERB must consider the following Minimal Conditions for Research Involving Minors when receiving an application:

Participation of children in research should only be considered in the following instances:

I. When the participation of children is scientifically indispensable to the research.
II. The research problem investigated is relevant to children.
III. When clinical research addresses an important paediatric health need and the necessary information cannot be extrapolated from research using consenting adults.
IV. A condition or disease that does not occur among adults.
V. Important safety and dosing information that cannot reliably be extrapolated from adverse event information obtained in equivalent adult research.
VI. The protocol should provide sufficient information to justify clearly why children should be included as participants.
VII. Equipoise in clinical interventional research whereby the research context uncertainty prevails amongst health care experts about whether a particular treatment or intervention is better than another.
VIII. Research poses acceptable risks of harm.
IX. The research, including observational research, is not contrary to the best interest of the minor.
X. The research, including observational research, places the minor at no more than minimal risk of harm.

XI. The research involves greater than minimal risk of harm but provides the prospect of direct benefit for the minor.

XII. The research, including observational research, involves greater than minimal risk of harm, with no prospect of direct benefit to the minor, but has a high probability of providing significant generalisable knowledge. The degree of risk of harm should be justified by the risk-knowledge ratio.

XIII. Greater than minimal risk of harm should represent no more than a minor increase over minimal risk.

XIV. Where appropriate, the minor will assent to participation.

XV. The proper written permissions have been obtained.

The consent process for a minor's participation in research requires
• Permission in writing from parents or legal guardian for the minor to be approached and invited to participate (in accordance with s 10 of the Children's Act 38 of 2005);
• Assent from the minor in writing (i.e. agreement to participate) if he or she chooses to participate.
NOTE that an unmarried minor mother may not agree to the participation of her child in research without assistance. Her guardian (usually her parent) is also the guardian of her child while she is a minor and must consent to the child's participation. In other words, pregnancy and childbirth do not change the legal status of the minor mother. When the mother reaches the age of majority (18 years), she may consent to her child's participation in research.(UCT, 2018)

Research involving children must be reviewed appropriately. The National Health Act distinguishes research with children as 'therapeutic' and 'non-therapeutic' research. The intention is to ensure that UHERB provides due consideration to the degree of risk of harm posed by a proposal and the likelihood of benefit to the child-participant.

'**Therapeutic research**' means research that includes interventions that may hold out the prospect of direct health-related benefit for the participant (Regulation 135).

'**Non-therapeutic research**' means research that includes interventions that will not hold out the prospect of direct health-related benefit for the participant but may produce results that contribute to generalisable knowledge (Regulation 135).

The degree of risk of harm should be evaluated against the likelihood of benefit to the child-participant. According to the Minister's delegated power, UHERB has permission to exercise authority to approve research with children that includes non-therapeutic components. However, UHERB must ensure that its deliberations on these components are properly minuted and recorded

as required by the Regulations. This includes the review of the researcher's detailed explanation and justification for the proposed non-therapeutic study. UHERB must include members with appropriate paediatric research experience.

UHERB must also ensure that the research will take cognizance of their legal obligation to report child abuse and neglect.

Permission & Consent

- Parents or guardians may not decide whether their minor child should participate in research without the minor's contribution to the decision.
- The process should be that the parent or guardian is requested to give permission for the minor to be approached to be invited to participate in the study. The factual decision whether to participate is the minor's and not the parent's.
- Parental permission and minor's decision must be consistent (UCT, 2018).

21. RESEARCH INVOLVING VULNERABLE PERSONS

UHERB will pay special attention to protecting the welfare of participants from vulnerable populations and/or participants requiring additional attention.

Personal circumstances, such as mental or intellectual impairment, acute illness, advanced age, and pregnancy and childbirth may increase vulnerability.

South Africa is home to a number of vulnerable communities.

Vulnerable participants may include but not limited to the following:

I. Minors (children and adolescents)
II. Women especially those that are pregnant
III. Adults with an incapacity to provide informed consent
IV. Persons in dependent relationships
V. Persons highly dependent on medical care
VI. Persons with physical disabilities
VII. Prisoners
VIII. Collectivities (DoH, 2015)

UHERB will follow the guidelines from the Department of Health, Ethics in Health Research: Principles, structures and processes, available at http://www.nhrec.org.za/index.php/grids-preview

22. DATA COLLECTION AND STORAGE OF BIOLOGICAL MATERIALS

The collection of data and/or biological specimens for research purposes may require additional protection. The most prevalent is genetic studies where findings may carry psychological, social or economic risks for an individual, a family or a community. These studies will require a detailed plan of how confidentiality would be protected. In studies using anonymous specimens and the perceived risks are lower, the protocol would need to state what measures will be taken to de-identify samples to render them anonymous.

'**Biological material'** means material from a human being including DNA, RNA, blastomeres, polar bodies, cultured cells, embryos, gametes, progenitor stem cells, small tissue biopsies and growth factors from the same.[1]

'Donor' means a person from whose body human biological material has been removed or withdrawn for the purpose of genetic testing, genetic training, genetic health research and therapeutics (DoH, 2015).

When reviewing such studies, UHERB will follow the guidelines from the Department of Health, (2015) Ethics in Health Research: Principles, structures and processes. Second Edition, available at http://www.nhrec.org.za/index.php/grids-preview

23. DATABASES, REGISTRIES AND REPOSITORIES

Databases, registries (data banks) and repositories (tissue banks) all involve the collection of information and/or biological specimens over time. Databases, registries and repositories may be created for research, diagnostic or clinical purposes or both.

Databases are collections of information elements (i.e. data) arranged for ease and speed of search and retrieval. Databases may be maintained electronically or as paper-based systems.

Registries or data banks are collections of information or databases whose organisers:

I. Receive information from multiple sources.
II. Maintain the information over time.
III. Control access to and use of the information by multiple users or for multiple purposes which may change over time.

Registries often contain codes that link information and specimens to their donors' identity. Examples of South African registries include the National Cancer Registry, the Hereditary Colorectal Cancer Registry and the South African Bone Marrow Registry.

Repositories collect, store and distribute human materials for research purposes. Human biological material may include blood, urine, faeces, bone marrow and cell aspirates. In research protocols, human biological materials are usually referred to as 'tissues' or 'specimens'. Repositories usually include demographic and/or medical information about the individuals from whom the specimens were obtained, and often contain codes that link the information and specimens to the donors' identity.

Databases and tissue banks are exclusively concerned with obtaining, maintaining and accessing participant health information, often including personal health information, for research, over long periods of time. This may pose particular risks to participants' privacy and confidentiality. UHERB will require researchers to explain in the initial repository protocol and informed consent form:

I. What information will be collected.

II. How it will be stored.

III. Who will have access for research purposes (UCT, 2018).

UHERB also requires that new protocols be submitted for each future use of stored data or specimens which include personal identifying details. See the related policy on 'Databases, Registries and Repositories' for more detailed guidance on maintaining confidentiality when collecting, storing and sharing information in studies which use databases, registries and repositories. http://www.nhrec.org.za/index.php/grids-preview

Informed Consent

Since a repository with linked or identifiable information may be used by many researchers and for many studies over time, donor-participants' informed consent should include the following information in simple language:

1. The general concept and purpose of repositories:
    - Name and purpose of specific repository for which consent is requested.
    - How the repository works.
    - Types of research the repository supports.
2. Conditions and requirements under which data/specimens will be shared with researchers.
3. How participants' privacy and confidentiality will be protected.
4. Specific risks related to use and storage of data/specimens, particularly if personal identifiers are retained.
5. When human genetic research is anticipated, information about potential consequences of genetic testing (e.g. paternity determinations, insurance risks, reproduction decisions) and associated confidentiality risks.
6. Potential benefits, if any:
    - Inform participants if there is no direct benefit.
    - Include other potential benefits such as societal benefit through the advancement of knowledge.
7. Where applicable, the fact those specimens may be:
    - Used for future research not yet identified.

- Shared with or transferred to other institutions.

8. A statement that participants may withdraw their consent at any time either by requesting that data or tissue be destroyed or that all personal identifiers be removed.
9. Information about the length of storage.
10. When consent to use information or specimens will expire.
11. Information about possible secondary use of stored tissue or the possible creation of an immortalised cell line based on the specimen.
12. Obtaining informed consent to use data or specimens stored in a repository created for non-research purposes may be problematic since research was not intended at the time of collection. Where feasible, the Committee may require a researcher to obtain informed consent. However, the Committee may approve a waiver of consent requirements if:
13. The research involves no more than minimal risk (e.g. anonymous use of samples); and
14. The waiver will not adversely affect participants' rights and welfare; and
15. The research could not practically be carried out without the waiver. (UCT, 2018)

24. COMPLAINTS PROCEDURES

UHERB may receive complaints about researchers, the conduct of research, or about the conduct of the UHERB. Complaints may be made by participants, researchers, staff of the institution, or others. All complaints should be handled promptly and sensitively.

Possible complaints cover a broad spectrum from 'inadvertent technical deviations' from established protocols to allegations of scientific misconduct or fraud. The primary concern in response to any complaint is the extent to which research participants are endangered. There may also be concerns about the degree to which researchers are fulfilling their responsibilities, questions around culpability for misconduct and misleading reports being published by a researcher accused of misconduct or fraud. Often UHERB will be the most appropriate body to consider complaints in the first instance, although ultimately, the responsibility lies with the Department of Health (DoH).

The Chairperson of UHERB will receive the complaints; he/she may delegate this responsibility to a member of UHERB. All complaints will be dealt with and may require the assistance of other persons (not necessarily members of UHERB). The letter of information and consent (Appendix B & C) provided to study participants will provide the contact details of the UHERB Administrator should

participants wish to lodge a complaint. The UHERB Administrator will forward the complaint on to the Chairperson/complaints officer. (DuT, 2015)

Complaints may be lodged via email to the UHERB Administrator or the UHERB Chairperson on the following email addresses:

uherbadmin@kznhealth.gov.za or

uherbchair@knzhealth.gov.za

PROCEDURE FOR COMPLAINTS:

- Complaint is referred to the Chairperson of UHERB
- The Chairperson would consider the complaint - including, where necessary, reference to original protocol, contact with researchers, contact with complainant
- Action would be taken including, if warranted, implementing an investigation with the complainant being advised accordingly
- A report will appear at the next UHERB meeting.
- Where the complainant is not satisfied with the actions taken, the complaint would be referred to the Chairperson of the Provincial Health Research and Ethics Committee (PHREC).

PROCEDURE FOR RESPONDING TO COMPLAINTS:

The Chairperson will respond urgently when there is any suggestion of harm to research participants, researchers or any other person. In extreme circumstances, an immediate demand to suspend a research study may be necessary while concerns are adequately investigated. In other cases, prompt action may be required to rectify or remove the cause of concern. Having determined the urgency of the need for action, the Chairperson should take any, and possibly all, of the following steps according to the circumstances:

- Make a clear and full written record of the complaint;
- Seek further information from all relevant parties;
- Convene an urgent meeting of the UHERB; and
- If necessary, confer with the highest level of management and authority within the relevant institution.

PROCEDURE FOR INVESTIGATING COMPLAINTS

Where initial investigations reveal a situation that requires further investigation and review, the following procedures are recommended:

- Invite the researcher(s) to explain the situation to UHERB and to demonstrate why the project should not be discontinued and ethical approval withdrawn.
- Advise researcher(s) that they may be accompanied by one or more colleagues.

- Reconsider the original research proposal and seek additional information from the researcher(s) in relation to the conduct of the study, or any other relevant factors, before making a final decision whether to revise or reconfirm the original decision to approve the project.

Having considered the matter, the committee may:

- Withdraw approval resulting in suspension of the project,
- Require amendments to the original research proposal or to the conduct of the research; or
- Allow the project to continue without amendment.

(DuT, 2015)

UHERB will inform the principal investigator in writing of the decision of UHERB explaining the reasons for the recommendations. It may be necessary to inform research participants that the research they have been participating in has been modified or discontinued. In this instance UHERB will take advice from the researcher(s) about the wording of the notice to participants.

An appeal against a decision can be made and should be referred to a mediator independent of the UHERB and related activities.

ALLEGATIONS AND COMPLAINTS OF SERIOUS RESEARCH MISCONDUCT

Research misconduct includes any of the following:

- Fabrication, falsification, plagiarism, or deception in proposing, carrying out, or reporting results of research.
- Deliberate, dangerous, or negligent deviations from accepted practice in carrying out research. This includes failure to follow established protocols if this results in unreasonable risk or harm to human beings, animals or the environment and also the facilitating of misconduct by collusion in, or concealment of, such actions by others.
- Misrepresentation of data and/or interests and/or involvement
- Non-approved deception in the carrying out of research
- Failure to follow accepted procedures to exercise due care in avoiding unreasonable harm or discomfort to participants or research staff
- Failure to obtain voluntary and informed consent
- Negligent management of data security.

- Breaches of confidentiality.
- Deception in research process.
- Misrepresentation or falsification of credentials.

(HSSREC, 2014)

Misconduct does not include honest error or honest differences in the design, execution, interpretation, judgment in evaluating research methods or results of misconduct (including gross misconduct) unrelated to the research process.

Where there has been an allegation of serious misconduct, the institution should ensure the following:

- Protection of participants;
- Appropriate confidentiality (in case the allegation proves to be groundless);
- Protection of 'whistle-blowers'; and
- Natural justice for those who are the subject of any allegations or complaints.

Confidentiality, protection for complainants and natural justice for the person complained about will be dealt with by the review process outlined as follows:

(1) Determine whether the allegation falls within scientific misconduct.

(2) Determine whether there is prima facie evidence of scientific misconduct.

(3) Institute a formal investigation to evaluate all relevant facts to determine whether scientific misconduct has been committed and, if so, by whom, as well as the seriousness of the misconduct. The integrity of the research data must be evaluated and all appropriate groups advised if inaccurate, misleading or invalid data have been published or submitted to other agencies.

COMPLAINTS CONCERNING UHERB REVIEW PROCESSES

Concerns regarding the UHERB review process of applications or the manner in which their projects have been considered and dealt with may arise. Researchers may complain about the following issues:

- When UHERB has rejected a proposed project,
- When UHERB is perceived to be taking undue time considering a proposal,

- Or when conflict has arisen between UHERB and researchers.

In many situations the problem may simply be one of inadequate communication between the committee and the complainant(s).

(1) Researchers should seek to resolve complaints with UHERB procedures or decisions informally through the Chair in the first instance.

(2) The Chairperson/complaints officer will attempt to deal with the concern or complaint without formal investigation where possible.

(3) If the matter remains unresolved the principle investigator may lodge a formal complaint with the Chairperson of the Provincial Health Research and Ethics Committee (PHREC).

(4) If the complainant is dissatisfied with the decision of the Chairperson of PHREC, an appeal maybe lodged with the Chief Director: Health Service Delivery, Planning, Monitoring & Evaluation, DoH.

All complaints that are being investigated will be dealt with: fairness, confidentiality, integrity and prevention of detriment.

Complaints can be directed via email to the following authorities:

- UHERB Chairperson: uherbchair@kznhealth.gov.za
- PHREC Chairperson: Elizabeth.lutge@kznhealth.gov.za
- KwaZulu-Natal Department of Health Head: nozipho.mchunu@kznhealth.gov.za
- National Health Research and Ethics Council: NhreC@health.gov.za

25. WHISTLEBLOWER PROTECTION

"Whistleblower" refers to an individual who makes an allegation or demonstrates intent to make an allegation (or what is perceived to be an allegation) while a member of the institution at which the alleged scientific misconduct occurred. Anyone with a reasonable basis for believing that an irregular act has occurred or is occurring has a responsibility to report this immediately. It should be noted that whistle-blowing is not a conduit for recording criticisms or general complaints.

UHERB strongly believes in the importance of protecting whistleblowers that make good faith allegations of scientific misconduct. In particular, UHERB is committed to protecting good faith whistleblowers from retaliation by covered institutions and their members.

The identity of the individual who raises awareness of research misconduct will be protected and will be made known to the Chair and members of UHERB only, under conditions of strict confidentiality.

Anyone making a report must act in good faith when reporting an allegation, and must disclose all information available to him or her relevant to the matter. UHERB encourages potential whistleblowers to consider making a confidential disclosure whereby their identity is disclosed. However, UHERB will also accept an anonymous disclosure.

PROCEDURES FOR REPORTING

The following procedure for both confidential and anonymous disclosures that must be reported is outlined as follows:

- Whistle blower may contact the UHERB Chairperson via email on the following address: uherbchair@kznhealth.gov.za
- If the whistleblower fears that their anonymity will be compromised via email correspondence, the whistleblower should seek the UHERB's chairpersons contact number by contacting the UHERB administrator on the number provided on UHERB's webpage http://portal.kznhealth.gov.za/components/sps/hrkm/umgungundlovuhealthethicsreviewboard/Home.aspx .
- When making an allegation, the whistleblower should provide their identity (optional), contact details (optional), pertinent information regarding the allegation, including the department(s), institution(s), and individual(s) involved, what has occurred and when it occurred.

(UCT, 2010).

The date of the call and all appropriate information will be recorded. The allegation will either be investigated by UHERB or forwarded for possible investigation to the following reporting authorities:

- The Chairperson of the Provincial Health Research and Ethics Committee (PHREC)
- The KwaZulu-Natal Department of Health's Head
- National Health Research and Ethics Council (NHREC)

26. CHANGES TO UHERB TERMS OF REFERENCE, STANDARD OPERATING PROCEDURES, AND/OR MEMBERSHIP

UHERB reserves the right to develop policy documents to provide for any complexity in research-related ethical issues as they develop.

UHERB will perform its functions according to UHERB Terms of Reference (TORs) and Standard Operating Procedures (SOPs) and will maintain written records of its activities and minutes of its meetings and will comply with GCP and applicable regulatory requirements.

This document will be reviewed and updated annually or as required.

27. SELECTED REFERENCES:

1. Department of Health (2015). *Ethics in health research: Principles, structures and processes*. *Second Edition.* Pretoria.
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4. Department of Health, Education, and Welfare (1979). *Belmont Report: Ethical principles and guidelines for the protection of human subjects of research. Report of the National Commission for the protection of human subjects of biomedical and behavioral research*. Washington: Author.
5. Council for International Organizations of Medical Sciences (CIOMS) (2002). *International ethical guidelines for biomedical research involving human subjects.* Geneva: Author
6. Medical Research Council: (2000). *Guidelines on ethics for medical research: General principles. Cape Town: Author.*
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8. Durban University of Technology. 2017. Institutional Research Ethics Committee Standard Operating Procedures Available at: http://www.dut.ac.za/wp-content/uploads/2012/06/SOP-IREC-8-February-20171.pdf
9. University of KwaZulu-Natal Humanities and Social Science Research Ethics Committee (HSSREC). 2014. Terms of reference and standard operating procedures Available at: http://research.ukzn.ac.za/Libraries/Human_Sciences_Documents/HSSREC_Terms_of_Reference_and_Standard_Operating_Procedures_2014.sflb.ashx
10. Biomedical Research Ethics Committee (BREC). (2010). Terms of reference and standard operating procedures. University of KwaZulu-Natal, Durban, South Africa.

11. Humanities And Social Science Research Ethics Committee (HSSREC). (2014). Terms Of Reference And Standard Operating Procedures. University of KwaZulu-Natal, Durban, South Africa.

12. University of Cape Town (UCT). 2018. Manual of Standard Operating Procedures. Available at: http://www.health.uct.ac.za/fhs/research/humanethics/sop

13. University of Cape Town (UCT). 2010. Whistleblowing procedures. Available at: http://www.health.uct.ac.za/fhs/research/humanethics/sop

28. APPENDIX A: UHERB PARTICIPANT INFORMATION LEAFLET TEMPLATE

LETTER OF INFORMATION

Title of the Research Study:

Principal Investigator/s/researcher: (Name, qualifications)

Co-Investigator/s/supervisor/s: (Name, qualifications)

BRIEF INTRODUCTION AND PURPOSE OF THE STUDY:

OUTLINE OF THE PROCEDURES: (Responsibilities of the participant, consultation/interview/survey details, venue details, inclusion/exclusion criteria, explanation of tools and measurement outcomes, any follow-ups, any placebo or no treatment, how much time required of participant, what is expected of participants, randomization/ group allocation)

RISKS OR DISCOMFORTS TO THE PARTICIPANT: (Description of foreseeable risks or discomforts to for participants if applicable e.g. Transient muscle pain, VBAI, post-needle soreness, other adverse reactions, etc.)

BENEFITS: (To the participant and to the researcher/s e.g. publications)

REASON/S WHY THE PARTICIPANT MAY BE WITHDRAWN FROM THE STUDY: (Non-compliance, illness, adverse reactions, etc. Need to state that there will be no adverse consequences for the participant should they choose to withdraw)

REMUNERATION: (Will the participant receive any monetary or other types of remuneration?)

COSTS OF THE STUDY: (Will the participant be expected to cover any costs towards the study?)

CONFIDENTIALITY: (Description of the extent to which confidentiality will be maintained and how will this be maintained)

RESEARCH-RELATED INJURY: (What will happen should there be a research-related injury or adverse reaction? Will there be any compensation?)

PERSONS TO CONTACT IN THE EVENT OF ANY PROBLEMS OR QUERIES:

(Supervisor and details) Please contact the researcher (Name), (Tel No.), My supervisor (Name), (Tel no.) or the Umgungundlovu Health Ethics Research Board (UHERB) Administrator on 033 395 2102.

Complaints can be reported to the Chairperson of UHERB:

General:

Potential participants must be assured that participation is voluntary and the approximate number of participants to be included should be disclosed. A copy of the information letter should be issued to participants. The information letter and consent form must be translated and provided in the primary spoken language of the research population e.g. isiZulu.

29. APPENDIX B: UHERB INFORMED CONSENT TEMPLATE

CONSENT

Statement of Agreement to Participate in the Research Study:

- I hereby confirm that I have been informed by the researcher,____(name of researcher), about the nature, conduct, benefits and risks of this study - Research Ethics Clearance Number:_____,
- I have also received, read and understood the above written information (Participant Letter of Information) regarding the study.
- I am aware that the results of the study, including personal details regarding my sex, age, date of birth, initials and diagnosis will be anonymously processed into a study report.
- In view of the requirements of research, I agree that the data collected during this study can be processed in a computerised system by the researcher.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.
- I understand that significant new findings developed during the course of this research which may relate to my participation will be made available to me.

_____ _____ _____ _____

Full Name of Participant **Date** **Time** **Signature / Right Thumbprint**

I,_____(name of researcher) herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

_____ _____ _____

Full Name of Researcher **Date** **Signature**

_____

Full Name of Witness (If applicable) **Date** **Signature**

Full Name of Legal Guardian (If applicable) **Date** **Signature**

30. APPENDIX C: UHERB APPLICATION CHECKLIST

CHECKLIST FOR RESEARCH STUDY ETHICS APPLICATIONS TO UHERB

Date Received: _____

UHERB Reference Number: _____

	Document	Tick if any	Comment
1.	Cover letter that indicates the title, researcher(s), the type of research ethics application, which documents are attached, and that adds any explanations to clarify the application		
2.	Completed UHERB application form for full ethical review or for expedited review		
3.	Copy of research proposal		
4.	Copy of applicant's current CV(s) in abbreviated format		
5.	Copy of evidence of research ethics training /GCP in the last three years		
6.	Copies of all questionnaires to be used in the study		
7.	Copies of the participant information leaflet		
8.	Copies of informed consent forms		

9.	Information about payments to participants, if applicable.		
10.	Information on compensation for research related injury (insurance) for participants, if applicable		
11.	Other documentation necessary for UHERB to make an informed decision regarding the research proposal		
12.	Proposal approved by a scientific/proposal committee		
13.	Advertisements or recruitment materials		
14.	Institutional support letters		
15.	**Submitted as hard or scanned copies:** Printed and signed pages of the ethics application form for the declarations by the PI		

31. APPENDIX D: UHERB PROTOCOL REVIEW PROFORMA

PROTOCOL REVIEW PROFORMA

CONFIDENTIAL

Reviewer Name:	
Date of Review:	
Subsequent Review Date:	
Title of study:	
STUDY RISK ASSESSMENT	
• No risk	Yes ☐ No ☐ _____
• Low	Yes ☐ No ☐ _____
• Medium	Yes ☐ No ☐ _____
• High	Yes ☐ No ☐ _____
APPLICATION CHECKLIST	
• Research proposal/ protocol	Yes ☐ No ☐ N/A ☐
• UHERB Application Form	Yes ☐ No ☐ N/A ☐
• DoH Institutional Support	Yes ☐ No ☐ N/A ☐
• Information Letter	Yes ☐ No ☐ N/A ☐

• Consent Form	Yes ☐ No ☐ N/A ☐
• Questionnaire (English)	Yes ☐ No ☐ N/A ☐
• If relevant, translated questionnaire	Yes ☐ No ☐ N/A ☐
• A letter from a translator where applicable	Yes ☐ No ☐ N/A ☐
• A letter from a statistician consulted	Yes ☐ No ☐ N/A ☐
• C.V. of Applicant/ Investigator	Yes ☐ No ☐ N/A ☐
• C.V. of Supervisor	Yes ☐ No ☐ N/A ☐
• C.V. of Research Assistant if applicable.	Yes ☐ No ☐ N/A ☐
REVIEW TYPE: **As per Indication per applicant**	Exempted from Review ☐ Expedited Review ☐ Full Review ☐
REVIEW TYPE: **As per Reviewer**	Exempted from Review ☐ Expedited Review ☐ Full Review ☐

		YES	NO	N/A	COMMENTS
1	Is the title clear about what the researcher/s wish to study?				
2	Is the study being undertaken for quality assurance purposes?				
3	Is the study being conducted as a requirement for an educational qualification?				
4	Is the research problem clearly stated?				
5	Did the researcher apply to any other ethics committee for ethical clearance?				
6	Is the significance of the study well explained/ is the reason for the study clearly motivated?				
7	Is the purpose/aim of the study clearly explained and relevant to the title?				
8	Are there relevant research objectives set that would achieve the aim?				
9	Will the research questions achieve the objectives of the study?				
10	Is there a hypothesis and is it relevant to the title?				
11	Is the research methodology described in a logical manner?				
12	Is the research design, sound and in line with the title or does it suit the study?				
13	Will the research design yield the data that is required?				
14	Is the research population described?				
15	Is the sampling frame described?				
16	Is the sample representative of the research population?				
17	Will the sample be selected free of any bias or prejudice?				
18	Is there a clear justification for the choice of the sample?				

19	Are inclusion and exclusion criteria clearly stated?				
20	Has a statistician been consulted regarding the sampling frame?				
21	Is the research setting described?				
22	Will privacy of the participants be ensured during the data collection stage?				
23	Did the researcher/s stipulate which gatekeepers they will require consent from?				
24	Will the safety of the participants be ensured?				
25	Will the interests of the participants outweigh the interests of the researcher/s?				
26	Will the researchers prepare the participants before the study?				
28	Does the letter of information stipulate how autonomy will be maintained?				
29	Does the letter explain that participation is voluntary and that participants may withdraw at any stage of the research process?				
30	Does the consent form attached include the necessary information?				
31	Will the participants be inclusive of minors or other vulnerable groups?				
32	Is the process of obtaining consent for studies involving minors and vulnerable groups proposed within a legal and ethical framework?				
33	Did the researcher/s explain how anonymity of participants will be ensured?				
34	Did the researcher/s provide additional information on how anonymity of participants will be maintained during qualitative studies?				

35	Did the researcher/s describe how confidentiality of raw data will be maintained?				
36	Is the process of data collection well explained?				
37	Did the researcher/s provide additional information on how confidentiality of data obtained during interviews will be maintained?				
38	If historical data such as patient records or registers are to be used, does the research proposal describe how confidentiality will be maintained				
39	Did the researcher describe how raw data will be stored?				
40	Did the researcher/s explain how data will be analysed?				
41	Did the researcher/s outline how the results of the study will be disseminated?				
42	Will a copy of the study be forwarded to PHREC?				
43	Does the researcher/s have the necessary credentials to conduct this study?				
44	Does the study require more experienced researchers to be involved in the study?				
45	Does the research proposal provide a sound scientific background to the study?				
46	Is the study to be conducted valid and will build on the body if scientific knowledge?				
47	Do the benefits of the study outweigh the risks?				
48	Are there any possible risks?				
49	Did the researcher/s outline how would they deal with any risk factor/s confronted?				
50	Will the participants receive any form of remuneration?				

51	Are the criteria for awarding remuneration clearly described?				
52	Will biological specimens be collected?				
53	Does the protocol specify how the above specimens will be used and stored?				
54	Is there a need for the allocated reviewers to consult with other specialists?				
55	Are the items on the data collection instrument clear and free of ambiguity?				
56	Will the items on the data collection tool provide the data to answer the aim, objectives and research question?				
57	Will the data collection tool need to be piloted too ensure reliability and validity?				
58	Does the proposal stipulate who will be the sample for the pilot of the data collection tool?				
59	Does the study require that a portion of the study be piloted?				
60	Does the proposal specify who will be the sample for the above pilot?				
61	Will research assistants be trained in the data collection process?				
62	SCIENTIFIC RIGOR OF THE PROPOSAL: • There is a flow of information				
	• Written in a scientific manner e.g. using terms such as “the researchers” instead of “we”				
	• Written in an objective style throughout				
	• Information presented in a logical manner				
	• Acceptable punctuation and grammar				
	• Evidence of referencing and citations				

	• A reference/bibliography attached				
63	Is there a list of abbreviations used and operational terms or concepts described?				

REVIEWER STATUS OF PROPOSAL:

☐ Approved ☐ Terminate ☐ Suspend

☐ Provisional Approval Subject to Modification

_____

☐ Rejected _____

Additional Comments (risks identified, concerns etc, areas that need further clarity).

_____

_____

_____

Reviewer Signature:_____Date:_____

Remarks by Chairperson:

_____

_____

_____

Date presented: _____

32. APPENDIX E: UHERB RECERTIFICATION APPLICATION FORM

UHERB RECERTIFICATION APPLICATION			
To be completed electronically by the principal investigator/researcher in accordance with the Standard Operating Procedures of UHERB.			
Ethical approval number:			
Title of the study:			
Date of UHERB ethics approval:			
Study Period: (*Date from – Date to)*			
Name of Principal Investigator (PI)/Researcher:			
Department & Institution of PI:			
Name of Co- Investigator , if applicable			
Telephone Number:			
E-mail Address:			
Research site:			
Brief Description of Project Aims, Sample And Methods:			
Section A			
	YES	**NO**	**N/A**
Has sufficient progress been made with respect to anticipated timeframes in the research protocol? (If not, please specify and explain why in an attached report)			
Have there been any deviations (intentional/unintentional) from the approved research protocol (If yes, please detail in an attached report)			
Has recruitment been on schedule?			
If closed to recruitment, how many enrolled?			
If recruitment is slow or delayed, please give reasons:			
Have any adverse events occurred since commencing the research?			
If yes to the above, has an adverse event report been Submitted to UHERB?			

Have there been any unforeseen events or circumstances which have/may jeopardise participant safety or result in contravention of the approved research protocol. (If yes, please detail in an attached report)			
Are you aware of any complaints (formal/informal) from participants or staff or stake holders regarding the conduction of the research? If yes please detail in an attached report)			
Are you aware of any incidents whereby participants have been managed/treated in a manner other than that stated in the approved research protocol? (If yes, please detail in an attached report)			
Has appropriate informed consent been obtained from all participants in keeping with the method stated in the research protocol and is documentary evidence thereof available for inspection? (If no, please detail in an attached report)			
Has it been necessary to exclude any participants who were previously recruited for the study? (If yes, please detail in an attached report)			
Have any participants requested to be withdrawn from the study prematurely? If yes, please details the reasons for such			
Is there any new information, not previously submitted, relevant to the recertification of this project?			
If 'yes', please describe below or attach an appendix to this form.			

DECLARATION:

I, the undersigned declare that:

1. To the best of my knowledge the above information accurately represents the past years' experience and future plans with regard to this protocol.

2. The research procedures and design have not changed without approval of UHERB.

3. Changes to research procedures and/or design from those approved by UHERB will be submitted in advance for approval, on the standard UHERB Amendment Application Form

Signature of Principal Investigator: _____ **Date:**_____

Signature of Supervisor (Postgraduate studies only) _____ **Date:**_____

Send this application form and supporting documents to the UHERB Administrator:

33. APPENDIX F: UHERB AMENDMENT APPLICATION FORM

UHERB APPLICATION FOR AMENDMENT OF PROTOCOL		
To be completed electronically by the Principal Investigator/Researcher in accordance with the Standard Operating Procedures of UHERB.		
Date:		
Title of the study:		
Institution:		
Name of Principal Investigator/Researcher:	Name of supervisor(s):	
PI Qualification:	Supervisor Qualification:	
Ethical Approval Number:		
Research Site (S):		
Nature Of Amendment:		
Effect On Risk Benefit Profile Of Participants:		
Please submit the following documentation: • Amended proposal **(changes to be underlined)** • Changes to letter of information and consent **(changes to be underlined)** • Any other relevant documentation		
Signature of PI:	**Date:**	
Signature of Supervisor:	**Date:**	
TO BE COMPLETED BY THE CHAIRPERSON OF THE UHERB		
Date received:		
Review required:	Yes	No
Type of Review Required:	Expedited	Full
TO BE COMPLETED BY THE CHAIRPERSON OF UHERB		
UHERB DECISION REGARDING AMENDMENT		
◯ Approved – there are no evident grounds for concern or further investigation.		
◯ Approved subject to minor changes		
◯ Needs to be re-submitted after recommendations are met		

◯ Approved however a site inspection is recommended.	
◯ Denied (please see attached)	
Signature of Chairperson of UHERB:	**Date:**