Standard Operating Procedures and Guidelines

Health Sciences Research Ethics Committee

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HEALTH SCIENCES
UFS

ACKNOWLEDGEMENTS

This document *'Standard Operating Procedures and Guidelines (HSREC SOPs)* provide an updated and strengthened guide to ensure that health-related research involving the University of the Free State is conducted responsibly and ethically.

Drawing on local and international ethics codes and guidelines, the Health Sciences Research Ethics Committee (HSREC) developed this locally relevant document.

Mandated by the National Health Research Ethics Council (NHREC), the basic expectations of the HSREC SOPs include that:

- Proposals to conduct research involving humans undergo HSREC review before research begins
- Proposed health research promote health, contribute to prevention of communicable or non-communicable diseases or disability or results in cures or alleviation of suffering
- Proposals to conduct health research stand up to scientific and ethical scrutiny appropriate to the disciplines concerned
- Harm to research participants is prevented or at least minimised and balanced against the likelihood of benefit
- Researchers are accountable for their research activities
- Social and ethical values are promoted

The HSREC is grateful to all HSREC members and HSREC Administration for their role in development of the HSREC SOPs and for their expert and technical input.

With thanks to the Stellenbosch University Health Research Ethics Office for extensive use of the HREC Terms of Reference and SOP document, towards the development of this version.

PROF A SHERRIFF
CHAIR: HEALTH SCIENCES RESEARCH ETHICS COMMITTEE
DATE: 24 November 2021

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1. THE HEALTH SCIENCES RESEARCH ETHICS COMMITTEE OF THE UNIVERSITY OF THE FREE STATE

1.1 Note

1.1.1 This section (1) should be read in conjunction with the Terms of Reference and Code of Conduct of the HSREC

1.2 Name of The Committee

1.2.1 The Health Sciences Research Ethics Committee of the University of the Free State, hereafter called the HSREC.

1.3 Objectives

1.3.1 The objectives of the HSREC are:

1.3.1.1 to protect the human participant in research;
1.3.1.2 to acknowledge human rights in health research;
1.3.1.3 to maintain high ethical standards in health research;
1.3.1.4 to foster an awareness of ethical aspects in the health sciences; and
1.3.1.5 to prevent impermissible research and research practices.

1.4 Policy

1.4.1 The HSREC reports to Faculty Management of the Faculty of Health Sciences on administrative matters.

1.4.2 The HSREC honours and respects current national and international ethical norms, standards and principles as specified in relevant documents of the Standard Operating Procedures (SOPs) regarding the evaluation of protocols. The HSREC functions in compliance with, but not limited to, the following documents and guidelines:

1.4.2.1 The Constitution of the Republic of South Africa;
1.4.2.2 The South African National Health Act. No. 61 of 2003 (2017);
1.4.2.3 Department of Health, 2015. Ethics in Health Research: Principles, Processes and Structures. Department of Health: Pretoria, South Africa;
1.4.2.4 Department of Health, 2006. Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa. Department of Health: Pretoria, South Africa;
1.4.2.5 Declaration of Helsinki;
1.4.2.6 The Belmont Report;
1.4.2.7 The Singapore Statement on Research Integrity;
1.4.2.8 H3Africa (2013). Guidelines for Informed Consent. H3Africa Working Group on Ethics and Regulatory Issues for the Human Heredity and Health (H3Africa) Consortium;
1.4.2.9 CIOMS (2002). International Ethical Guidelines for Biomedical Research Involving Human Subjects. Council for International Organisations of Medical Sciences and WHO: Geneva;
1.4.2.10 ICH Harmonised Tripartite Guideline: Guideline for Good Clinical Practice E6 (R2) 2016;
1.4.2.11 ICH Harmonised Tripartite Guideline: Clinical Investigation of Medicinal Products in the Paediatric Population E11 2000;
1.4.2.12 The International Conference on Harmonization and Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH Tripartite);
1.4.2.13 Final Framework for African genomics and biobanking (2017);
1.4.2.14 Guidelines of the South African Health Products Regulatory Authority (SAHPRA) as well as Laws and Regulations with regard to the Control of Medicines; and
1.4.2.15 The HSREC Terms of Reference
1.4.2.16 The HSREC Code of Conduct.

1.4.3 When strict compliance with the letter of a particular requirement of these declarations and codes is not possible, the HSREC will ensure that the proposed research is nonetheless in keeping with the spirit of the declarations and codes.

1.4.4 The essential purpose of the HSREC is to protect the dignity, rights, safety, and well-being of all human participants in health-related research. A high premium is placed on the transcultural differences, identity and confidentiality of subjects. Attention is also paid to measures for the protection of researchers. The HSREC will do this through independent,

prospective and ongoing ethics review of all health research projects undertaken by members of staff, registered students and affiliates of the University of the Free State.

1.4.5 The HSREC carefully guards against aspects that could result in serious side-effects, could offend, be dangerous or discriminatory or involve risks, as well as against poorly or vaguely formulated protocols and information documents for subjects.

1.4.6 The HSREC may, at the discretion of the Chair or HSREC Administration, accept for the purposes of review research protocols involving human participants submitted to it by researchers from other institutions who are not UFS staff members, students or affiliates.

1.5 Composition and Membership

1.5.1 The HSREC is authorised to follow the DOH 2015 and to establish a membership that complies with the regulatory framework and is appropriate for the scope and nature of research conducted under the auspices of the UFS.

1.5.2 Criteria for membership:

1.5.2.1 able to contribute by means of qualifications, experience and expertise to review and evaluate the scientific, medical, legal, psychosocial and ethical aspects of research applications;

1.5.2.2 persons of good standing and who have a working knowledge of research ethics codes and guidelines;

1.5.2.3 a lay person who is representative of the communities that the HSREC serves;

1.5.2.4 reflect the demographic profile of the population of South Africa;

1.5.2.5 either gender, although not more than 70% should be either male or female.

1.5.3 Nomination and election of members

1.5.3.1 Members of the HSREC are elected every three years according to Faculty/School procedures.

1.5.3.2 In case of a vacancy, an interim nomination and election will take place.

1.5.3.3 Nomination of suitable members is informed by criteria for membership, HSREC membership, terms of reference and code of conduct

1.5.3.4 A potential member may be nominated by any member of staff in the School that the nominee represents, from the position of lecturer and higher

1.5.3.5 A nomination should be seconded by a member in good standing of the HSREC

1.5.3.6 Following this process, the name of the nominee is presented at the next HSREC meeting. If any member objects to the recommendation of the nominee, this should be raised at the meeting or within 7 working days of the meeting in writing addressed to the Chair of the HSREC. If no objections to the nomination are received within this time, the nominee will go through the appointment process.

1.5.4 Appointment of HSREC members:

1.5.4.1 Elected members will be presented to the Faculty Management for approval at the last Faculty Management meeting of the preceding year.

1.5.4.2 Following this, membership ratified at the following Faculty Board meeting.

1.5.4.3 Once approved by Faculty Management as well as the Faculty Board, the newly appointed members are informed in writing that they have been appointed on the HSREC within 5 working days of the Faculty Board meeting.

1.5.4.4 Following this, the nominee becomes an official member of the HSREC of the Faculty of Health Sciences and is required to start training and attend the next HSREC Meeting.

1.5.4.5 On appointment, HSREC members sign the:

1.5.4.5.1 Confidentiality and Non-disclosure Agreement and

1.5.4.5.2 Member Code of Conduct

1.5.4.6 A newly appointed member will only be eligible to review protocols once they have:

1.5.4.6.1 Current Good Clinical Practice certification

1.5.4.6.2 Completed the SA GCP training on TRREE

1.5.4.6.3 Completed HSREC member training

1.5.4.6.4 Performed two shadow reviews

1.5.4.6.5 Signed confidentiality and non-disclosure document

1.5.4.6.6 Member code of conduct

1.5.4.7 If a newly appointed HSREC member is not able to fulfil the requirements to review protocols (above) within 3 months of appointment, that persons' membership will be terminated.

1.5.4.8 A member may serve for a maximum of two three-year terms consecutively. A

member may be re-elected after a recess of one year.

1.5.4.9 In the absence of a valid reason, members who do not attend two consecutive meetings or who do not accept or submit accepted reviews will be contacted by the HSREC office and asked to furnish a reason for this. If the member does not attend the subsequent meeting or again fails to accept or submit accepted reviews, the chair will contact the member and ask for an explanation. Simultaneously, the chair will send a letter informing the member that failure to attend the next meeting or failure to accept or submit accepted reviews will result in termination of membership by the Faculty Management Committee.

1.5.4.10 The University of the Free State obtains professional liability insurance to cover both affiliated and non-affiliated members when carrying out any professional duties under the auspices of the HSREC.

1.5.5 HSREC Chair and Vice-Chair:

1.5.5.1 The Chair is nominated and elected from the members at the first meeting after the election of members.

1.5.5.2 A Vice-Chair is nominated and elected from the members at the first meeting after the election of members.

1.5.5.3 The Chair and Vice-Chair(s) are elected by HSREC members, for a renewable term of three years.

1.5.6 HSREC Membership:

1.5.6.1 The HSREC shall:

1.5.6.1.1 Always have at least 20 voting members;

1.5.6.1.2 Not only have members from senior ranks

1.5.6.1.3 Be diverse in terms of age, race, gender

1.5.6.1.4 Have at least one member with knowledge of, and current experience in, the professional care, counselling or health-related treatment of people. Such a member might be a medical practitioner, psychologist, social worker or nurse;

1.5.6.1.5 Have at least one member with professional training and experience in qualitative research methodologies

1.5.6.1.6 Have members with professional training in quantitative research methodologies

1.5.6.1.7 Have at least one member with expertise in bio-statistics

1.5.6.1.8 Have at least one member with expertise in research ethics

1.5.6.1.9 Have at least one member who is legally qualified

1.5.6.1.10 Have at least one lay representative who has no affiliation with the University of the Free State or the Academic Hospital Complex, and who is not involved in medical, scientific or legal work, and who is from the community that the HSREC represents.

1.5.6.1.11 Have sufficient membership to address all considerations arising from the categories of research likely to be submitted to it.

1.5.6.1.12 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 ground and conforms to the principles of this document.

1.5.6.1.13 Have a Chair and a Vice-Chair;

1.5.6.1.14 Have an EXCO consisting of the Chair and the Vice-Chair, one representative each from the School of Pathology, School of Biomedical Sciences, School of Health and Rehabilitation Sciences, School of Nursing and School of Clinical Medicine.

1.5.6.1.15 Define a quorum as:

1.5.6.1.15.1 A simple majority of the members listed on the HSREC membership roster. When the membership roster consists of an even number (N), a quorum is defined as (N/2) +1.

1.5.6.1.15.2 A quorum should include at least one, but preferably more than one member who has knowledge of and current experience in the processional care, counselling or health-related treatment of people;

1.5.6.1.15.3 Meetings will only be conducted when a quorum is

present.

1.5.6.1.16 Expect all members to provide the following documents annually:
- 1.5.6.1.16.1 provide proof of current Good Clinical Practice certification
- 1.5.6.1.16.2 signed confidentiality and non-disclosure agreements
- 1.5.6.1.16.3 signed HSREC member code of conduct
- 1.5.6.1.16.4 proof of registration with the relevant professional board

1.5.6.1.17 Members will be required to sign a statement undertaking:
- 1.5.6.1.17.1 that any conflicts of interest, which exist or may arise during his/her tenure on the HSREC will be declared;
- 1.5.6.1.17.2 that he/she will notify the EXCO of the HSREC of any criminal conviction or disciplinary action in writing

1.5.6.1.18 Require members to provide proof of continuous professional development in research ethics.

1.5.6.1.19 Invite non-members with expertise in special areas for assistance/advice.

1.5.6.1.20 Strive to retain expertise within the HSREC as far as possible.

1.5.6.2 HSREC membership will include:
- 1.5.6.2.1 Representation from the five Schools in the Faculty
  - 1.5.6.2.1.1 School of Clinical Medicine: 15
  - 1.5.6.2.1.2 School of Pathology: 3
  - 1.5.6.2.1.3 School of Biomedical Sciences: 4 (including at least one biostatistician)
  - 1.5.6.2.1.4 School of Nursing: 5
  - 1.5.6.2.1.5 School of Health and Rehabilitation Sciences: 5
- 1.5.6.2.2 One representative from the Faculty of Health and Environmental Sciences of the Central University of Technology, Free State and his/her secundus
- 1.5.6.2.3 One representative from the Provincial Health Research Committee and his/her secundus.

1.5.6.3 Voting members:
- 1.5.6.3.1 All members, except ex office members are voting members

1.5.6.4 Termination/resignation:
- 1.5.6.4.1 At the end of the three-year term of a member, their membership automatically terminates and their availability for re-election is determined during the July meeting of their last serving term.
- 1.5.6.4.2 The policy and procedures regarding the election of members for the HSREC are followed to elect new members on the HSREC.
- 1.5.6.4.3 In a case of resignation, the resigning member must inform the HSREC in writing of his/her intention to resign from the HSREC.
- 1.5.6.4.4 The resigning member must submit his/her letter of resignation at least one month before the actual resignation date.
- 1.5.6.4.5 The resignation is referred to the next HSREC meeting for notification and HSREC Administration will inform the secretariat of Faculty Management accordingly.
- 1.5.6.4.6 The HSREC could also decide to terminate the services of an appointed member. The specific case must be discussed at a Faculty Management meeting. If the Faculty Management accepts the recommendation, an official letter will be written by the secretariat of the HSREC to the said HSREC member informing him/her of the decision by the HSREC as well as the Faculty Management.
  - 1.5.6.4.6.1 The member has failed to provide a valid reason for meeting non-attendance, refused to accept reviews or failed to review accepted reviews on two occasions, and was contacted by the HSREC admin office and then subsequently failed to provide a reason for meeting non-attendance, refused to accept reviews or failed to review accepted reviews, and was contacted by the Chair of the HSREC in writing and then subsequently failed to provide a reason for meeting non-attendance, refused

to accept reviews or failed to review accepted reviews on a fourth occasion;

1.5.6.4.6.2 The member has failed to produce documentation or certification required for a member to be a functional member of the HSREC despite being asked for it in writing three times over a period of three months

1.5.6.5 The membership and composition of the HSREC will be continuously monitored to ensure appropriate representation. When a member resigns from the HSREC, the choice of a replacement takes into account the overall balance of the HSREC and specific expertise that is needed.

1.5.6.6 Faculty Management or delegate may terminate the appointment of any member of the HSREC if the Faculty Management is of the opinion that:

1.5.6.6.1 it is necessary for the proper and effective functioning of the HSREC;

1.5.6.6.2 the person is not fit to serve on an HSREC;

1.5.6.6.3 the person has failed to carry out his/her duties as an HSREC member as described above.

1.5.7 Remuneration: Members are not offered remuneration, except lay members who are reimbursed for meeting attendance. Refer to Terms of Reference.

1.6 HSREC Policies and Procedures

1.6.1 The HSREC will perform its functions, including monitoring of research and management of complaints, according to its written standard operating procedures (SOPs) available on the Faculty of Health Sciences website.

1.6.2 These procedures shall be reviewed continuously and amended and updated as necessary.

1.6.3 All HSREC members shall have access to and/or be provided with copies of the SOPs and shall be consulted with regard to changes thereto.

1.6.4 All issues involving research governance will be dealt with in accordance with the HSREC Standard Operating Procedures.

1.7 Conflict of Interest

1.7.1 Members of the HSREC are expected to make decisions and conduct their oversight responsibilities in an independent manner, free from bias and undue influence. HSREC members (and members of their immediate families) may be involved in activities that could be perceived as conflicting with their HSREC responsibility. The integrity of the HSREC review process can be compromised if such conflicts of interests are not disclosed and where necessary, avoided.

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

1.7.2.1 Personal Relationship: The HSREC member has a personal relationship with the principal investigator or key personnel of a research protocol under review by the HSREC.

1.7.2.2 Relationship to the research study: The HSREC member (his/her spouse or immediate family member) is the principal investigator or co-investigator of the research protocol under review by the HSREC.

1.7.2.3 Business relationship or affiliation: The HSREC 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 the HSREC.

1.7.2.4 Financial interest: The HSREC member has a financial interest that could be affected by the outcome of the research protocol under review by the HSREC. 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.

1.7.3 HSREC members should make disclosures to the Chair. The Chair and HSREC shall determine whether a conflict exists. The determination of whether or not a conflict exists shall be reflected in the minutes.

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

1.7.5 Recusal: HSREC members who have a conflict of interest related to any research protocols that the HSREC is about to consider will refrain from participating in any discussion of the protocol or related matters, except to the extent necessary to provide relevant factual

information requested by the Chair. Unless requested by the Chair to provide such information to the HSREC, the member with a conflict of interest will leave the meeting during the discussion and decision process. The outcome of the HSREC 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.

1.7.6 HSREC members assigned as a reviewer for a protocol or related matters, with respect to which a conflict of interest has been identified, will notify HSREC Administration so that the protocol can be reassigned.

1.7.7 In the event that the conflict of interest involves the Chair, he or she will appoint the Vice-Chair, or another member as acting chair (with approval of the HSREC). The acting chair will conduct the meeting, for the remainder of the discussion of the item in question.

1.8 Confidentiality

1.8.1 All HSREC members and HSREC Administration shall sign a standard confidentiality and non-disclosure agreement on appointment to HSREC.

1.8.2 All HSREC business, documents, discussions and correspondence are considered confidential.

1.9 Continuous Professional Development of HSREC members and administration in Research Ethics

1.9.1 Should be managed according to the SOP Orientation, education and training of HSREC Members and Staff.

1.9.2 Funding for continuous professional development shall be funded from the Faculty Management of the Faculty of Health Sciences.

1.9.3 An annual training budget shall be allocated to the HSREC from the Faculty Management.

1.10 Consultants and Ad Hoc Reviewers

1.10.1 The HSREC may use consultants or *ad hoc* reviewers where additional or specialised expertise is needed to review specific protocols. Reasons for seeking additional or special competence may include but are not limited to the need for:

1.10.1.1 Additional scientific, clinical or scholarly expertise.

1.10.1.2 Particular knowledge about potentially vulnerable populations.

1.10.1.3 Broader understanding of gender or cultural issues.

1.10.1.4 Greater sensitivity to community perceptions.

1.10.1.5 A statistical opinion.

1.10.2 Consultants and *ad hoc* reviewers:

1.10.2.1 Must have access to all documents submitted to the HSREC relevant to the specific study under review.

1.10.2.2 May take part in deliberations and may make recommendations concerning the study.

1.10.2.3 May not vote unless required by a particular protocol and such voting status is confirmed by the HSREC in advance on a case-by-case basis.

1.10.2.4 Must affirm that they have no conflict of interest with respect to the specific studies that they are invited to review.

1.10.2.5 Must maintain strict confidentiality with respect to the specific protocol and the meeting's proceedings and will be required to sign a confidentiality agreement.

1.10.2.6 May provide information about a specific study by written reports and/or by attending the meeting.

1.11 Evaluation of HSREC Members and Chairpersons

1.11.1 **The HSREC Chair:** The HSREC Chair will be evaluated annually. This will be done by means of both an objective and subjective assessment.

1.11.1.1 Objective assessment: At the end of each academic year, HSREC Administration will provide the following metrics for the HSREC Chair and vice-chair:

1.11.1.1.1 Number of meetings attended and chaired out of the total number of meetings.

1.11.1.1.2 Number of protocols reviewed that went to the convened HSREC meeting.

1.11.1.1.3 Number of reviews completed.

1.11.1.1.3.1 Final approval

1.11.1.1.3.2 Modifications required
1.11.1.1.3.3 Conditional Approval
1.11.1.1.3.4 Amendments
1.11.1.1.3.5 Notifications
1.11.1.1.3.6 Study closure
1.11.1.1.4 Number of letters reviewed
1.11.1.1.4.1 Final approval
1.11.1.1.4.2 Modifications required
1.11.1.1.4.3 Conditional Approval
1.11.1.1.4.4 Amendments
1.11.1.1.4.5 Notifications
1.11.1.1.4.6 Study closure
1.11.1.1.5 Number of EXCO meetings managed/ attended
1.11.1.1.6 Number of meetings with researchers
1.11.1.1.7 Number of meetings or letters with reviewers or faculty
1.11.1.1.8 Number of Provincial Ethics committee attended,

1.11.1.2 At the end of each academic year, the HSREC Chair and vice-chair will complete self-evaluation forms.

1.11.1.3 The results of these assessments will be presented at the HSREC Executive Committee (EXCO) meeting and will be used to make decisions regarding training development, overall improvement of the HSREC, and the composition of the HSREC itself.

1.11.2 HSREC Members: The HSREC Members will be evaluated annually. This will be done by means of both an objective and subjective assessment.

1.11.2.1 Objective assessment: At the end of each academic year, HSREC Administration will provide the following metrics for each HSREC Member:

1.11.2.1.1 Number of meetings attended out of the total number of meetings.
1.11.2.1.2 Number of times that members availed themselves for review
1.11.2.1.3 Number of protocols reviewed that went to the convened ethics committee meeting.
1.11.2.1.4 Number of reviews completed.

1.11.2.2 At the end of each academic year, each HSREC Member will complete a self-evaluation form.

1.11.2.3 Anonymised results of these assessments will be presented at a HSREC meeting and will be used to make decisions regarding training development and other needs

1.11.2.4 The EXCO will review the identified results of outliers

1.11.3 The results of these assessments will be shared with the HSREC Chair and presented at the HSREC Executive Committee (EXCO) meeting and will be used to make decisions regarding training development and the composition of the HSREC itself.

1.12 Meetings

1.12.1 Meetings will be held in accordance with the procedures as set out in this document.

1.12.2 The HSREC agenda will be distributed no later than seven working days prior to the HSREC meeting.

1.12.3 Decisions by the HSREC will be informed by the exchange of opinions from each of the members that constitute the minimum membership of the HSREC (20 members).

1.12.4 The contribution of information and opinion from an HSREC member unable to attend a face-to-face meeting will be considered along with those opinions and feedback of other HSREC members in the final decision making.

1.12.5 In general, decisions of the HSREC will be reached by general agreement and consensus. If there is a difference of opinion and there is not a two-thirds agreement from voting members, the decision will be postponed. The decision will be made after expert opinion has been gathered and the matter will be reverted to the committee for voting. If the decision is time sensitive the feedback and voting will take place on the virtual platform.

1.12.6 Members of the HSREC will be required to declare any conflict of interest prior to or at any time during a meeting. The Chairperson will determine the action to be taken.

1.12.7 Dates and venue:

1.12.7.1 At least 10 meetings per year.

1.12.7.2 Meeting dates will be available on the Faculty of Health Sciences website.

1.12.7.3 The venue and time will be confirmed.

1.12.8 Secretarial Support:

1.12.8.1 Secretarial support will be provided by HSREC Administration.

1.12.9 Decisions from HSREC meetings:

1.12.9.1 The minutes of meetings will be recorded in writing and audio.

1.12.9.2 Minutes will record major issues discussed, concerns expressed, decisions taken and reasons for rejection or requirement for change to the protocol.

1.13 Continuous Monitoring

1.13.1 Continuous monitoring of research given institutional authorisation should be managed as set out in this document.

1.14 Complaints and Appeals

1.14.1 Research complaints concerning the conduct of a project and / or a Committee's review process, including the Committee's rejection of an application should be managed as set out in this document.

APPROVAL

Prof A Sherriff
Chair: Health Sciences Research Ethics Committee (HSREC)

2. HSREC POLICIES AND PROCEDURES

2.1 Purpose

This section describes the policies and procedures for developing, implementing, and revising written policies and procedures for the Health Sciences Research Ethics Committee (HSREC) of the University of the Free State.

2.2 Policy

2.2.1 The HSREC holds and maintains written policies and procedures for the major functions of the HSREC. As required by regulations, this includes procedures which the HSREC will follow for:

2.2.1.1 Conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and institution;

2.2.1.2 Ensuring prompt reporting to the HSREC of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which HSREC approval has already been given, may not be initiated without HSREC review and approval except when necessary to eliminate apparent immediate hazards to subjects.

2.2.2 HSREC policies and procedures must be consistent with:

2.2.2.1 Applicable national and international regulations;

2.2.2.2 The terms of the UFS Federalwide Assurance (FWA).

2.2.3 HSREC Administration has delegated authority from the HSREC Chair to develop, implement, and revise policies and procedures for the HSREC.

2.2.4 Procedures should provide sufficient step-by-step description with key operational details so that an independent observer can understand how the HSREC operates and conduct their major functions.

2.3 Definitions

2.3.1 Federalwide Assurance for the protection of human subjects (FWA): A written assurance of compliance with federal human subjects' regulations that is provided by an institution conducting federally-supported, non-exempt, human subjects research. Through the FWA, an institution commits to federal agencies that it will comply with the regulations and requirements.

2.3.2 Guidance: Written discussion of issues. Guidance may be free-standing documents or may be embedded within a Standard Operating Procedure (SOP). When embedded within a SOP, guidance is clearly labelled as "guidance".

2.3.2.1 Guidance enhances policies and procedures by providing additional information about specific ethical, regulatory or administrative issues.

2.3.3 Documentation: In a SOP, this section refers to any material needed to perform the activities described in the SOP. Examples: forms, checklists, templates, other SOPs.

2.3.4 Policy: A guiding principle of operation, broad decision-making, or service.

2.3.5 References: This section can be found at the end of the SOP document and lists reference documents that are referred to, that provide the basis for the procedure, or that describe related or additional information.

2.3.6 Standard Operating Procedure (SOP): The term used by the HSREC to refer to documents containing HSREC policies and procedures.

2.3.7 HSREC Administration: Employees appointed to support the HSREC function.

2.4 Responsibilities

2.4.1 The HSREC Chair and/or designee(s) is/are responsible for reviewing all HSREC policies, prior to implementation.

2.4.1.1 A subcommittee may be appointed as deemed necessary.

2.4.2 HSREC Administration is responsible for the following areas, though any of these responsibilities may be delegated to others in HSREC on a routine or ad hoc basis:

2.4.2.1 Overall management of HSREC policies and procedures. This includes:

2.4.2.1.1 drafting new and revised documents;

2.4.2.1.2 obtaining consultation; and

2.4.2.1.3 feedback and communication.

2.4.2.2 Promoting and ensuring consistency in interpretation and implementation of the policies and procedures.

2.4.3 HSREC Administration members are required to follow implemented HSREC policies and procedures.
2.4.4 All HSREC members are responsible for following implemented HSREC policies and procedures.

2.5 Procedures

2.5.1 New policies and procedures (SOPs):
- 2.5.1.1 New SOPs are written using the standard format. Variations in structure and content are permissible when appropriate for the content or for ensuring clarity.
- 2.5.1.2 Initial content is drafted by the Head of HSREC in consultation with HSREC Administration and HSREC EXCO.
- 2.5.1.3 The template: SOP specifies the required content sections.
- 2.5.1.4 The SOP may (optionally) include guidance in addition to the template-specified sections.
- 2.5.1.5 Consultation and feedback are obtained as appropriate to the content.
- 2.5.1.6 Consultation and feedback may be obtained through any methods and mechanisms that seem appropriate. For example, this may include: emailed draft documents and presentations at HSREC meetings.
- 2.5.1.7 The HSREC Chair obtains approval from the HSREC members by providing the members with a copy of the final SOP document. This may be preceded or accompanied by a briefing – e.g., about the content, the feedback and consultation obtained, implications, regulatory basis, etc.
  - 2.5.1.7.1 Approval is documented by the HSREC Chair's dated signature on the first page of the printed SOP, as well as in the HSREC Minutes of the meeting at which the SOPs were presented for approval.
- 2.5.1.8 SOPs may be implemented after approval and after being posted on the HSREC website.
  - 2.5.1.8.1 In rare circumstances, a SOP may instead be implemented by posting it to the secure internal HSREC shared server. This implementation route is used only for a few SOPs that describe internal HSREC processes not tied to regulatory requirements.
- 2.5.1.9 SOPs are formally distributed to their audiences (e.g., HSREC Administration, HSREC members, researchers, etc.) by being posted on the HSREC's website. Implementation is formally communicated to all audiences through email.
  - 2.5.1.9.1 Exception: the rare SOPs that are implemented by being posted on the HSREC internal server. These are communicated to HSREC staff through internal email and/or HSREC meetings.

2.5.2 Revision of SOPs:
- 2.5.2.1 Revisions of existing SOPs follow the same process as described above for new SOPs.
- 2.5.2.2 SOPs are revised as needed, but no less than once every two years.

2.5.3 Management of SOPs:
- 2.5.3.1 HSREC SOPs are maintained by HSREC Administration.
- 2.5.3.2 The implemented documents are stored as electronic documents in the HSREC's shared folder as well.
- 2.5.3.3 SOP management information is created, maintained and revised for each update of the document.
- 2.5.3.4 The management information is maintained in the document itself and on the HSREC shared folder.

2.5.4 Retirement of SOPs:
- 2.5.4.1 SOPs are retired for many possible reasons, such as regulatory changes that eliminate the need for the SOP.
- 2.5.4.2 The HSREC EXCO is responsible for making the decision to retire a SOP.
- 2.5.4.3 The retirement process consists of:
  - 2.5.4.3.1 Removing the section from the SOP document.
  - 2.5.4.3.2 Moving the retired version of the SOP document into the "Archived" section of the document library;

2.5.4.3.3 Updating the document version.

2.5.5 HSREC Practices

2.5.5.1 HSREC staff and HSREC members may occasionally develop practices for doing certain operations or managing certain issues.

2.5.5.2 Such practices are not necessarily considered official HSREC SOPs, even when they exist in writing and have been widely adopted.

2.5.5.3 Practices must be consistent with implemented HSREC SOPs.

2.5.5.4 Practices that arise out of interpretation of regulations or policies should be evaluated by HSREC members:

2.5.5.4.1 for consistency with existing SOPs, and

2.5.5.4.2 as a possible indication of the need for a new or revised SOP.

2.5.5.5 Practices should not be construed as limitations on the flexibility or range of possibilities inherent in regulations and in official SOPs.

3 ORIENTATION, EDUCATION, AND TRAINING OF HEALTH SCIENCES RESEARCH ETHICS COMMITTEE MEMBERS

3.1 Purpose

This section describes the procedures used to train Health Sciences Research Ethics Committee (HSREC) of the University of the Free State members and staff.

3.2 Policy

3.2.1 It is policy of the HSREC that all involved in the review and oversight of human subject research (voting HSREC Members, HSREC Chairs and HSREC Administration) must complete initial and continuing education in human research protections.

3.2.1.1 Initial orientation to be completed within 6-8 weeks from the date the appointment was confirmed by the Faculty Board.

3.2.2 Opportunities for training and refresher courses in human research ethics should be made available or accessible for voting HSREC members and HSREC Administration.

3.3 Definitions

3.3.1 A new member is defined as someone whose appointment on the HSREC has been confirmed by the Faculty Board, but has not yet completed the required orientation process.

3.3.2 Orientation process is defined as the completion of the following:

3.3.2.1 The completion of the TRREE modules as stipulated in the procedures;

3.3.2.2 The completion of shadow reviews;

3.3.2.2.1 Shadow reviewing: the new HSREC member serves as a third reviewer in addition to the two main reviewers. The new HSREC member is not regarded as a formal reviewer on this research study, but may submit comments or questions if there is an issue, he/she believes has not been addressed.

3.4 Responsibilities

3.4.1 HSREC Administration is responsible for compiling the training files and arranging the sessions.

3.4.2 HSREC members are responsible for attending sessions, and following the self-paced programme as set out by this document.

3.5 Procedures

3.5.1 Orientation:

3.5.1.1 New HSREC members are required to complete an orientation process prior to reviewing any research studies.

3.5.1.2 New member orientation should include meetings with the HSREC Chair, and HSREC Administration. The focus of the meetings will include:

3.5.1.2.1 Regulations and purpose of the HSREC

3.5.1.2.2 Other regulations that pertain to human subject research

3.5.1.2.3 Key issues in the protection of human subjects

3.5.1.2.4 Day-to-day operations of the HSREC

3.5.1.2.5 Research management system training

3.5.1.2.6 Data/information management in terms of POPIA

3.5.1.3 New HSREC members are also provided with access to an online reference binder available through the UFS intranet. Links to appropriate documentation are available.

3.5.1.4 New HSREC members are required to complete specific research ethics courses using the Training and Resources in Research Ethics Evaluation (TRREE) training program. At a minimum, all users must complete the following modules and submit their certificates to the HSREC office:

3.5.1.4.1 Module 1: Introduction to Research Ethics

3.5.1.4.2 Module 2.1: Research Ethics Evaluation

3.5.1.4.3 Module 3.1: Informed consent

3.5.1.4.4 National Supplement Module: South Africa

3.5.1.4.5 Initial TRREE training is valid for three years and must be refreshed by repeating the modules and submitting the new certificates to HSREC Administration.

3.5.1.5 As part of the training process, new HSREC members perform a shadow review of new initial applications.

3.5.1.6 The orientation procedure for the HSREC Chair will vary by level of Research Ethics Committee experience and familiarity with the HSREC review process.

3.5.2 Ongoing education:

3.5.2.1 The HSREC will provide and support continuing educational opportunities as appropriate.

3.5.2.2 Maintenance of certification of TRREE and a Good Clinical Practice certificate (GCP) must be submitted to HSREC Administration.

3.5.3 Good Clinical Practice Certification (GCP)

3.5.3.1 HSREC members who review clinical trial proposals should have completed GCP training, evidenced by a valid certificate. GCP must be refreshed every three years to obtain a valid certificate.

3.5.4 Fulfilment of requirements

3.5.4.1 Education requirements are monitored by the HSREC Chair and HSREC Administrator. HSREC members who do not complete the required HSREC training within the allotted time frames will not be involved in reviewing research studies or voting at the convened meetings until the requirement is satisfied.

3.5.4.2 If an HSREC member does not fulfil his/her initial and/or continuing education requirements, the HSREC Executive Committee (EXCO) may recommend actions to the Faculty Board.

4 APPLICATION AND ADMINISTRATIVE REQUIREMENTS

4.1 Purpose

4.1.1 This section provides guidelines for submitting the required documents to the HSREC with regard to research activities involving human participants.

4.2 Procedure

4.2.1 Application information and guidelines for submission are available from HSREC Administration, Dean's Division, Block D, Room 104, Francois Retief Building, Faculty of Health Sciences or visit the webpage for further information

4.2.2 Applications can be submitted on an ongoing basis, but must be received by the set due dates in order to be considered for the agenda of the relevant meeting.

4.2.3 ***NOTE:*** Submission of a research application by the submission due date does not guarantee that application will be incorporated into a specific agenda. If the application is incomplete, it will not be accepted for review and will be sent back to the researcher.

4.2.4 The dates of meetings are available from HSREC Administration and from the webpage.

4.2.5 For information on specific submission types, refer to the Preparation Guidelines available on the webpage and from HSREC Administration.

4.3 Review Fees

4.3.1 The HSREC has a graded administrative fee structure in place, which is revised annually.

4.3.2 Student projects and projects funded solely from a University of the Free State departmental budget are exempt from fees.

4.3.3 The current administrative fee structure is available on the HSREC webpage.

4.3.4 The HSREC reserves the right to not review a research application if administrative fees are outstanding.

4.4 Signatures on HSREC Forms

4.4.1 It is HSREC policy to require the signature of the investigator(s) and student supervisor(s) (if the research is for qualification) on the Investigator Declaration document. This form is available from HSREC Administration and the webpage. The application will not be accepted for review if this document is not signed and submitted.

4.4.2 The investigator's Head of Department must provide a letter of support which must be submitted with the initial application. The application will not be accepted for review if this document is not signed and submitted.

If the researcher is the Head of Department a letter of support must be provided by his/her senior member of their Departmental Management team.

4.4.2.1 Head of Department (HOD) signature/letter of support.

4.4.2.1.1 The purpose of the signature of the HOD is to provide HSREC with documentation of:

4.4.2.1.1.1 The HOD's approval of the investigator's qualifications for conducting the proposed research, based on knowledge of the investigator's academic position, education, resources for the research, and expertise.

4.4.2.1.1.2 The HOD's approval of the scientific merit of the proposed research.

4.4.2.2 Head of Department signature.

4.4.2.2.1 The Head of Department may delegate this signature responsibility to others.

4.4.2.2.2 The following describes who should sign as Head of Department in specific circumstances:

4.4.2.2.2.1 Standard: Head of Department or individuals with delegated authority.

4.4.2.2.2.2 Investigator has appointments in more than one department:

4.4.2.2.2.2.1 The Head of Department of the investigator's primary UFS department.

4.4.2.2.2.3 Student investigator whose supervisor is in a different department:

4.4.2.2.2.3.1 The head of the student's department.

4.4.2.2.2.4 Student investigator whose supervisor is the student's Head of Department:

4.4.2.2.2.4.1 The Head of Department needs to delegate the signatory power to a senior member of the department for the Head of Department letter.

4.4.3 The signature of a study supervisor within a faculty is required on the Investigator Declaration form when the investigator is an undergraduate or postgraduate student.

4.4.3.1 Faculty supervisor signature:

4.4.3.1.1 The faculty supervisor must be a member of the UFS faculty or senior University administration.

4.4.3.1.2 The purpose of the faculty supervisor's signature is to provide:

4.4.3.1.2.1 Confirmation that the faculty supervisor accepts responsibility, together with the student investigator, for ensuring that the research is performed in an ethical manner that complies with appropriate human subjects' regulations and with the information provided in the application. This may include assisting the HSREC if they are unable to effectively communicate with the student or if problems develop.

4.4.3.1.2.2 Confirmation that the faculty supervisor has reviewed and approved of the research, including the: purpose, design, methodology, procedures, and subjects.

4.4.3.1.2.3 Confirmation that the faculty supervisor will provide supervision, advice, and guidance during the course of the research. This should include arrangements for appropriate periodic interaction with the student conducting the research.

4.4.4 Applications for HSREC approval of any research studies will not be accepted until the required signatures have been provided.

4.4.5 Investigator signature:

4.4.5.1 The purpose of the investigator's signature is to provide:

4.4.5.1.1 Authorization to begin a review process on behalf of the investigator;

4.4.5.1.2 Assurance that the project will be conducted as described in the protocol; and

4.4.5.1.3 Assurance that the investigator is aware of, and agrees to fulfil, his/her responsibilities for the project.

4.4.6 Responsibilities:

4.4.6.1 Investigators are expected to provide the appropriate signatures on application forms.

4.4.6.2 HSREC Administration is responsible for verifying that signatures have been provided.

4.4.7 Missing signatures:

4.4.7.1 HSREC Administration notifies the investigator (or investigator's contact person) about any missing signatures. If repeated attempts to obtain the missing signature are unsuccessful, the application is returned to the investigator.

4.4.7.2 Student research

4.4.7.2.1 PhD, Master's and MMed research

4.4.7.2.1.1 All PhD and Master projects must have undergone a scientific review process by an Evaluation Committee first before being submitted to the HSREC for ethics review and approval. The MMed project must be presented to the MMed Departmental research meeting. The final version of the protocol, as approved by the Evaluation Committee, should be submitted to HSREC accompanied by the Evaluation Committee report. Research projects will not be accepted for review if the Evaluation Committee report has not been submitted with the initial application.

4.4.7.2.1.2 A letter from the supervisor is required that states that all corrections advised by the Evaluation Committee or Departmental Research Committee have been implemented.

4.4.7.2.2 Undergraduate and postgraduate research for degree and diploma purposes

4.4.7.2.2.1 All undergraduate and postgraduate health research for degree and diploma purposes must be submitted to the HSREC for review prior to the start of study related activities.

4.4.7.2.2.2 Undergraduate student research:

4.4.7.2.2.2.1 The HSREC will regard the supervisor as the principal investigator who assumes ultimate responsibility for the project. The project will be registered under the name of the student and all correspondence will be addressed directly to the student. If the project is a group project, the project will be registered in the name of the supervisor and list the students as researchers.

4.4.8 Signature format.

4.4.8.1 The signature must preferably be provided in wet ink Electronic or digital signatures are accepted by the HSREC.

4.4.8.2 “Cut, copy and paste” signatures are not acceptable.

5 MATERIALS FOR REVIEW

5.1 Purpose

5.1.1 This section describes the documentation provided to the HSREC for review purposes.

5.2 Policy

5.2.1 Investigators are expected to use the guidance provided by the HSREC to provide sufficient information to the HSREC so that specific required determinations can be made and it can be decided (when appropriate) whether the applicable criteria for HSREC approval have been met.

5.2.2 Review materials are accessible via the research information system to allocated HSREC reviewers and review deadlines are provided from the HSREC office.

5.3 Responsibilities

5.3.1 Investigators are responsible for providing appropriate and sufficient materials so that the HSREC can make determinations and decide whether applicable criteria for approval have been met within the stipulated timeframe.

5.3.2 HSREC Administration is responsible for preparing and distributing the materials for review within the stipulated timeframe.

HSREC members are responsible for reviewing the materials appropriate to their role in a specific review within the stipulated timeframe.

5.4 Procedures

5.4.1 Preparation and distribution of materials:

5.4.1.1 Materials are prepared and provided to HSREC members via InfoEd RIMS.

5.4.2 Materials provided to HSREC Members:

5.4.2.1 General:

5.4.2.1.1 Meeting agenda

5.4.2.1.2 Minutes from previous meetings

5.4.2.1.3 Educational materials

5.4.2.1.4 Ethical principles

6 REVIEW PROCESSES

6.1 Review Process: New Applications

6.1.1 **Purpose**

The purpose of this section is to define and describe the application and review process for the various types of research reviewed by the HSREC.

6.1.2 **Policy**

The HSREC reviews research applications according to predefined review processes:

6.1.2.1 **Minimal Risk review:**

Definition: A new research application may be considered suitable for minimal risk review if the risk level of the proposed research meets the criteria outlined below. This will be reviewed by one reviewer.

6.1.2.1.1 Minimal risk is:

6.1.2.1.1.1 A file audit that is retrospective, excluding vulnerable groups

6.1.2.1.1.2 Retrospective analysis of laboratory data

6.1.2.1.1.3 Any testing of a device where no humans or biological material are involved

6.1.2.1.2 Minimal risk is not:

6.1.2.1.3 Research where genetic or any additional evaluations are done on any biological material

6.1.2.1.4 Research involving human participants or where any form of informed consent is required, including assent in the case of minors.

6.1.2.2 **Expedited review:**

6.1.2.2.1 Expedited review is a procedure through which certain kinds of research may be **reviewed** and approved without convening a meeting of HSREC. Depending on the type of research one or 2 reviewers may be allocated to review the protocol. The turnaround time for reviewers for expedited review is 24 hours (1 working day). The turnaround time for administrative functions for expedited review is 2 working days.

6.1.2.2.2 The expedited review process is an extraordinary process and should not be used as a way to circumvent the normal review process. A motivation for expedited review must accompany any expedited review application with compelling evidence of urgency. The research should address an urgent need and have a significant perceived scientific impact.

6.1.2.3 **Full committee review:**

6.1.2.3.1 Full committee review is intended for research that involves possible risks to participants which are greater than those found in everyday life. These may include: physical, psychological or social risks.

6.1.2.4 **Reciprocal review:**

6.1.2.4.1 Studies that have received ethical approval from another accredited REC, will require evaluation by our HSREC for suitability within the local population. It will be reviewed by one reviewer.

6.1.3 **HSREC Review Process: Minimal Risk Research**

6.1.3.1 Any application for minimal risk research will follow the normal submission procedures as set out by the HSREC. Applications that were not marked for minimal risk specifically may be at the discretion of the HSREC Chair converted to a minimal risk.

6.1.3.2 HSREC Administration captures each minimal risk research application and allocates the application to one HSREC reviewer.

6.1.3.3 An HSREC member reviews the minimal risk research application and submits their proposed review outcome to HSREC Administration.

6.1.3.4 The research application and review outcome are ratified at the next available convened HSREC meeting.

6.1.3.5 If the HSREC member responsible for review of a minimal risk project has any concerns regarding the study, the project will revert to the standard review process and sent to a second reviewer

6.1.3.6 Applicants are notified in writing of the HSREC review decision and may commence with their research once their application has been approved.

All other standard operating procedures of the HSREC are applicable to minimal risk projects. Minimal risk studies will still require relevant approvals (e.g., from the Free State Department of Health, UFS Gatekeepers, etc.)

6.1.4 **HSREC Review Process: Expedited Review**

6.1.4.1 The criteria used to approve an expedited procedure is the same as the criteria used for review by a convened HSREC.

6.1.4.2 The application for expedited review must be accompanied by a motivation for such a review, as well as the motivating reason for this request.

6.1.4.3 If the HSREC member(s) responsible for review of an expedited project has any concerns regarding the study, the project will revert to the standard review process.

6.1.5 **HSREC Review Process: Reciprocal review process**

6.1.5.1 The normal review processes will apply. This application must be accompanied by the full report of the original research ethics committee approval. Different ethics committees may come to different conclusions on the same protocol based on local values, issues or policies.

6.2 Full Committee Review (Convened HSREC Meeting)

6.2.1 **Purpose**

This section describes the review processes and full convened meetings of the HSREC.

6.2.2 **Policy**

6.2.2.1 The HSREC must review all of the following:

6.2.2.1.1 Initial applications, status reports, and amendment requests;

6.2.2.1.2 Unexpected problems, noncompliance, continuing noncompliance, and other problems/information in previously approved studies reported to the HSREC;

6.2.2.1.3 Responses to deferral letters;

6.2.2.1.4 Continuing Review Reports: Continuation Reports for active research and Final Reports for closing/finalised research;

6.2.2.1.5 General and policy matters; and/or

6.2.2.1.6 Allegations of misconduct in research or other complaints.

6.2.2.2 An HSREC meeting cannot occur unless the following conditions are met:

6.2.2.2.1 A quorum consisting of a simple majority of the members is participating (when a simple majority is not possible, the HSREC may revert to National Department of Health quorum requirements, which is 33% of the voting membership)

6.2.2.2.2 The quorum must be maintained for the duration of the meeting.

6.2.2.2.3 The appropriate expertise will be available at the meeting.

6.2.2.3 The HSREC meets every month except with anticipated inability to fulfil the meeting requirements, or special circumstances.

6.2.2.3.1 The schedule of HSREC meetings for the year commencing on 1 January should be agreed between the Senior Administrator and the Chair by 31 October in the previous year. The schedule should set out the dates, times and venues of meetings and the closing date for applications to each meeting. All members of the HSREC should be issued with details of the schedule.

6.2.2.4 Minimum membership requirements and meeting attendance. Requirements with respect to voting members are:

6.2.2.4.1 The HSREC Chair votes as a regular member.

6.2.2.4.2 Voting members must be listed on the HSREC roster at the time of the meeting, as documented by the following:

6.2.2.4.2.1 A membership appointment letter that has been signed by the HSREC Chair.

6.2.2.4.3 When voting members have a conflict of interest on an item, they may neither serve as the primary or secondary reviewer nor vote on the item. See Conflict of Interest.

6.2.2.4.4 A co-opted member/secundus who is attending in place of a designated member should be counted towards quorum requirements and is considered a voting member for that meeting. (6.2.2.5)

6.2.2.4.5 If the quorum requirements for meetings of the HSREC has not been satisfied, the HSREC may not commence, continue or conclude any discussion with the purpose of determining the decision on an application for ethical review or matters involving policy.

6.2.2.4.6 The HSREC meeting, or part of the meeting, may proceed with any other business on the agenda as if it were a sub-committee meeting, provided that the Chair (or Vice-Chair) and at least one other member is present.

6.2.2.4.7 The HSREC Administration should keep a record of attendance, indicating which members and co-opted members were present for the discussion of each application for ethical review.

6.2.2.4.8 Where HSREC Administration is concerned that a forthcoming meeting may not be quorate due to foreseen absences, he/she should report the matter to the Chair and consider the following options:

6.2.2.4.8.1 Co-opting additional members who have the necessary expertise to fulfil the membership criteria

6.2.2.4.8.2 Postponing and re-arranging the meeting

6.2.2.4.8.3 Cancelling the meeting.

6.2.2.5 Co-opted members:

6.2.2.5.1 The HSREC may co-opt additional members in each category at any HSREC meeting for the purposes of that meeting. A person may be co-opted as a member only if he/she has had prior experience and/or training as a member of the HSREC and/or has expert scientific or clinical knowledge relevant to the protocols being discussed.

6.2.2.5.2 Procedures for co-opting members are the responsibility of HSREC Administration. HSREC Administration should maintain records of members within the area who would in principle be willing to be co-opted where required.

6.2.2.5.3 To ensure a co-opted member is provided with indemnity and insurance coverage and is aware of their roles and responsibilities they should be formally appointed to the HSREC.

6.2.2.5.3.1 The co-opted member must sign a Confidentiality Agreement as well as the attendance list of the specific meeting to provide proof of HSREC membership for the meeting.

6.2.2.6 Written comments from members: A member who is unavailable to attend a meeting may submit comments in writing on any agenda item. These should normally be received by HSREC Administration at least three working days prior to the meeting. Where later comments are received, they may be discussed at the meeting at the discretion of the Chair.

6.2.2.7 External Expert Reviewers:

6.2.2.7.1 The HSREC may seek the written advice of an expert reviewer on any aspects of an application that are relevant to the formation of an ethical decision, and which lie beyond the expertise of the members or on which the HSREC is unable to agree. This may necessitate going outside the required membership of the HSREC. These expert reviewers may be specialists in ethics, specific diseases or methodologies, or they may be representatives of

communities, patients or special interest groups.

6.2.2.7.2 Advice from expert reviewers may be sought at any time by the HSREC.

6.2.2.7.3 Expert reviewers are not voting members of the HSREC, and should not be involved in the business of the HSREC other than that related to the application on which their advice is sought.

6.2.2.7.4 HSREC Administration or the Chair should ensure that the expert reviewer(s) has/have declared any conflict of interest and agreed to UFS Terms of Confidentiality.

6.2.2.7.5 If possible, a copy of the advice received should be made available to members prior to the meeting or discussed at the meeting. The substance of the advice should be recorded in the minutes.

6.2.2.7.6 The expert reviewer may be invited to attend the meeting in person for discussion of the application concerned. The attendance of the expert reviewer and the substance of his/her advice at the meeting should be recorded in the minutes. The expert reviewer should not have a vote in the decision taken by the HSREC.

6.2.2.8 Investigators at HSREC meetings. The HSREC does not routinely require investigators to attend HSREC meetings at which their materials will be reviewed. However, on occasion the HSREC may require an investigator's presence to answer specific questions and provide information. In addition, investigators may ask to attend a meeting. The HSREC Chair makes the decision about whether such attendance would be appropriate and helpful.

6.2.2.8.1 On review of a research project, it might be identified that a meeting with the researcher outside of a committee meeting may be required. Such a meeting should be attended by the principal investigator, reviewer(s) as well as the Chair or Vice-chair. Such a meeting might contribute to greater understating of the processes and guide the researcher/reviewer with clarity on the way forward.

6.2.2.9 Guests and observers. The HSREC meetings are not considered "public meetings". However, the HSREC allows guests and observers at convened HSREC meetings, at the discretion of the HSREC Chair and HSREC Administration. Guests and observers are expected to follow the guidelines outlined in Guests at HSREC Meetings. Guests and observers may be asked to leave the meeting during review and discussion of highly sensitive issues.

6.2.2.10 Declarations of interest:

6.2.2.10.1 Members and co-opted members should declare to the HSREC any interests they may have in relation to an application for ethical review or any other matter for consideration at that meeting. Such a declaration may be made verbally at the meeting, prior to the matter being considered or in writing to the Chair prior to the meeting.

6.2.2.10.2 Where the member concerned is the Principal Investigator or another key investigator/collaborator named on the application form, the HSREC should not proceed with the review until the member has recused himself/herself from the meeting room. If necessary, the member can be invited back into the room to answer questions raised by the HSREC, but should again leave the room when the discussion resumes.

6.2.2.10.3 In the case of any other declared interest, the HSREC should collectively consider whether or not it is appropriate for the member concerned to take any part in the review of the application. Account should be taken of the closeness of the member's interest in the application and the potential for a conflict of interest. In some cases, the declaration of the interest may in itself be sufficient to ensure that the decision of the HSREC is not unduly influenced.

6.2.2.10.4 The minutes should record any declaration of interest and the decision of the HSREC on the procedure to be followed.

6.2.2.10.5 Any conflict of interest pertaining to researchers, institutions, HSREC members and all other stakeholders should be considered in accordance with Conflict of Interest.

6.2.2.11 Confidentiality of proceedings: HSREC members do not sit on the HSREC in any representative capacity and need to be able to discuss freely the applications submitted to them. For this reason, HSREC meetings should be held in private, and members should be encouraged to raise any matters of concern.

6.2.2.11.1 The Statement and Undertaking Contract for members and co-opted members include requirements to keep confidential the business of the HSREC.

6.2.2.11.2 The Statement and Undertaking Contract shall also include confidentiality agreement regarding online meetings.

6.2.2.12 Conduct of business and decision making: The Chair is responsible for the conduct of the business and for ensuring that the HSREC reaches clearly agreed decisions on all matters. Where the Chair is unavailable, the meeting should normally be chaired by the Vice-Chair or, if the Vice-Chair is also unavailable, by the alternate Vice- Chair/other designee.

6.2.2.12.1 All members present, both expert and lay, should be allowed reasonable opportunity to express relevant views on matters on the agenda.

6.2.2.12.2 The HSREC should endeavour to reach decisions by general consensus. Generally, the Minutes will record discussion of significant issues and the decision taken.

6.2.2.12.3 Where any member wishes to record his/her formal dissent from the decision of the HSREC, this should be recorded in the minutes.

6.2.3 **Definitions**

6.2.3.1 Quorum: A simple majority of the members listed on the HSREC membership roster. When the membership roster consists of an even number (N), a quorum is defined as (N/2) +1.

6.2.3.2 Primary reviewer: The HSREC member with the most appropriate expertise for reviewing a specific item. The primary reviewer:

6.2.3.2.1 Provides a brief summary of the item to the HSREC.

6.2.3.2.2 Leads a discussion of the criteria for approval with respect to the item, including the identification of any concerns.

6.2.3.2.3 Usually makes the first motion proposing specific HSREC actions (for example, approval).

6.2.3.2.4 May assist in writing or reviewing the correspondence to the investigator that communicates the HSREC's decisions, requirements, and questions.

6.2.3.2.5 May assist in verifying that the investigator's responses to a Conditional Approval outcome satisfactorily meet the HSREC's conditions.

6.2.3.3 Secondary reviewer: An HSREC member who fulfils the same responsibilities as the primary reviewer on a given item, and who is chosen to ensure an appropriate balance of scientific and/or non-scientific expertise for a specific item.

6.2.3.4 Recusal: An HSREC member's absence from the HSREC meeting due to a conflict of interest with respect to the item under consideration. The member no longer counts towards the quorum. Recusals are indicated in the minutes as "Recusal".

6.2.3.5 Present (as used with respect to an HSREC meeting): Means that an HSREC member is participating in the meeting.

6.2.4 **Responsibilities**

6.2.4.1 Unless otherwise specified, all procedures are performed by the HSREC Chair of the meeting.

6.2.4.2 HSREC Administration: The secretary to the meeting will normally be the HSREC Senior Administrator or an assistant administrator.

6.2.4.2.1 The responsibilities of HSREC Administration in relation to HSREC meetings are as follows:

6.2.4.2.1.1 Publishing the schedule of HSREC meetings;

6.2.4.2.1.2 Preparing the agenda;

6.2.4.2.1.3 Allocating reviewers;

6.2.4.2.1.4 Distributing the agenda and documentation for review;
6.2.4.2.1.5 Preparing the venue;
6.2.4.2.1.6 Recording apologies for absence prior to the meeting;
6.2.4.2.1.7 Raising with the Chair any concern that a meeting may not be quorate;
6.2.4.2.1.8 Recording attendance by members and co-opted members for the discussion of each application for ethical review;
6.2.4.2.1.9 Advising the meeting as necessary on compliance with standard operating procedures and relevant national/international requirements;
6.2.4.2.1.10 Making a written record of the meeting;
6.2.4.2.1.11 Preparing the minutes of the meeting for review and approval at the following meeting.
6.2.4.2.1.12 The secretary records all decisions in the minutes. The secretary also documents any member leaving or entering the room during the meeting, in order to record and ensure that a quorum is always present.

6.2.5 **Procedures**

6.2.5.1 Pre-meeting process

6.2.5.1.1 New research applications must be received by HSREC Administration by the published due dates in order to be considered for the agenda of that meeting. Due dates are published in conjunction with meeting dates but do not guarantee that applications will be incorporated into a specific agenda. If the application is not complete and as stipulated in HSREC submission guidelines, the application will be sent back to the researcher. If a response is not received within the specified turnaround time, the application will stand over until the next meeting's review cycle.

6.2.5.1.2 HSREC Administration reviews the application for completeness and may request additional information from the applicant.

6.2.5.1.3 HSREC Administration captures each new research project and allocates each research application to reviewers of the HSREC, at most 4 working days after the deadline for submission.

6.2.5.1.4 The Chair may, at her/his discretion, co-opt an external consultant for a particular review, if s/he feels the HSREC does not have the necessary expertise to adequately evaluate all aspects of a particular research application.

6.2.5.1.5 HSREC Administration collates all the available reviews into the meeting agenda and distributes the agenda to the full committee at least 2 working days prior to the meeting.

6.2.5.2 Quorum and other meeting requirements.

6.2.5.2.1 The secretary or delegate refers to the current HSREC Membership Roster to monitor and ensure the following requirements:

6.2.5.2.1.1 A quorum is present and maintained throughout the meeting. (See HSREC Terms of Reference).

6.2.5.2.1.2 The secretary records those present and also notes apologies.

6.2.5.2.1.3 The Attendance Register is circulated to obtain all HSREC members' signatures.

6.2.5.2.2 This monitoring occurs:

6.2.5.2.2.1 At the beginning of the meeting. The HSREC Chair is informed when the requirements are met, so that the meeting can be called to order.

6.2.5.2.2.2 With a member recusal. Members who have a conflict of interest are recused from the discussion and decision on the item presenting a conflict. HSREC Administration inform the HSREC Chair whether all meeting requirements are still met before the decision

is made.

6.2.5.2.2.3 With a member absence. Members may leave the meeting (an absence) for reasons other than a conflict of interest. HSREC staff inform the HSREC Chair whether all meeting requirements are still met before decisions are made. Absent members do not count towards the quorum.

6.2.5.2.3 No vote can be taken, nor determinations made, on an item if the meeting requirements are not met for the item.

6.2.5.2.4 The fulfilment of the meeting requirements is documented in the meeting minutes.

6.2.5.3 Meeting minutes

6.2.5.3.1 HSREC Administration take sufficient notes during the meeting to later prepare meeting minutes.

6.2.5.4 The Meeting: Opening business

6.2.5.4.1 The Chair calls the meeting to order.

6.2.5.4.2 A quorum, as described earlier must be present for all decision making.

6.2.5.4.3 The secretary records those present and also notes apologies.

6.2.5.4.4 The Chair introduces any observers or guests.

6.2.5.4.5 The Chair asks whether any members have a conflict of interest with respect to any of the items to be reviewed.

6.2.5.4.6 The Chair reminds the members, staff, and any guests that the discussion and decisions are confidential.

6.2.5.4.7 The Chair asks the members for any corrections or revisions to any minutes from previous meetings (if provided). A motion is made, and voted upon, to accept, accept with corrections, or not accept the minutes. Voting is not restricted to those members who were present at the meeting described by the minutes. The minutes are accepted when at least two HSREC members accept it.

6.2.5.4.8 The Chair facilitates the conduct of any other business, including education and training activities, announcements, etc.

6.2.5.5 Reviewing items

6.2.5.5.1 The Chair tables an item when:

6.2.5.5.1.1 The requirements for a meeting are not met (for example, a member's departure from the meeting results in the loss of quorum); or

6.2.5.5.1.2 Appropriate expertise is not available at the meeting (for example, when the primary reviewer is unexpectedly unable to participate in the meeting).

6.2.5.5.2 Information presentation The Chair performs the following actions, in a sequence that is appropriate to the item and circumstances:

6.2.5.5.2.1 New applications are introduced;

6.2.5.5.2.2 Asks the primary reviewer to provide a short descriptive summary of the item;

6.2.5.5.2.3 If the investigator is a member of the HSREC, s/he may answer any specific queries that members wish to address but should voluntarily recuse him or herself prior to discussion and decision-making. This recusal is recorded in the minutes.

6.2.5.5.3 Discussion of criteria for approval, and required determinations

6.2.5.5.3.1 A reviewer (preferably the primary reviewer) leads a discussion of the criteria for approval, referring as needed to the Criteria for Approval Checklist (Appendix 1).

6.2.5.5.3.2 This reviewer also leads a discussion of any determinations that the HSREC is required to make (examples: waiver of consent; device risk determination).

6.2.5.5.3.3 Experienced senior HSREC staff provide regulatory

clarification and guidance as needed.

6.2.5.5.3.4 The only individuals, who may participate in the discussion, unless otherwise invited by the Chair, are the HSREC members and HSREC Administration. For example, guests and observers may not participate in the discussion unless specifically requested to do so.

6.3 Student Research

All health research, whether undergraduate or postgraduate, for degree and diploma purposes must be submitted to the HSREC for review prior to the start of study-related activities.
Student research will follow the same review processes depending on the type of research planned.

6.3.1 PhD Research

6.3.1.1 All PhD projects must have undergone a scientific review process first before being submitted to the HSREC for ethics review and approval. The final version of the protocol, as approved by the scientific committee, should be submitted to HSREC. A letter from the supervisor should accompany the submission stating that the corrections to the protocol as recommended by the scientific review committee have made to his/her satisfaction.

6.3.2 Postgraduate Research (Degree and Diploma)

6.3.2.1 Honours-and BTech projects are regarded by the HSREC as undergraduate projects, and should follow the undergraduate application process.

6.3.2.2 HSREC review process:

6.3.2.2.1 HSREC Administration accepts new postgraduate research applications at any time, on an ongoing basis.

6.3.2.2.2 The postgraduate research applicant should submit all necessary documentation for a new application as specified in the Preparation Guidelines.

6.3.2.3 A signed supervisor declaration (HSREC 19), current professional registration and CV is required for all student research applications.

6.3.2.4 HSREC Administration reviews the application for completeness and may request additional information from the applicant.

6.3.2.5 HSREC Administration allocates each postgraduate research application, via InfoEd RIMS to evaluators of the HSREC for review.

6.3.3 Undergraduate, Honours, and BTech Research

6.3.3.1 Many undergraduate students are required to complete small research projects or educational exercises during the course of their studies.

6.3.3.2 Undergraduate students are encouraged to conduct minimal risk research.

7 HSREC DECISIONS

7.1 Purpose

This section describes the decisions available to the HSREC. It also describes specific procedures associated with each action.

7.2 Policy

7.2.1 Relevant regulations and South African Health law give the HSREC the authority to take specific action in connection to research activities, including research on human subjects. The laws and regulations require investigators to also take specific action, to make changes, and/or provide relevant information in order to obtain HSREC approval.

7.2.2 The HSREC's actions are taken as the result of:

- 7.2.2.1 The review of all research activities, including research on humans;
- 7.2.2.2 The receipt of new information (which may or may not come from the investigator) provided to the HSREC.

7.2.3 One of the following decisions must be made:

- 7.2.3.1 Approval
- 7.2.3.2 Conditional approval
- 7.2.3.3 Modifications required
- 7.2.3.4 Modifications required - Held over
- 7.2.3.5 Disapproval
- 7.2.3.6 Suspension
- 7.2.3.7 Termination.

7.2.4 The Chair should ensure that one of the above decisions is made on every application considered at an HSREC meeting.

7.2.5 Where the HSREC decides that further information or clarification is required, the Chair should ensure that:

- 7.2.5.1 The further information or clarification required is specifically identified at the meeting.
- 7.2.5.2 The investigator provides a summary of changes (template available on RIMS) clearly addressing the questions asked by the HSREC. All changes made need to be indicated by highlighting them in 'yellow' and must provide all the revised documentation e.g., study protocol, participant information sheets, consent forms, etc.
- 7.2.5.3 Delegation of responsibility for considering the further information and confirming the HSREC's final decision is clearly agreed, i.e., whether the information will need to be re-submitted to the full HSREC, several HSREC members, HSREC Administration or the Chair only.

7.2.6 Final decision following consideration of the information:

- 7.2.6.1 On receipt of a complete response from the applicant, the HSREC should confirm its final decision with the application. The procedures set out above should be followed.

7.2.7 Further advice from an external expert reviewer(s):

- 7.2.7.1 Where the HSREC decides that it cannot give a decision until it has obtained further advice from an external expert reviewer, the following procedure should be adopted:
  - 7.2.7.1.1 Advice should be sent to the applicant following the meeting, explaining that no decision has been taken on the application pending consultation with an expert reviewer.
  - 7.2.7.1.2 The letter may notify the applicant of the issues of concern to the HSREC, but should not at this point request further information or clarification.
- 7.2.7.2 The HSREC may decide at the meeting whom it wishes to consult, and this should be recorded in the minutes. Alternatively, the Chair and/or HSREC Administration should be appointed to urgently identify a suitable expert reviewer following the meeting.
- 7.2.7.3 The Chair and/or HSREC Administration should initially contact the prospective expert reviewer(s) by phone or e-mail to establish whether he/she is willing and

able to provide expert advice within the required timeline. It should be established that the prospective expert reviewer has no conflict of interest regarding the research. Advice should be given about confidentiality.

7.2.7.4 Once a suitable and willing expert reviewer has been identified, the Chair or HSREC Administration should write to the expert reviewer. This letter should be as specific as possible about the issues of concern and the expert advice required.

7.2.7.5 The HSREC should not disclose the nature of the reviewer's advice to the applicant. The decision of the HSREC on the application is its own. It may not disclose the identity of the reviewer/s except with his/her express permission.

7.2.8 Notification of the decision to the principal investigator (or coordinating principal investigator):

7.2.8.1 HSREC Administration should ensure that, following confirmation of the Minutes by the Chair, notification of the decision is sent to the principal investigator (or coordinating principal investigator for multi-centre studies) in writing within 7 working days of the meeting.

7.2.8.2 Initial HSREC approval notification to the researcher may be via email from HSREC Administration or the HSREC Chair.

7.2.8.3 The following information should in all cases be included in the letter or in enclosures for ethical and scientific approval of a new application:

7.2.8.3.1 The decision reached by the HSREC;

7.2.8.3.2 On request, a list of the membership of the HSREC which includes the membership category, gender and institutional affiliation of each member is made available;

7.2.8.3.3 Any interests declared by members who were present or any member recusals during the discussion of the application.

7.2.8.4 The letter should also include the HSREC's decision on any relevant issue on which the applicant has specifically asked for its decision.

7.2.8.5 It is not necessary to include all the questions raised at the meeting in the letter. However, it is important to record any ethical concerns, with reference to applicable national/international human subject research requirements, that the HSREC collectively discussed and resolved at the meeting in the minutes for future reference.

7.2.8.6 The letter should not attribute comments or questions to individual members of the HSREC.

7.2.8.7 The letter contains standard conditions for research approved by the HSREC.

7.2.8.8 Any additional approval conditions specified by the HSREC for a particular application, for example a requirement for more frequent progress reports, should be included in the letter.

7.2.8.9 Where the final decision is disapproved, the applicant should be given a full explanation of the HSREC's reasons with reference to applicable national/international human subjects research requirements. The applicant should also be informed of the options available for further review.

7.2.9 Studies requiring Department of Health or another provincial department approval:

7.2.9.1 Authorisation of research projects to be conducted within or in association with public healthcare institutions will be granted in line with the regulations of the provincial department. The research must not commence until this authorisation has been granted (See HSREC webpage for more information).

7.2.10 Delegation of responsibility by the HSREC:

7.2.10.1 Where the HSREC has made the decision to request the clarification of information, the provision of further information to the HSREC and/or amendment(s) to the study, the HSREC will establish a procedure for considering interim correspondence received from the principal investigator which may include one of the following:

7.2.10.1.1 Delegation of the authority to review the interim correspondence and approve the study between meetings at the discretion of the Chair alone.

7.2.10.1.2 Delegation of the authority to review the interim correspondence and approve the study between meetings at the discretion of one or more HSREC members;

7.2.10.1.3 Delegation of the authority to review the interim correspondence and approve the study between meetings at the discretion of a sub-

committee of the HSREC;

7.2.10.1.4 Consideration of the interim correspondence at a further meeting of the HSREC (in exceptional circumstances or where those delegated authority to review interim correspondence recommend reference back to a further meeting of the HSREC);

7.2.10.1.5 Delegation of the authority to HSREC Administration.

7.2.10.2 To provide suitable oversight of this delegated authority to review the interim correspondence and approve the study between meetings, the HSREC must ratify the final decision taken on its behalf at the next available meeting.

7.2.10.3 In deciding the procedures to be followed, the HSREC should consider the significance of the information further and the degree of ethical judgement necessary to evaluate it. Where the information is straightforward, it is acceptable for the matter to be delegated to the Chair alone or HSREC Administration. Where questions of ethical judgement are likely to arise, or specific clinical or scientific expertise is required, consideration should be given to involving other members, such as the reviewer(s) or a relevant expert member. Where these questions are likely to be significant, the HSREC may decide that the information should be considered at a further meeting of the HSREC.

7.2.10.4 Where possible, the HSREC should encourage informal communication with researchers, and should consider face-to-face meetings to resolve issues about research proposals that have not been resolved by written or telephone communication.

7.2.10.5 Signing of HSREC letters:

7.2.10.5.1 Projects processed via the research information system receive letters from the system. The signature of the Chair is part of the letter template.

7.2.10.5.2 All HSREC formal meeting letters must be authorized by the Chair or designate.

7.2.10.5.3 The following letters may be authorized by HSREC Administration on behalf of the Chair:

7.2.10.5.3.1 Final approval letters of projects that have satisfied all conditions of approval and HSREC Administration has delegated authority from the HSREC to approve. This decision must be ratified at the next meeting.

7.2.10.5.3.2 Conditional approval letters of projects that have satisfied all requests for modifications to the project documentation and HSREC Administration has delegated authority from the HSREC to grant conditional approval.

7.2.10.5.3.3 Request for modification letters of projects that have not yet satisfied HSREC criteria of approval and HSREC Administration has delegated authority from the HSREC to issue the letter.

7.2.10.5.3.4 Any other letters as requested/delegated by the Chair or designate.

7.2.11 Confidentiality:

7.2.11.1 Once an application has been validated for review, all further correspondence with the applicant relating to the application should be treated confidentially by the HSREC.

7.2.11.2 No copies of letters should be sent directly by the HSREC, providing the decision reached, or requesting further information, to the sponsor(s) of the research.

7.2.11.2.1 All HSREC correspondence must be addressed to the principal investigator or delegated signatory.

7.2.11.3 Response deadline: The HSREC sets a deadline for receipt of the investigator's response. The date is typically 60 calendar days from the date on the HSREC letter. The investigator may negotiate a later deadline by contacting HSREC Administration.

7.2.11.4 Investigator response not received by the deadline: Failure to meet the deadline (or make alternative arrangements) is interpreted as failure to meet the conditions of approval. The HSREC approval for the item is not effective. The item may be

administratively closed, depending upon the circumstances, unless there are unresolved issues related to compliance or subject safety and rights.

7.3 Procedures

7.3.1 **Approval**

7.3.1.1 Definition The item is approved. The activity may be conducted within the constraints (if any) established by the HSREC. No changes or additional information are required, and all of the applicable criteria for HSREC approval are met (or continue to be met).

7.3.1.2 Requirements All of the applicable criteria for HSREC approval are met (or continue to be met) without any changes, requests for confirmation or additional information, or conditions that must first be fulfilled.

7.3.1.3 Outcomes All approved activities may be initiated. If the item is associated with a new source of funding, the funds may now be released for spending.

7.3.1.4 Procedures If the item is an initial application or a Status Report, the HSREC makes the following determination in connection with the approval:

7.3.1.4.1 The approval period granted by the HSREC, which determines the frequency of continuing review. Final ethical clearance is valid for one year from the date of approval.

7.3.1.5 Issues and guidance

7.3.1.5.1 Approval of components instead of the whole The HSREC may choose to approve some components of the activity and allow the investigator to initiate (or continue) those components. To do so, the HSREC must believe that the approved components will yield scientifically meaningful results and satisfy all criteria required for HSREC approval, even if the other components are never approved and conducted. The investigator may later submit an amendment to request approval for the other components.

7.3.1.5.2 The purpose of the review of informational items is to confirm (or not) that the criteria for HSREC approval continue to be met in light of the new information. A decision to “approve” means that the HSREC has determined that the criteria for approval continue to be met.

7.3.1.5.3 Approval periods and dates with each review of an entire project (i.e., at initial and continuing review), the HSREC is required to specify the duration of the approval period. This determines the date of the next continuing review (i.e., Continuation Report).

7.3.1.5.3.1 The approval date is the date when the research is approved (after all conditions have been met).

7.3.1.5.3.2 The expiration date of the approval period is at 11:59 PM on the last day of the approval period as communicated by HSREC Administration on the Approval Letter.

7.3.1.5.3.3 The approval period granted by the HSREC cannot be any longer than one calendar year. See **Continuing Review** for additional information.

7.3.1.5.3.4 The approval period of a study does not change when the HSREC approves an amendment or when the HSREC suspends the HSREC approval of the study.

7.3.2 **Conditional Approval**

7.3.2.1 Definition: The HSREC has determined that the applicable criteria for HSREC approval have been met, based on the assumption that specific conditions will be met by the investigator and subsequently verified.

7.3.2.2 Requirements: The HSREC requires as a condition of approval that the investigator: (1) make specified changes; (2) confirm specific assumptions or understandings on the part of the HSREC; and/or (3) provide additional or revised information or documents such that, based on the assumption that the conditions are satisfied, the applicable criteria for approval would be met and required determinations would be made.

7.3.2.3 Outcomes

7.3.2.3.1 Initiation of research: The research activities or changes cannot be initiated until the conditions have been met and verified as required by the HSREC.

7.3.2.3.2 No further need for full HSREC review of the item. For items that are granted Conditional Approval by a full convened HSREC, the investigator's response is verified by individual(s) designated by the HSREC rather than returning to another full HSREC meeting.

7.3.2.3.3 Approval dates: The approval period starts at the time that the conditions of approval have been verified, defined as:

7.3.2.3.3.1 HSREC receives the investigator's response to the Conditional Approval letter.

7.3.2.3.3.2 The designated individual(s) have verified that the HSREC's conditions have been satisfactorily met; and

7.3.2.3.3.3 The verification confirmation has been communicated to the investigator.

7.3.2.3.4 Approval period: The HSREC specifies the approval period granted by the HSREC, which determines the frequency of continuing review.

7.3.2.3.5 HSREC designation of verification: When it grants Conditional Approval, the HSREC also designates the individual(s) who will evaluate the investigator's response and verify whether the conditions of approval have been satisfied. This is documented in the HSREC meeting minutes. The HSREC selects individual(s) who have the appropriate expertise. For example, the evaluation of some responses may require medical, scientific or technical expertise. When such expertise is not required, senior HSREC Administrators commonly fulfil this role.

7.3.2.3.6 When granting Conditional Approval to a status report or an amendment, the HSREC must specify whether any conditions need to be satisfied before the investigator can continue particular research activities related to those conditions. These constraints are not considered a suspension.

7.3.2.3.7 Unsatisfactory investigator response: The individual(s) evaluating the investigator's response may conclude that it does not satisfactorily meet the conditions of the HSREC. This is communicated to the investigator and documented for the file.

7.3.2.3.7.1 The investigator may provide additional materials and information, or the investigator may choose to provide an amended proposal. An amended proposal must return to the full convened HSREC for review. This is considered 're-review'. Approval criteria and waivers must be reconsidered and the application is re-signed.

7.3.2.3.7.2 If the investigator and the verifying individual(s) are unable to agree on whether the investigator's response satisfies the conditions, they consult with the HSREC Chair. If no agreement can be reached, the response to the conditional approval letter must come back to the full convened HSREC for review. This is considered 're-review'. Approval criteria and waivers must be reconsidered and the application is re-signed.

7.3.2.3.8 Completion of the verification process: The HSREC communicates in writing to the investigator when the verification process has been completed and the conditions are considered satisfactorily met. The communication includes the date when the conditions were determined to be satisfied (which is also the date on which the approval becomes effective), and the date by which continuing review must occur (if the item was an initial application

or status report).

7.3.2.3.9 Amendments submitted before completion of initial review cycle: The HSREC will not review new amendments to a new project before all of the HSREC's conditions for initial approval have been satisfied. However, amendments may be submitted as a review response.

7.3.2.3.10 Issues and guidance

7.3.2.3.10.1 The investigator's response to Conditional Approval is not considered an amendment. Similarly, the verification that the response has met the conditions of approval is not considered an HSREC expedited review process.

7.3.3 **Modifications Required**

7.3.3.1 Definition: The HSREC is unable to approve the research because it cannot make the determinations required for approval (i.e., the applicable criteria for HSREC approval have not been met.) The HSREC defers the item for further review after amendments and/or additional information have been provided by the investigator.

7.3.3.2 Requirements: Amendments, clarification, revised documents and/or additional information are required from the investigator in order to determine that the applicable criteria for HSREC approval are met.

7.3.3.3 Outcomes

7.3.3.3.1 Initiation of research: The research activities under review cannot begin.

7.3.3.3.2 If the item was reviewed by a full convened HSREC meeting, the investigator's response must be reviewed by both initial reviewers of the HSREC and it is eligible for expedited review.

7.3.3.4 Procedures: The HSREC specifies what changes, information, or new/revised materials are needed, in a written review letter to the investigator. These should be directly relevant to the HSREC criteria for approval and required determinations.

7.3.3.4.1 When an amendment or status report is being reviewed, the information and requirements may include the HSREC's need for verification from sources other than the investigator that no material changes have been made to the project since the last HSREC review. The criteria and procedures for this are described in the Continuing Review.

7.3.4 **Modifications Required - Held Over (Deferral)**

7.3.4.1 Definition: The HSREC is unable to approve the research because it cannot make the determinations required for approval (i.e., the applicable criteria for HSREC approval have not been met.) The HSREC defers the item for further review at a future date after amendments and/or additional information have been provided by the investigator.

7.3.4.2 Requirements: Amendments, clarification, revised documents and/or additional information are required from the investigator in order to determine that the applicable criteria for HSREC approval are met.

7.3.4.3 Outcomes

7.3.4.3.1 Initiation of research. The research activities under review cannot begin.

7.3.4.3.2 If the item was reviewed by a full convened HSREC meeting, the investigator's response must be reviewed by the full convened HSREC; it is not eligible for expedited review.

7.3.4.4 Procedures: The HSREC specifies what changes, information, or new/revised materials are needed, in a written review letter to the investigator. These should be directly relevant to the HSREC criteria for approval and required determinations.

7.3.4.4.1 When an amendment or status report is being reviewed, the information and requirements may include the HSREC's need for verification from sources other than the investigator that no material

changes have been made to the project since the last HSREC review. The criteria and procedures for this are described in the Continuing Review.

7.3.4.4.2 If the deferral action was taken by the full convened HSREC, the investigator's response to the deferral review letter must come back to the full convened HSREC for review. If the deferral was part of an expedited review, the deferral response may be reviewed by the expedited process.

7.3.5 **Disapproval**

7.3.5.1 Definition: The applicable criteria for HSREC approval are not met, and the HSREC is not willing to re-consider the item. The disapproval action is not available as part of expedited review.

7.3.5.2 Requirements: An item is disapproved rather than deferred when the HSREC believes that it is very unlikely that:

7.3.5.2.1 The applicable criteria for approval will be met even with substantial amendments and/or additional information; or

7.3.5.2.2 It is not possible to obtain (or the investigator is unwilling to provide) the substantial amendments or additional information that would be necessary to meet the criteria for approval.

7.3.5.3 Outcomes

7.3.5.3.1 No actions proposed in the item may be initiated.

7.3.5.3.2 The activity may not be re-submitted to the HSREC for another review, unless the investigators wishes to appeal the determination. Only one appeal is allowed. See Appeal of HSREC Determination.

7.3.5.4 Procedures

7.3.5.4.1 The HSREC generally does not disapprove an item until there has been at least one attempt to work with the investigator to find mutually acceptable changes (i.e., at least one review with a Modifications Required decision) that will allow the HSREC to determine that the criteria for approval have been met.

7.3.5.4.2 The HSREC strongly prefers to communicate any suggestions it has, even with a Disapproval decision. For example, the HSREC may suggest that the investigator seek scientific review, redesign the project, and then submit a new application.

7.3.5.5 Issues and guidance: Examples of circumstances in which a disapproval may be appropriate are when the HSREC determines:

7.3.5.5.1 The science is clearly inadequate.

7.3.5.5.2 The resources to conduct the activity are not available.

7.3.5.5.3 The risks of the research outweigh the benefits, and the risks cannot be reduced or mitigated sufficiently.

7.3.6 **Suspension**

7.3.6.1 Definition: HSREC approval for some or all parts of an approved research study is temporarily withdrawn. Suspension is not available through an expedited review process.

7.3.6.2 Requirements: Suspension may be imposed at any time, when:

7.3.6.2.1 The research is not being conducted in accordance with the HSREC's requirements or HSREC-approved procedures.

7.3.6.2.2 New information suggests the benefits of the research may be significantly less than previously expected, or that the risks may be significantly greater than previously known. In such cases, the suspension may be placed in order to allow for investigation and gathering of additional information.

7.3.6.3 Who can suspend HSREC approval:

7.3.6.3.1 The action of suspension may be taken by the full HSREC or the HSREC Chair. Relevant materials are provided to the HSREC for discussion at its next convened meeting, when the full HSREC will review the matter and determine whether to continue or lift the suspension.

7.3.6.3.2 Individual HSREC members do not have the authority to suspend a

study, or any parts of a study (such as enrolment of new subjects).

7.3.6.3.3 When HSREC Administration learn of a situation in which it would be appropriate to temporarily halt an activity (such as enrolment of new subjects) while a problem is being resolved, they may:

7.3.6.3.3.1 Recommend to the study staff (but do not have the authority to require) that the activity be halted, and point out the potential consequences of not halting the activity.

7.3.6.3.3.2 Inform the HSREC Chair and recommend that they suspend approval.

7.3.6.3.4 A suspension may be lifted only by a full convened HSREC, even if the suspended study is otherwise eligible for expedited review.

7.3.6.4 Outcomes

7.3.6.4.1 The suspended activities must be immediately halted, except for those activities the HSREC requires for the safety or welfare of the subjects.

7.3.6.4.2 The HSREC may require the investigator to take certain actions in connection with the suspension. For example, the investigator may be required to quickly develop a plan for discontinuing subject participation in the study.

7.3.6.4.3 Suspended studies remain subject to the requirement for continuing review (status reports). The date by when the continuing review must occur does not change due to either a suspension or the lifting of a suspension, unless the HSREC specifically makes a change.

7.3.6.5 Procedures

7.3.6.5.1 The suspension must include a statement of the reasons for the suspension. The HSREC must specify the specific activities that are suspended; otherwise, the suspension is assumed to be a "full" suspension of all research activities. If the decision is to withdraw approval, the HSREC 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.

7.3.6.5.2 Subject safety: The HSREC must identify and require any appropriate actions to protect the safety and welfare of past or currently enrolled subjects, together with a timeline for fulfilling these requirements. The HSREC may consult with the investigator in these issues. The HSREC should always consider:

7.3.6.5.2.1 What activities (if any) should be allowed to continue (for example, follow-up visits that involve important monitoring assessments of subject safety);

7.3.6.5.2.2 What information and additional procedures (if any) should be provided to past or currently enrolled subjects or other parties, as well as how and by whom.

7.3.6.5.3 Criteria for lifting the suspension: The HSREC must specify and communicate to the investigator the actions or information that are required to address the HSREC's concerns, so that the HSREC can consider lifting the suspension. The timeline for fulfilling these requirements should also be specified.

7.3.6.5.4 Documentation: When a suspension is imposed by the HSREC Chair, the suspension is documented with a detailed note to file and any other relevant documents. Suspension by the full HSREC is documented in the same way as any other HSREC action (i.e., meeting minutes; written communication to researcher and other appropriate parties).

7.3.6.6 Issues and guidance

7.3.6.6.1 Other types of suspension: A suspension imposed by any entity other than the HSREC is not considered a suspension of HSREC approval. Examples of non-HSREC suspensions include suspensions imposed

by: a Sponsor, Data and Safety Monitoring Board, Head of Department, University Dean or designee, or the any relevant regulatory bodies.

7.3.6.6.2 Relationship between lapsed HSREC approval and suspension: A lapse of HSREC approval due to lack of continuing review (i.e., a status report) is not considered a suspension.

7.3.6.7 Relationship between conditional approval of status reports and suspension: It is not considered a suspension when the HSREC grants conditional approval to a status report that includes a condition that certain activities may not continue until a specific condition is met.

7.3.6.8 Review of status reports when a study is suspended: A status report should be submitted as usual, if the expiration of the approval period is near. See Continuing Review for the appropriate procedures.

7.3.7 **Termination**

7.3.7.1 Definition: HSREC approval for some or all parts of an approved research study is permanently withdrawn.

7.3.7.2 Requirements: Termination may not be imposed through the expedited process. It may be imposed when the full HSREC determines that the actions required to adequately address the following issues cannot, or will not, occur:

7.3.7.2.1 New information about a significant increase in risk and/or a significant decrease of benefits;

7.3.7.2.2 Serious or continuing non-compliance with National/International regulations or HSREC requirements; or

7.3.7.2.3 Other circumstances of significant concern to the HSREC.

7.3.7.3 Outcomes: The terminated activities must be immediately halted, except for those activities and actions the HSREC requires for the safety and welfare of the subjects. Terminated research is permanently closed and no longer requires continuing review (status reports). However, the HSREC may require a closure report from the investigator before it closes the research and the HSREC file.

7.3.7.4 Procedures

7.3.7.4.1 The termination must include a statement of the reasons for the termination. The HSREC must specify the specific activities that are terminated; otherwise, the termination is assumed to be a “full” termination of all research activities.

7.3.7.4.2 Subject safety: The HSREC must identify and require any appropriate actions to protect the safety and welfare of past or currently enrolled subjects, together with a timeline for fulfilling these requirements. The HSREC may consult with the investigator in these issues. The HSREC should always consider:

7.3.7.4.2.1 What activities (if any) should be allowed to continue (for example, follow-up visits that involve important monitoring assessments of subject safety);

7.3.7.4.2.2 What information and additional procedures (if any) should be provided to past or currently enrolled subjects or other parties, as well as how and by whom.

7.3.7.4.3 Communication: The termination is immediately reported in writing (and, usually, by phone) to the investigator. A copy of the formal HSREC termination letter is sent to the National Health Research Ethics Council (NHREC), South African Health Products Regulatory Authority where applicable (SAHPRA), the relevant UFS Research Committee, Head of the School, Dean of Faculty and the investigator’s Head of academic department.

7.3.7.5 Issues and guidance

7.3.7.5.1 Other types of termination: A termination imposed by any entity other than the HSREC is not considered a termination of HSREC approval. Examples of non-HSREC terminations include termination imposed by: a Sponsor, Data and Safety Monitoring Board, Head of Department, University Dean or designee, or any relevant regulatory bodies.

7.3.7.5.2 Examples of situations in which termination may be appropriate:

7.3.7.5.2.1 New information about an investigational drug or device shows that it is unsafe for use with the specific patient population being studied.

7.3.7.5.2.2 The researcher is unable, or persistently unwilling, to comply with the HSREC's requirements for resolving suspension of HSREC approval.

8 REVIEW CRITERIA

8.1 Purpose

The purpose of this section is to outline the considerations and factors that may influence the scientific validity and ethical acceptability of the research.

8.2 Policy

8.2.1 The essential policy of HSREC is to protect the dignity, rights, safety, and well-being of all human participants in health-related research. The HSREC will do this through independent, prospective and ongoing ethics review of all health research projects undertaken by members of staff, registered students and affiliates of the University of the Free State.

8.2.2 The HSREC Ethical Principles template (Appendix 1) is referenced by reviewers during project evaluation.

8.3 Review Criteria

8.3.1 The HSREC uses the following criteria for review:

8.3.1.1 Social and scientific value

8.3.1.1.1 The proposed research is relevant to:

8.3.1.1.1.1 The community involved and/or the greater South African and/or African community; and

8.3.1.1.1.2 The advancement of knowledge/the scientific field in the proposed area of study and/or related areas of study.

8.3.1.2 Scientific validity

8.3.1.2.1 The proposed research is scientifically valid; and

8.3.1.2.1.1 Research must be well designed and conducted (e.g. clear aims, rigorous design, adequate sample, adherence to GCP, sound data analysis). Even a valuable research question can be poorly researched, resulting in unreliable data. Poorly designed research that is not scientifically sound is unethical because it wastes resources and exposes participants to risks and inconvenience for no purpose if the research yields inaccurate conclusions/ misleading answers;

8.3.1.2.1.2 To meet ethical requirements, research ought not to expose patients and volunteers to inconvenience or risk of harm without possible benefit to society or where the research will not generate the intended knowledge.

8.3.1.2.2 The proposed investigators/researchers/study coordinators are:

8.3.1.2.2.1 Suitably qualified to undertake the research. 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; and

8.3.1.2.2.2 Registered with the Health Professions Council of South Africa (HPCSA) or other South African statutory body, as appropriate. If not registered with HPCSA or another statutory body, the HSREC 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; or

8.3.1.2.2.3 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.

8.3.1.3 Reasonable risk-benefit ratio

8.3.1.3.1 The potential risks to individual subjects in the proposed research are outweighed by the benefits to the individual or society. ALL the following requirements are satisfied:

8.3.1.3.1.1 The potential risks to individual subjects or society are identified and minimized;

8.3.1.3.1.2 The proposed research involves procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk;

8.3.1.3.1.3 Risk minimization measures are undertaken and stated in the protocol;

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

8.3.1.3.1.5 Whenever possible / appropriate, minimize risk by utilizing already performed diagnostic and treatment procedures

8.3.1.3.2 The potential benefits of the research to individual subjects or society are identified and maximized.

8.3.1.3.2.1 NOTE: Compensation for time and inconvenience, and reimbursement for expenses such as travel are not considered research benefits.

8.3.1.3.3 The potential risks to individual subjects should be outweighed by the benefits to the individual or society. Risks to participants are reasonable in relation to:

8.3.1.3.3.1 The anticipated benefits, if any, to participants and/or the wider community; and

8.3.1.3.3.2 The importance of the knowledge that may reasonably be expected to result.

8.3.1.3.4 In evaluating risks and benefits, the HSREC shall consider only those risks and benefits that may result from the research itself (as distinguished from risks and benefits of therapies participants would receive as standard clinical practice, even if not participating in the research). The HSREC 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 and benefits that fall within the purview of its responsibility.

8.3.1.4 Fair selection of participants

8.3.1.4.1 The selection of research participants for the proposed research must be fair and just. In making this assessment the HSREC 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 challenges of research involving vulnerable populations, such as children, prisoners, pregnant women, intellectually impaired persons, or economically or educationally disadvantaged persons.

8.3.1.4.2 Participants must be selected:

8.3.1.4.2.1 According to the scientific goals of the study (not for non- scientific reasons e.g., convenient, vulnerable, less able to protect their rights); and

8.3.1.4.2.2 To minimize risks (some participants may be eligible for scientific reasons, but at substantially higher risk of harm, e.g., impoverished and vulnerable to undue inducements).

8.3.1.4.2.3 The research has avoided involving the vulnerable when less vulnerable persons could be involved; or

8.3.1.4.2.3.1 When some or all of the participants are likely to be vulnerable, such as children, prisoners, pregnant women,

mentally disabled persons, or economically or educationally disadvantaged persons, the applicant has:

8.3.1.4.2.3.1.1 Justified why vulnerable individuals /communities are included;

8.3.1.4.2.3.1.2 Included, and clearly articulated, additional safeguards in the proposed research to minimize risks for, and protect the rights and welfare of, these participants.

8.3.1.4.2.4 To fairly distribute benefits and burdens

8.3.1.4.2.4.1 Research can provide direct and indirect benefits. Participants should be selected so that these benefits are fairly distributed;

8.3.1.4.2.4.2 Participants and/or communities should not be excluded without sound justification. Unfair exclusion from research may deny these participants and/or communities relevant knowledge/ health interventions;

8.3.1.4.2.4.3 Individuals and groups who bear the burden of the research should share in its benefits (new knowledge or products). Those who stand to benefit from research must contribute to its risks and discomforts. No group of persons should be asked to bear more than their fair share of the burden of research; no group (e.g. impoverished) should be asked to bear research risks in order that others (e.g. the wealthy) enjoy benefits (new knowledge or products).

8.3.1.5 Informed consent process

8.3.1.5.1 The informed consent process for the proposed research allows for:

8.3.1.5.1.1 An informed and voluntary decision from each prospective participant, or the participant's legally authorized representative, in accordance with, and as required by the section on Informed Consent of this document; and

8.3.1.5.1.2 Appropriately documented written informed consent and assent if applicable, in accordance with, and as required by the section on Informed Consent of this document.

8.3.1.6 Respect for participants

8.3.1.6.1 The proposed research demonstrates respect for the dignity of participants throughout the course of the research.

8.3.1.6.2 There are adequate provisions to protect the privacy of participants and to maintain the confidentiality and security of participant data; and

8.3.1.6.2.1 Participants may withdraw from the study at any time without prejudice; and
8.3.1.6.2.2 There are adequate measures in place to monitor participant welfare throughout; and
8.3.1.6.2.3 Participants are informed of research results.

8.3.1.6.3 Maintaining confidentiality respects participants' rights to choose to whom, and what personal information, is disclosed. Participants must consent to the ways in which confidentiality will be maintained (e.g., using codes instead of identifiers, restricted access to data), as well as to how the results will be published, and to any limits to confidentiality where these apply.

8.3.1.7 Respect for communities

8.3.1.7.1 The proposed research demonstrates respect for communities by appropriate community interaction and feedback of results.

8.3.1.7.2 There are adequate provisions to respect the autonomy of communities and to maintain the confidentiality and security of community data;

8.3.1.7.3 There is appropriate community consultation, for example, discussions with Community Advisory Boards (CABs) and/or other community representatives during the planning phase of the research, before the commencement of the research, i.e., the community should be part of the research process; and

8.3.1.7.4 Communities are informed of research results.

9 UNRESPONSIVE RESEARCHERS

9.1 Purpose

This section describes the policies and procedures followed by the HSREC for preventing, identifying, and managing researchers' lack of response to HSREC communications.

9.2 Policies

9.2.1 Researcher responsibility

9.2.1.1 Researchers are responsible for tracking and responding to communications from the HSREC about items that the researchers have submitted for review. Failure to receive or notice correspondence does not absolve researchers of this responsibility, nor does it change the consequences of not responding.

9.2.2 Sixty (60) calendar days deadline

9.2.2.1 It is HSREC policy to require researcher responses to communications from the HSREC about an item submitted for review, within 60 calendar days of the date of the communication.

9.2.2.2 Examples of the communications requiring a response include:

9.2.2.2.1 A review letter or email of any type from HSREC, such as a Conditional Approval letter;

9.2.2.2.2 An email from HSREC;

9.2.2.2.3 Any request for information from HSREC.

9.2.2.3 Negotiable circumstances

9.2.2.3.1 The HSREC recognizes that circumstances may prevent the researcher from meeting the response deadline. In such cases, the researcher should negotiate in advance with HSREC Administration for an alternate deadline.

9.2.2.4 Missed deadline

9.2.2.4.1 When the response deadline has passed, HSREC Administration will withdraw the item from further consideration or will administratively close the item. These actions mean that the item does not have HSREC approval and that the human subjects research activities described in the item cannot occur or continue. The researcher may resubmit the project as a new application.

9.3 Definitions

9.3.1 Administrative closure: Closure of a study that does not have HSREC approval (due to an expired approval, or failure to respond to conditions of approval).

9.3.2 Withdrawn: The full term is "Withdrawn from further consideration". This status is given to items that:

9.3.2.1 Were submitted to HSREC;

9.3.2.2 Were reviewed with an outcome of "held over" or deferred;

9.3.2.3 Have not yet been approved or conditionally approved; and

9.3.2.4 For which the researcher has not provided a timely response to the screening or review communication.

9.4 Procedures

9.4.1 Communication of the 60-day deadline

9.4.1.1 The 60-day deadline is included in clear, prominent language in all relevant communications from the HSREC. Communications are sent to the email and/or campus mail addresses provided by the researcher. It is the researcher's responsibility to ensure that the correct email address is provided.

9.4.2 Negotiable circumstances

9.4.2.1 Circumstances may prevent the researcher from meeting the response deadline. When the researcher contacts HSREC Administration in advance of the deadline, HSREC Administration may negotiate a later deadline with the researcher.

9.4.3 Identification of missed deadlines

9.4.3.1 HSREC Administration uses the HSREC database and other means to track researcher response deadlines.

9.4.3.2 HSREC Administration will, if workload permits, remind the researcher about a response deadline that is near via emails or InfoEd RIMS. However, researchers should not rely on such reminders. There is no automated system for such reminders.

9.4.4 Notification of researcher

9.4.4.1 As soon as possible after the passed deadline of 60 days, HSREC Administration sends a letter to the researcher, study supervisor, Academic Head of Department, Postgraduate Office and Research Support Structure. See the definitions of "Administrative Closure" and "Withdrawal" for a description of the circumstances appropriate for each type of letter.

9.4.4.2 The letter can be sent by email, through campus mail or InfoEd RIMS.

9.4.4.3 The researcher will be given a final 30 days to respond in writing. If no response was received during this time, the study will be closed in InfoEd RIMS.

9.4.4.4 The item is considered withdrawn or administratively closed on the date and time when the letter is sent.

9.4.4.5 Appropriate data entry is performed in the HSREC database.

9.4.5 Physical disposition of the item

9.4.5.1 Items that were submitted for an already-approved study (e.g., Amendments; Continuation Reports)

9.4.5.1.1 The item is appropriately annotated by HSREC Administration (e.g., "response not received by deadline") and then filed in the study's HSREC file. A copy of the notification letter and any reminder attempts are also placed in the file.

9.4.6 Initial applications

9.4.6.1 If the application received HSREC review, it is considered an HSREC record. It is annotated by HSREC Administration ("response not received by deadline"). A copy of the notification letter (which may be either a Withdrawal Letter or an Administrative Closure Letter) and documentation of any reminder attempts are also placed in the file.

9.4.6.2 If the application did not receive HSREC review (for example, it was an HSREC application that underwent only pre-review screening), the application is considered an HSREC record. A copy of the Withdrawal Notification letter and documentation of any reminder attempts are attached to the application.

10 COMMUNICATION OF REVIEW DECISIONS

10.1 Purpose

The purpose of this section is to outline the procedure for the communication of HSREC decisions to investigators.

10.2 Policy

10.2.1 To ensure that investigators are appropriately informed about HSREC review decisions.

10.3 Procedure

10.3.1 Decisions taken at an HSREC meeting are communicated in writing to the applicant.

10.3.2 R can address any queries to HSREC Administration, which will attempt to resolve problems and liaise with the Chair when necessary.

10.3.3 The average turnaround times for notifying research applicants of the review outcome are 7 working days after the HSREC meeting. The research applicant should only follow up with the HSREC office if they have not received an HSREC letter within the 7 working day period.

10.3.4 The research applicant may start the project only once a **final** HSREC approval letter has been received. If modifications are required, then all requested changes must be made before a final letter of approval is issued.

10.3.5 It is not unusual for the HSREC to request some changes to the project, information and consent form, or clarification of certain issues. Only once these requirements are satisfactorily fulfilled, a formal letter of approval will be issued.

10.3.6 It is the responsibility of the research applicant to comply with all requests and return the requested documentation with a covering letter responding to the points raised, to the HSREC according to the Preparation Guide (available on the webpage) as soon as possible but not later than 60 calendar days from the date of issue. The application may be cancelled if no feedback is received from the research applicant within 60 calendar days.

10.3.7 All requested protocol and other document changes must be clearly marked by highlighting the changes in the re-submitted document. The track changes facility in the word processing programme should be used.

10.3.8 The Summary of Changes template on the application form must be used when responding to the HSREC.

10.3.9 One HSREC member or delegate as appointed by the Chair will carefully check all amended documentation, including participant information and consent forms.

10.3.10 If correct, the project will receive final approval that will be confirmed by the final approval letter issued by the HSREC administration.

10.3.11 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 HSREC requested major alterations to the protocol i.e., deferred the protocol, it must be resubmitted to a full sitting of the HSREC within 60 calendar days. In the event that the project fails to be re-submitted within the time period of 60 calendar days, a new and full application may need to be submitted unless arrangements have been made with HSREC Administration.

10.3.12 The initial period of approval is one year from the date of final approval. A continuation report and request for re-approval should be submitted at least 8 weeks before expiry of approval.

10.3.13 The final HSREC approval date will be recorded as the date on which the final approval letter is issued, and approval will expire in 1 year from this date.

10.3.13.1 HSREC Administration reserves the right to not issue approval letters if administrative fees are outstanding.

11 REVIEW PROCESS: CONTINUING REVIEW

11.1 Routine Continuing Review (Continuation Reports)

11.1.1 **Purpose**
The purpose of this section is to provide guidance on the continuing review process.

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

11.1.3 **Procedure**

11.1.3.1 Ethics approval is valid for one year only from the date of approval on the official final approval letter. An annual continuation report must be submitted to the HSREC a minimum of 8 weeks before the ethics approval expiry date, so that the submission can be reviewed and the project re-approved for the next year prior to the expiry date. No research may continue without this process and re-approval.

11.1.3.2 Continuation reports:

11.1.3.2.1 All clinical trials falling under the jurisdiction of SAHPRA must submit a progress report to SAHPRA six monthly. Copies of these SAHPRA progress reports should accompany the annual continuation report submitted to the HSREC. This six monthly SAHPRA progress report should not be submitted outside of this annual reporting to the HSREC, unless necessary for safety reasons.

11.1.3.2.2 In the case of all other research, yearly continuation reports are required, unless the HSREC deems the project to be of particularly high risk and requests more frequent progress reports.

11.1.3.2.3 The HSREC continuation report form should be used for the purposes of this submission.

11.1.3.2.4 The continuation 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.

11.1.3.2.5 For multi-centre studies the information in the continuation report must pertain specifically to local (UFS) sites. A site-specific continuation report must be submitted annually, for ethics approval, using the HSREC continuation report form.

11.1.3.2.6 Copies of published abstracts, may be submitted as attachments, if appropriate and self-explanatory.

11.1.3.2.7 Information that must be included in the continuation report:

11.1.3.2.7.1 For multi-site studies: For each of the reporting requirements listed below, the principal investigator must report specifically for the local site(s), while putting these local reports into perspective by reporting them relative to the larger study;

11.1.3.2.7.2 the number of participants recruited;

11.1.3.2.7.3 a summary of any unexpected problems and available information regarding adverse events (in many cases, such a summary could be a simple brief statement that there have been no unexpected 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);

11.1.3.2.7.4 a summary of any withdrawal of participants from the research since the last HSREC review;

11.1.3.2.7.5 a summary of any complaints about the research since the last HSREC 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 HSREC review; any relevant multi-centre trial reports;

11.1.3.2.7.6 any other relevant information, especially information about risks associated with the research;

11.1.3.2.7.7 A copy of the current informed consent document and any newly proposed consent document.

11.1.3.2.8 The above information will be distributed to HSREC members as assigned by the Chair or designated person prior to each meeting for discussion and renewal of approval.

11.1.3.2.9 The HSREC has the authority to place restrictions on, suspend, or terminate any study in which the investigator fails to comply with the review process or where such actions are deemed appropriate and justified by a fully convened HSREC meeting.

11.1.3.2.10 A study is considered active while analysis of any data collected or resulting from the study is ongoing.

11.1.3.2.11 Continuation reports are required annually until such time as the investigator submits a final study report or a notice of termination of the study.

11.2 Protocol Amendments

11.2.1 **Purpose**

The purpose of this section is to outline the procedures involved in applying for an amendment to an approved protocol including amendments to researchers.

11.2.2 **Policy**

11.2.2.1 Prospective HSREC approval requirement HSREC review and approval is required in advance of implementing any changes (amendments) in approved research, except when necessary to eliminate apparent immediate hazards to the human subjects. The HSREC review process, criteria for approval, and HSREC actions are the same as for other types of applications.

11.2.2.1.1 Approval cannot be granted retrospectively, after a change has been made. This applies to all amendments, including those that may appear to investigators to be largely administrative in nature.

11.2.2.2 The approval period of a study does not change when the HSREC approves an amendment or when the HSREC suspends the HSREC approval of the study.

11.2.2.3 Timing of Amendments: Amendment applications may be submitted at any time after the study has been granted final approval.

11.2.2.3.1 Changes that are related to an unexpected problem, adverse event, or non-compliance should be submitted as a Protocol Amendment together with an Adverse Event or Unanticipated Problem Report.

11.2.2.3.2 Amendment submitted at the same time as a Continuation Report (i.e., at the time of continuing review) are considered to be separate items and will be reviewed separately (even if reviewed at the same meeting).

11.2.2.4 Amendment versus a new application: Investigators sometimes use the amendment process to add secondary/sub studies, repositories, registries, or other major new activities to an already-approved study. HSREC Administration and the HSREC have the authority to determine that these activities should be submitted as a new application rather than an amendment to an existing application.

11.2.2.5 All applications for an amendment must include the rationale or justification for the proposed change(s). The justification for an amendment must clarify how it will change the study, how it will affect risks to participants and what safeguards will be introduced to protect participants from additional risks. If the revision requires a change in the informed consent process, a revised consent form must be submitted with the amendment. Terms such as amendments, revisions, addenda, administrative changes, additions and amendments will be referred to in this document as changes or amendments.

11.2.2.6 All proposed changes must be indexed and highlighted in the revised protocol and consent documents. Major changes must be incorporated in the protocol and a revised protocol submitted. The approval of an amendment does not alter the original approval or expiry dates assigned to the protocol.

11.2.2.7 The final decision as to whether an amendment is minor or major and whether it requires expedited or full committee review rests with the HSREC Chair or a person delegated this authority by the HSREC.

11.2.3 **Definitions**

11.2.3.1 Minor changes: Minor changes may be reviewed by the expedited process rather than a full HSREC.

11.2.3.1.1 A minor change:

11.2.3.1.1.1 Does not change the risk benefit profile of the study in any way;

11.2.3.1.1.2 Neither materially increases risk, nor materially decreases benefit, when considered in light of any changes proposed to mitigate risk and improve benefit;

11.2.3.1.1.3 Does not materially decrease scientific merit; and

11.2.3.1.1.4 Does not adversely affect the assessment of the research with respect to the criteria for approval.

11.2.3.1.2 Examples of typical minor amendments:

11.2.3.1.2.1 Administrative or informational amendments

11.2.3.1.2.1.1 Changes in research staff

11.2.3.1.2.1.2 Changing the study title or contact information

11.2.3.1.2.1.3 Addition or removal of qualified investigators and/or study sites

11.2.3.1.2.1.4 Revision of format of consent documents, recruitment materials or questionnaires

11.2.3.1.2.1.5 Correction of typographical errors

11.2.3.1.2.1.6 Change in background information or update of literature review

11.2.3.1.2.2 Procedural amendments

11.2.3.1.2.2.1 Drawing slightly different amounts of blood.

11.2.3.1.2.2.2 Changing frequency at which blood is drawn.

11.2.3.1.2.2.3 An increase or decrease in proposed number of participants supported by a statistical justification

11.2.3.1.2.2.4 Stricter inclusion or exclusion criteria

11.2.3.1.2.2.5 Changing the amount of compensation, within reasonable limits

11.2.3.1.2.2.6 Revisions to the informed consent documents to improve clarity, to include missing elements or to revise lay language

11.2.3.1.2.2.7 Decreasing drug dosage or frequency of administration

11.2.3.1.2.2.8 Decrease in number of study visits provided such a decrease does not affect collection of relevant safety-related data

11.2.3.1.2.2.9 Extension of period of study

11.2.3.1.2.2.10 Other changes that do not affect study design and will not affect study outcomes or results.

11.2.3.2 Major or substantive changes: Major or substantive changes require a change(s)

to the study methodology or procedure that may result in an alteration of the risk benefit profile of the study. Major changes must be reviewed by the full HSREC review process.

11.2.3.2.1 Examples include:

11.2.3.2.1.1 Change in study aims, objectives or design
11.2.3.2.1.2 Resulting changes to consent documents
11.2.3.2.1.3 Easing of inclusion or exclusion criteria
11.2.3.2.1.4 Adding a new activity that may increase risk to participants
11.2.3.2.1.5 Changing drugs or medications as well as dosages
11.2.3.2.1.6 Changing levels of radiation exposure
11.2.3.2.1.7 Adding a vulnerable population
11.2.3.2.1.8 Adding or changing invasive procedures
11.2.3.2.1.9 Adding a research arm to the study
11.2.3.2.1.10 Substantially extending the duration of exposure to the test material or intervention.

11.2.4 **Procedure**

11.2.4.1 Pre-review - Amendment or new application: The pre-review process by HSREC Administration includes consideration of whether the amendment should be reviewed as a separate study rather than an amendment to an existing approved study. The HSREC may also make this determination.

11.2.4.1.1 HSREC Administration and the HSREC consider the following factors when making this decision:

11.2.4.1.1.1 The degree of overlap with the already-approved study.
11.2.4.1.1.2 Most importantly, the impact of the amendment on the complexity of the study, and the HSREC's consequent ability to adequately track and oversee the study activities.

11.2.4.1.2 Amendments that may be best reviewed as separate studies are most likely to be: secondary studies (sub-studies), repositories, and registries. However, it is not always necessary requirement for these to be separate studies.

11.2.4.1.3 A decision to require a new application is communicated in writing to the investigator.

11.2.4.2 Pre-review - Level of review: An amendment may be reviewed by the expedited process instead of a full convened HSREC, if the amendment is a minor change.

11.2.4.3 Amendments are reviewed using the same procedures, criteria for approval, and HSREC actions as for all other HSREC-reviewed items.

11.2.4.4 Emergency deviation from HSREC-approved procedures: If a deviation is required to eliminate an apparent immediate hazard to a subject(s), then the investigator should make whatever changes are needed to protect the safety and welfare of the subject, without prior HSREC review and approval. However, a report of the deviation (including rationale and outcome) must be provided to the HSREC.

11.2.4.5 Planned (anticipated) deviation from HSREC-approved procedures, for a single subject: On rare occasions, an investigator will anticipate the need to deviate from the HSREC-approved procedures for a single subject. The specific deviation, rationale, and impact on risks and/or benefits must be provided. The investigator and the HSREC should also consider whether the currently-approved consent form (if any) needs revision for the single subject.

11.3 Reporting Requirements on HSREC Approved Research

11.3.1 **Purpose**

This section describes the information and events that must be reported to the HSREC as well as the time frame and procedures for the reporting.

11.3.2 **Policy**

11.3.2.1 The HSREC requires researchers to promptly notify the HSREC of the following

information and events, for any HSREC approved human subjects' research:

11.3.2.1.1 Unexpected problem;
11.3.2.1.2 Unexpected adverse medical device effect;
11.3.2.1.3 Adverse Events and Serious Adverse Events;
11.3.2.1.4 Serious non-compliance by researcher (or allegation of serious non-compliance);
11.3.2.1.5 Continuing non-compliance (or allegation of continuing non-compliance);
11.3.2.1.6 Emergency deviation from HSREC-approved procedures made without prior HSREC review to eliminate an apparent immediate hazard to a subject or others;
11.3.2.1.7 Continuation of research procedures after HSREC approval has lapsed, because the procedures are of direct benefit to individual subjects or withholding the research intervention (if any) may increase risks to subjects;
11.3.2.1.8 Breach (or risk of breach) of subject confidentiality or privacy;
11.3.2.1.9 Complaint of a subject that cannot be resolved by the study team;
11.3.2.1.10 Audit, inspection, compliance-related inquiry, or safety-related inquiry from a federal agency;
11.3.2.1.11 New information that has implications for the risks of the research. For example:
11.3.2.1.11.1 A publication in the literature indicates an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk;
11.3.2.1.11.2 An investigator brochure, package insert, or device labelling is revised to indicate an increase in the frequency or magnitude of a previously known risk, or to describe a new risk;
11.3.2.1.11.3 A withdrawal, restriction or modification of the marketing approval or SAHPRA/FDA labelling of a drug, device, or biologic being used in the research;
11.3.2.1.11.4 Premature suspension or termination of some or all of the research by the sponsor, researcher, or institution;
11.3.2.1.11.5 Safety monitor or Data and Safety Monitoring Board (DSMB) reports;
11.3.2.1.11.6 Protocol deviations, Violations and Exceptions.

11.3.2.2 The HSREC relies upon the expertise of the researcher to make an initial assessment of the information/event, to determine whether it meets the reporting requirements described above, and to determine the relationship of the information/event to the research.

11.3.3 **Definitions**

11.3.3.1 Unexpected Problem: An unexpected problem is any incident, experience or outcome that meets all the following three criteria:
11.3.3.1.1 Unexpected in terms of its nature, severity or frequency, or the research population being studied; or if anticipated it is not fully addressed or specified in information provided to the HSREC or to participants such as in initial protocol applications, any amendments, investigator brochures, scientific literature, product labelling, package inserts and HSREC-approved informed consent documents or any existing documentation regarding the research conducted to date under the protocol;
11.3.3.1.2 Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience or outcome may have been caused by the procedures involved in the research);
11.3.3.1.3 Suggests that the research places participants or others at a greater risk of physical, psychological, economic or social harm than was previously known or recognized.
11.3.3.1.4 Examples of unexpected problems include:

11.3.3.1.4.1 Loss of a laptop computer containing confidential information about participants or others;
11.3.3.1.4.2 A spouse physically abused by his or her partner for taking part in the study;
11.3.3.1.4.3 Publication in the literature or a Data and Safety Monitoring Report that indicates an unexpected change in the balance of risks and benefits in the study;
11.3.3.1.4.4 Finding that laboratory reports on blood or other samples were in error.

11.3.3.2 Unexpected Adverse Device Effect: Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with a medical device (if that effect, problem or death was not previously identified in nature, severity, or degree of incidence in the materials reviewed by the HSREC), or any other unexpected serious problem associated with a medical device that relates to the rights, safety, or welfare of subjects.

11.3.3.3 Adverse Event (AE): An adverse event is defined as any untoward medical or psychological occurrence in a human research participant, including any abnormal laboratory finding, symptom or disease, and which does not necessarily have a causal relationship with the research or any risk associated with the research.

11.3.3.3.1 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 the HSREC.

11.3.3.3.2 Adverse events can thus 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 event may obviously, in certain studies also include adverse drug events.

11.3.3.3.3 An adverse drug reaction is an adverse event which, in the investigator's opinion, has a causal relationship with the research.

11.3.3.3.4 An unexpected adverse event is one in which one or more of the following apply:

11.3.3.3.4.1 The specificity or severity is not consistent with the current investigator's brochure;
11.3.3.3.4.2 The event is not consistent with the risk information in the current protocol application;
11.3.3.3.4.3 The event is occurring more frequently than anticipated.

11.3.3.4 A serious adverse event (SAE): Any adverse drug experience, occurring at any dose that results in any of the following outcomes:

11.3.3.4.1 Death;
11.3.3.4.2 A life-threatening incident (places the participant at immediate risk of death from the event as it occurred);
11.3.3.4.3 Inpatient hospitalisation or prolongation of existing hospitalization;
11.3.3.4.4 Significant or persistent disability/incapacity;
11.3.3.4.5 Congenital abnormality/birth defect;
11.3.3.4.6 Requires medical or surgical intervention to prevent permanent impairment or damage (e.g., allergic bronchospasm requiring intensive treatment in the emergency room or at home);
11.3.3.4.7 Inadvertent disclosure of confidential information if this presents an immediate risk to a participant such as from spousal or child abuse.
11.3.3.4.8 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 the HSREC.

11.3.3.5 Non-compliance: A situation, event or process in human subjects' research that is under the researcher's control and that is inconsistent with the following. This can include inquiries and complaints directed to the researcher that involve an allegation of non-compliance as defined here:

11.3.3.5.1 The ethical principles of human subjects research as described in the

Belmont Report;

11.3.3.5.2 National and International regulations applicable to human subjects' research under the jurisdiction of the HSREC;

11.3.3.5.3 HSREC policies and procedures governing human subjects' research; or

11.3.3.5.4 The research activities as approved by the HSREC, including any HSREC requirements or determinations.

11.3.3.6 Serious non-compliance:

11.3.3.6.1 Non-compliance which could significantly:

11.3.3.6.1.1 Increase risks to, or jeopardize the safety, welfare, and/ or rights of subjects or others, or

11.3.3.6.1.2 Decrease potential benefits (including the scientific integrity of the research).

11.3.3.6.1.3 Conducting a research study without any prospective HSREC approval is always considered serious non-compliance.

11.3.3.7 Continuing non-compliance: A pattern of non-compliance that:

11.3.3.7.1 Suggests that non-compliance will continue, if there is no intervention, or

11.3.3.7.2 Increases the risk of serious non-compliance.

11.3.3.8 Minor non-compliance: Non-compliance that is neither serious nor continuing.

11.3.3.9 Study Deviation/Violation: A protocol deviation or violation is an unplanned or unforeseen failure of the principal investigator or other study personnel to follow the specified procedures approved by the HSREC. Protocol deviations differ from amendments because they usually apply to a single incident or participant and are not intended at the time to change the study.

11.3.3.9.1 The principal investigator must categorise a protocol deviation as major or minor.

11.3.3.9.2 Major Protocol Violations or Deviations: If a deviation meets any of the following criteria it should be classified as major (the list is not exhaustive):

11.3.3.9.2.1 The deviation has harmed or posed a significant or substantive risk of harm to a participant:

11.3.3.9.2.1.1 A participant received the wrong treatment or incorrect dose;

11.3.3.9.2.1.2 A participant met withdrawal criteria during a study but was not withdrawn;

11.3.3.9.2.2 The deviation compromises the scientific integrity of the study data:

11.3.3.9.2.2.1 A participant was enrolled but does not meet the protocol's eligibility criteria;

11.3.3.9.2.2.2 Failure to treat participants per protocol procedures that specifically relate to primary efficacy outcomes (if it involves participant's safety, it meets the category above);

11.3.3.9.2.2.3 Changing the protocol without HSREC approval;

11.3.3.9.2.2.4 Inadvertent loss of samples or data.

11.3.3.9.2.3 The deviation is a wilful or knowing breach of ethical or regulatory policies or guidelines:

11.3.3.9.2.3.1 Failure to obtain informed consent;

11.3.3.9.2.3.2 Falsifying research or medical records;

11.3.3.9.2.3.3 Performing tests or procedures beyond the investigator's professional scope;

11.3.3.9.2.3.4 Failure to follow the safety monitoring plan.

11.3.3.9.2.4 The deviation involves serious or continuing non-compliance with institutional or regulatory policies:

11.3.3.9.2.4.1 Working under an expired professional licence;

11.3.3.9.2.4.2 Repeated minor deviations.

11.3.3.9.3 Minor Protocol Violations or Deviations: Minor protocol deviations are deviations which do not affect a participant's safety, compromise the integrity of study data or affect a participant's willingness to continue taking part in the study.

11.3.3.9.3.1 Examples of minor deviations include, but are not limited to:

11.3.3.9.3.1.1 Missing pages of a completed consent form;

11.3.3.9.3.1.2 Inappropriate documentation of informed consent such as missing signatures;

11.3.3.9.3.1.3 Using an expired consent form that has not changed significantly;

11.3.3.9.3.1.4 Participant did not receive a copy of a signed consent form (but on discovery, a copy is given to participant);

11.3.3.9.3.1.5 Study procedure conducted out of sequence.

11.3.3.10 Study Exceptions: A protocol or study exception is a one-time intentional action or process that departs from the HSREC-approved protocol.

11.3.3.10.1 Occasionally investigators want to make a temporary change or a change which affects only one or a few participants. These temporary or limited changes are defined as 'study exceptions'. For example:

11.3.3.10.1.1 Enrolment of a participant who does not meet the eligibility criteria, for instance a participant whose age slightly exceeds the age inclusion criterion;

11.3.3.10.1.2 Changing the dose of a study medication when justified;

11.3.3.10.1.3 Changing a visit date;

11.3.3.10.1.4 Adding an extra visit or omitting a visit.

11.3.4 **Procedure**

11.3.4.1 When to report Unexpected Problems or Adverse Events: Table 1 below includes a list of information and events that need to be reported as well as the timelines.

11.3.4.1.1 Serious Adverse Events (SAE)/ Suspected Unexpected Serious Adverse Reaction (SUSAR)/ Council for International Organizations of Medical Sciences (CIOMS) reports of all South African centres have to be reported per event. This data must be submitted by the sponsor to the principal investigator who submits it to the HSREC.

11.3.4.1.2 SAE/SUSAR/CIOMS reports of worldwide centres have to be reported in a line listing format. Cumulative data is preferred. This data must be submitted by the sponsor to the principal investigator who submits it to the HSREC.

11.3.4.1.3 Any notifications/letters e.g. Dear Dr letters, Dear Investigator letters etc. have to be reported per event. This data must be submitted by the sponsor to the principal investigator who submits it to the HSREC.

11.3.4.1.4 The principal investigator must submit a written report of all serious adverse events or safety related matters as per HSREC approved

site.

11.3.4.2 When to report Protocol Violations/Deviations and Study Exceptions: Table 2 below includes a list of information and events that need to be reported as well as the timelines.

11.3.4.3 Research involving collaborators or multiple performance sites. When the components of the research are distributed across more than one institution or site, the reporting requirements depend upon the Research Ethics Committee (REC) review arrangements:

11.3.4.3.1 If the HSREC UFS and another REC are both reviewing the entire study: The researcher follows the UFS reporting requirements described in this document, regardless of the component or site at which the problem occurred.

11.3.4.3.2 If the HSREC UFS is the REC of record for another institution: The researcher follows the UFS reporting requirements described in this document, for problems involving the other institution or the UFS.

11.3.4.3.3 If the HSREC UFS is reviewing only the components of the research in which the UFS is engaged: The researcher follows the UFS reporting requirements described in this document, but only for problems relevant to the research components reviewed by the HSREC UFS with one exception of certain External (or, offsite) AEs.

11.3.4.3.3.1 External AEs: From the perspective of one particular institution engaged in a multi-centre trial, internal adverse events are AEs experienced by subjects enrolled by the researcher at that institution, whereas external adverse events are AEs experienced by subjects enrolled by researchers at other institutions engaged in the trial.

11.3.4.3.3.1.1 Researchers may routinely receive a large volume of reports of external AEs experienced by subjects enrolled in multicenter clinical trials. These individual reports often lack sufficient information to allow researchers or the HSREC to make meaningful judgments about whether the AE is unexpected or is related or possibly related to the research.

11.3.4.3.3.1.1.1 This means that it is neither useful nor necessary for many individual external AEs to be reported to HSREC UFS.

11.3.4.3.3.1.2 External AEs should only be reported to HSREC UFS if they meet the definition of an Unexpected Problem.

11.3.4.4 Cancellation or early termination of studies:

11.3.4.4.1 The terminated activities must be immediately halted, except for those activities and actions the HSREC requires for the safety and welfare of the subjects. Terminated research is permanently closed and no longer requires continuing review (Status Reports). However, the HSREC may require a Closure Report from the investigator before it closes the research and the HSREC file.

11.3.4.4.2 Procedures

11.3.4.4.2.1 The cancelation or early termination must include a statement of the reasons for the termination/cancelation. The investigator must specify the specific activities that are terminated/cancelled; otherwise, the termination is assumed to be a “full” termination of all research activities.

11.3.4.4.2.2 Subject safety. The HSREC must identify and require

any appropriate actions to protect the safety and welfare of past or currently enrolled subjects, together with a timeline for fulfilling these requirements. The HSREC may consult with the investigator in these issues. The HSREC should always consider:

11.3.4.4.2.2.1 What activities (if any) should be allowed to continue (for example, follow-up visits that involve important monitoring assessments of subject safety);

11.3.4.4.2.2.2 What information and additional procedures (if any) should be provided to past or currently enrolled subjects or other parties, as well as how and by whom.

11.3.4.4.2.3 Communication. The termination is immediately reported in writing to the HSREC.

11.3.5 **Guidance and Additional Information**

11.3.5.1 Consultation. Researchers may contact HSREC Administration if they are uncertain about whether specific information or events should be reported.

11.3.5.2 Determination of "unexpected". It may be difficult to determine whether a particular event is unexpected. For many studies, this determination can be done only through an analysis of appropriate data on all subjects enrolled in the research. Regulatory agencies state that the vast majority of adverse events are expected in light of:

11.3.5.2.1 The known toxicities and side effects of the research procedures;

11.3.5.2.2 The expected natural progression of subjects' underlying diseases, disorders, conditions; and

11.3.5.2.3 Subjects' predisposing risk factor profiles for the adverse events.

11.3.5.3 Determination of "relatedness". Determinations about the relatedness of adverse events or medical problems to participation in research commonly result in probability statements that fall along a continuum between definitely related to the research and definitely unrelated to participation in the research.

11.3.5.3.1 Researchers sometimes mistakenly define relatedness as "cannot rule out the possibility that it is related" or "cannot be explained by anything else".

11.3.5.3.2 The threshold for reporting an event is possibly related to participation in the research, defined as "more likely than not".

11.3.5.3.3 Sometimes researchers may not be able to determine whether a problem is possibly related to the research within the required time frame for reporting. In such cases, the researcher should report the problem and then provide a follow-up report after causality has been more fully addressed or is better understood.

Table 1: Timelines for Reporting Unexpected Problems or Adverse Events

Information or Event	When to report
Unexpected problems	All unexpected problems that increase the risk of harm to participants or others must be reported to the HSREC **within seven calendar days** after the investigator first learns of their occurrence
Fatal and life-threatening, unexpected adverse drug reactions	All fatal and life-threatening adverse drug reactions in clinical trials must be reported to the HSREC **as soon as possible but not later than seven calendar days** after the investigator first learns of their occurrence.
Serious and unexpected non-fatal adverse drug reactions	All serious unexpected drug reactions that are not fatal or life-threatening must be reported to the HSREC **as soon as possible but not later than fifteen calendar days** after first learning of their occurrence.
Expected adverse drug reactions	All adverse drug reactions that are expected but are judged to be occurring at a significantly higher frequency or severity than expected must be reported to the HSREC **within fifteen calendar days** after the investigator first learns of their occurrence. The basis for these assessments must be included in the investigator's report.
Serious and unexpected adverse device effects	All unexpected adverse device effects must be reported to the HSREC **as soon as possible but not later than seven calendar days** after first learning about their occurrence
New information that might impact the conduct of a clinical trial	Other unexpected adverse events, regardless of severity, that may alter the balance of risks and benefits in a study and as a result warrant consideration of substantive changes in the overall conduct of a clinical trial must be reported to the HSREC **within three calendar days** of first learning about their occurrence. The report could include individual case reports or a major safety finding from other sources.
Early termination or cancelation of studies	The termination is immediately reported in writing.

Table 2: Timelines for Reporting Protocol Violations/Deviations and Study Exceptions

Information or Event	**When to report**
Major protocol violations/deviations	The Principal Investigator must report major protocol deviations to the HSREC **within seven calendar days** of first hearing of the incident
Minor protocol violations/deviations	If the principal investigator determines the deviation is **minor** and has **no impact** on the study or welfare of participants, **no further action** is necessary and the **deviation can be reported in the next annual continuation report.**
Study exceptions	All study exceptions must receive HSREC approval **prior** to initiation and must be **listed** in the subsequent continuation report.

12 EXPIRED APPROVAL

12.1 Purpose

This section describes the procedures followed by the HSREC for preventing, identifying, and managing lapsed HSREC approvals. The final approval is valid for a year from date of approval.

12.2 Policies

12.2.1 Researcher responsibility

12.2.1.1 It is ultimately the researcher's responsibility to track HSREC approval periods and ensure that HSREC approval does not lapse. Failure to receive HSREC reminders does not absolve researchers of this responsibility, nor does it change the consequences of a lapsed approval.

12.2.2 Expired approval

12.2.2.1 If HSREC approval expires, all research must stop, except those activities that meet very specific criteria as described in the Continuing Review section of this document.

12.2.2.1.1 "All" includes (but is not limited to): participant contact, data collection, and data analysis. Activities that occur without current HSREC approval are considered non-compliance, with appropriate consequences.

12.2.3 Identification of lapsed approvals

12.2.3.1 HSREC Administration regularly monitors the approval status of all studies so as to identify studies with lapsed approval.

12.2.4 Administrative closure of lapsed studies

12.2.4.1 Studies will be closed 30 calendar days after the expiration of HSREC approval if a complete Continuation Report has not been submitted to the HSREC, unless other arrangements have been made between the researcher and the HSREC.

12.2.5 Re-opening of administratively-closed studies

12.2.5.1 Studies that have been administratively closed cannot be re-opened without submitting a new application unless there are extraordinary circumstances, then a formal request and rationale must be submitted, and the request must be approved by the HSREC. An adequate research status report must also be submitted with this request and approved by the HSREC.

12.3 Definitions

12.3.1 Administrative closure:

12.3.1.1 Closure of a study that does not have HSREC approval (due to a lapsed approval, or failure to respond to conditions of approval)

12.3.2 Expiration date:

12.3.2.1 HSREC approval expires at 11:59 PM on the last day of the HSREC approval period as communicated by HSREC Administration on the Approval Letter. HSREC approval is valid for one year from date of approval.

12.3.3 Lapsed approval:

12.3.3.1 The status of a study for which the HSREC approval has expired.

12.3.4 Continuation Report:

12.3.4.1 The form that investigators complete and submit to the HSREC to initiate the continuing review process.

12.3.5 Continuing review.

12.3.5.1 HSREC re-review of a study, for "renewal" of HSREC approval. Must occur at least once per year.

12.4 Procedures

12.4.1 Identification of reminder recipients

12.4.1.1 A report is generated once a month (January to November) in the HSREC database that identifies studies approximately 8 weeks before expiration of approval.

12.4.2 HSREC Administration manually sets the study status for those studies to "Lapsed Approval". The report is brought to the attention of the Chair for further attention.

12.4.3 Management of lapsed approvals

12.4.3.1 HSREC Administration is responsible for using the report to ensure that the

following activities are performed:

12.4.3.1.1 Contacting the principal investigator and/or the study coordinator about providing a Continuation Report. All contact attempts should be documented in RIMS. The following information is conveyed:

12.4.3.1.1.1 The HSREC approval has lapsed. Therefore, no research activities (recruiting, procedures, data collection, etc.) should have been, or may be, performed until HSREC approval has been renewed, except as necessary with currently enrolled participants to ensure that (1) their rights and welfare are protected; (2) they are not put at risk; and (3) they receive appropriate care during the lapsed approval.

12.4.3.1.1.2 Sending a warning letter of lapsed approval, if lapsed approval continues for 30 calendar days without submission of a Continuation Report or other arrangements made with the researcher.

12.4.4 Administratively closing the study, if lapsed approval continues for 30 calendar days without submission of a complete Continuation Report or other arrangements made between the researcher and HSREC.

12.4.4.1 A letter of study closure for lapsed approval is used to formally communicate the closure; a copy will be kept in RIMS.

12.4.4.2 The procedures are the same as described for the 30-calendar day warning letter, with the additions noted here:

12.4.4.2.1 The date of the letter must be the same as the date the researcher is sent the letter. This is also the official closure date entered in the HSREC database.

12.4.4.2.2 The following individuals are copied in the email:

12.4.4.2.2.1 Researcher's department chair, Dean, or Director (whomever is most appropriate);

12.4.4.2.2.2 The student supervisor (if the researcher is a student);

12.4.4.2.3 With the sending of the letter, the study is considered closed.

12.4.4.2.4 HSREC Administration performs appropriate data entry in the HSREC database.

13 STUDY CLOSURE

13.1 Purpose

This section describes the policies and procedures for closing an HSREC approved study.

- See the section on expired approval for administrative closure of studies whose HSREC approval has lapsed.
- See the section on unresponsive researchers for administrative closure of studies with conditional approval.

13.2 Policy

13.2.1 When a study may be closed.

13.2.1.1 Regulatory basis of closure

13.2.1.1.1 Continuing review and re-approval of a study is required so long as the project continues to involve human participants. When it no longer involves human participants, the study may be closed with the HSREC.

13.2.1.1.1.1 Research involves human participants while the researchers continue to obtain:

13.2.1.1.1.1.1 Data about the participants, through intervention or interaction with them, or

13.2.1.1.1.1.2 Identifiable private information (data, specimens, etc.) about the participants.

13.2.2 Closure report

13.2.2.1 HSREC policy requires the principal investigator of ALL studies to formally inform HSREC when a study has been completed. A study is considered active while data collection (human or other data) is ongoing.

13.2.2.2 The HSREC reviews a researcher's closure notification.

13.2.2.3 The HSREC acknowledges the researcher's closure by sending an official letter of acknowledgement.

13.2.3 Researcher responsibilities after study closure

13.2.3.1 The researcher continues to have some responsibilities for a study even when HSREC review and approval is no longer required. These include:

13.2.3.1.1 Records retention (including HSREC applications) must comply with all applicable regulations governing the study.

13.2.3.1.2 If the researcher is maintaining identifiable private data, the protections described in the HSREC application and to participants must be maintained, for the time frame described.

13.2.3.1.3 The researcher must continue to honour any commitments made to participants as part of the approved research. Examples might include: providing information about study results; payment for research participation and access to the investigational product.

13.3 Definitions

13.3.1 Administrative closure

13.3.1.1 Closure of a study that does not have HSREC approval (due to a lapsed approval or failure to respond to conditions of approval).

13.3.2 Closure date

13.3.2.1 The date when a non-lapsed study is considered closed (i.e., no longer has HSREC approval).

13.3.3 Expiration date

13.3.3.1 HSREC approval expires at 11:59 PM on the last day of the HSREC approval period as communicated by HSREC Administration on the Approval Letter.

13.3.4 Lapsed approval

13.3.4.1 The status of a study for which the HSREC approval has expired.

13.3.5 Continuation Report

13.3.5.1 The form that investigators complete and submit to the HSREC to initiate either the continuing review of the study, or the closure of the study.

13.3.6 Continuing review

13.3.6.1 HSREC re-review of a study, for "renewal" of HSREC approval. Must occur at least once per year.

13.3.7 Final/Study Closure Report

13.3.7.1 The form that investigators complete and submit to the HSREC to initiate the closure of the study.

13.4 Procedure

13.4.1 **Researchers**

13.4.1.1 Closure notification. Researchers notify HSREC of study closure by sending HSREC a Final Report for Academic Studies or a Study Closure Report for Contract Research Studies.

13.5 Procedures

13.5.1 **HSREC**

13.5.1.1 Continuation Reports requesting continuation of HSREC approval

13.5.1.1.1 HSREC Administration screen Continuation Reports that request a continuation of HSREC approval. The information in the Continuation Report may suggest that the study is eligible for closure. In such cases, HSREC Administration contact the researcher to obtain sufficient information to make a determination about closure eligibility.

13.5.1.1.2 When sufficient information can be obtained and documented, researchers are required to submit a revised Final Report or a Study Closure Report for Contract Research Studies requesting closure instead.

13.5.1.1.3 Evaluating closure eligibility for requested closure

13.5.1.1.3.1 HSREC Administration screen Continuation Reports to ensure that the study is eligible for closure.

13.5.1.1.3.2 Additional information may be required from the researcher to determine closure eligibility.

13.5.1.1.4 Closure

13.5.1.1.4.1 HSREC Administration formally closes the study by updating the project status.

13.5.1.1.4.2 HSREC Administration sends a letter of confirmation to the principal investigator as acknowledgment and documentation of closure.

14 RESEARCH ACTIVITIES PERFORMED WITHOUT HSREC APPROVAL

14.1 Purpose

This section defines the circumstances in which research activities are considered to have been performed by researchers without HSREC approval. It also describes the consequences of obtaining data without HSREC approval.

14.2 Policy

14.2.1 Data and/or specimens obtained for human research activities are considered to have been collected without HSREC approval when obtained under the following circumstances:
- 14.2.1.1 With no prior review or approval by the HSREC;
- 14.2.1.2 With outstanding conditions of approval pending;
- 14.2.1.3 With no informed consent from the subjects or their legally authorised representatives (and when the HSREC had not approved a waiver of consent);
- 14.2.1.4 Using procedures that were not described in the HSREC-approved consent document (and when the HSREC had not approved a waiver for excluding the procedure from the consent document);
- 14.2.1.5 After the expiration of HSREC approval;
- 14.2.1.6 After suspension or termination of HSREC approval.

14.2.2 The HSREC does not, and cannot, grant retrospective approval for use of data that was collected without HSREC approval. National and international regulations allow HSREC approval to be granted only when it is prior to the initiation of the research activities.

14.3 Procedure

14.3.1 The HSREC may identify data collected without HSREC approval in a variety of ways such as:
- 14.3.1.1 Self-reported by the researcher;
- 14.3.1.2 Screening by HSREC Administration;
- 14.3.1.3 Screening by HSREC Members; or
- 14.3.1.4 Concerns brought to the HSREC by individuals.

14.3.2 The HSREC then requires the researcher to submit a completed Protocol Violation/Deviation report, describing the unapproved activities, circumstances, and any proposed corrective or preventative action.

14.3.3 HSREC initial intake:
- 14.3.3.1 When a Protocol Violation/Deviation report is submitted for a study that appears to have been conducted without any HSREC approval, HSREC Administration determines whether an HSREC record for the study exists. If a record does not exist, a record will be created in the HSREC database.
- 14.3.3.2 All other Protocol Violation/Deviation reports go through the normal intake process for Problem Reports.

14.3.4 Review:
- 14.3.4.1 The Protocol Violation/Deviation report is reviewed by the HSREC.
- 14.3.4.2 In addition, the HSREC makes a formal determination as to whether data were collected without required HSREC approval. To do so, the Senior HSREC Administrator, HSREC Chair or designate assesses whether the activity constituted research involving human subjects.

14.3.5 Consequences of obtaining data without HSREC approval:
- 14.3.5.1 Non-compliance determination:
  - 14.3.5.1.1 The HSREC determines whether the data collection is minor, serious, or continuing non-compliance. Conducting a research study without any prospective HSREC approval is always considered serious non-compliance. The regulatory basis for non-compliance determinations includes (but is not limited to) the following:
    - 14.3.5.1.1.1 Obtaining human subjects' data without HSREC approval is always considered to be non-compliance with human subjects' regulations and HSREC policy.
    - 14.3.5.1.1.2 Accessing records for research purposes without HSREC approval is non-compliance with HSREC policy.
    - 14.3.5.1.1.3 Publications and presentations. Data collected without HSREC approval cannot be described as being part of

an HSREC-approved study. This may have implications for the publications or presentations, as many journals and conferences require Research Ethics Committee (REC) approval as a condition of publication or presentation of research that involved human subjects.

14.3.5.1.2 A statement to this effect is communicated to the researcher for determinations of serious or continuing non-compliance.

14.3.5.1.3 The HSREC reports serious or continuing non-compliance to appropriate regulators and/or funding agencies.

14.3.5.1.4 The HSREC may require corrective or preventative actions to address or prevent the collection of data without HSREC approval as well as any consequences of the data collection activity. The possible actions are:

14.3.5.1.4.1 Some or all parts of the research are modified.

14.3.5.1.4.2 The data are collected again, but with HSREC approval.

14.3.5.1.4.3 The subjects provide consent again, using appropriately revised procedures and documents.

14.3.5.1.4.4 Notification of subjects may be required in studies that obtained records without the prior consent or authorisation (or an HSREC -granted waiver) from the subjects. The researcher's department is responsible for the notification costs.

14.3.5.1.4.5 Recommendation to impose sanctions on use of the data. Although the HSREC cannot impose sanctions on the use of data, the HSREC can recommend that the appropriate institutional office(s) consider the following actions:

14.3.5.1.4.5.1 Require that data not be published or presented;

14.3.5.1.4.5.2 Require that data not be used for a thesis or dissertation;

14.3.5.1.4.5.3 Require that data be destroyed; and/or

14.3.5.1.4.5.4 Other actions for which the institutional office has authority.

14.3.5.2 Suspension of research activities. The HSREC may temporarily withdraw HSREC approval for some or all parts of an approved study.

14.3.5.3 Termination of research activities. The HSREC may permanently withdraw HSREC approval for some or all parts of an approved study.

14.3.5.4 Closure. If the entire research study was conducted without HSREC approval (e.g. only on Conditional Approval), HSREC Administration will administratively close the file per the procedures in the Study Closure section, after all review activity related to the matter has been concluded. The file is retained as an HSREC record.

15 INFORMED CONSENT

15.1 Purpose

This section describes the policies and procedures for obtaining and documenting informed consent from human research subjects.

15.2 Policy

15.2.1 Requirement for consent.

15.2.1.1 Investigators may not 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 authorized representative, where appropriate.

15.2.1.2 This requirement is one of the central protections provided by the human subjects regulations. It is based on the principle of respect for persons, one of the three ethical principles governing human subjects research described in the Belmont Report. The principle of respect requires that individuals be treated as autonomous agents.

15.2.1.3 The requirement for consent applies to all human research, including situations that involve:

15.2.1.3.1 Direct intervention or interaction with subjects.

15.2.1.3.2 Obtaining private identifiable data, specimens, or records from subjects (including medical records).

15.2.2 An investigator shall seek such consent only under circumstances that provide the prospective participant, or their representative, with sufficient opportunity/time to consider whether or not to participate and that minimise the possibility of undue influence or coercion.

15.2.3 The information that is given to the participant or the representative shall be presented in language and/or format that optimally promotes understanding of the proposed research by the participant or the participant's legally authorized representative, where appropriate.

15.2.4 Reading level.

15.2.4.1 Most consent forms should be written so they are understandable to a lay audience. This means 8th grade reading level. However, a higher reading level may be acceptable depending upon the study population (for example, a study population of physicians or other highly educated individuals).

15.2.5 Informed consent may not 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.

15.2.6 The process of recruitment and documentation of informed consent must be described clearly and in detail in the study protocol.

15.2.7 For multi-centre clinical trials, the participant information and consent form must be adapted to the requirements of the local community and potential participants.

15.2.8 Informed consent begins with the initial approach to the potential subject (e.g., through a flyer, brochure, discussion, or any advertisement) and continues until the subject decides to end his/her participation or the study ends.

15.2.9 Obtaining a signature on a consent form does not complete the consent process. Researchers are required to provide subjects with any new information that arises during the study that may affect the subject’s decision about whether to continue participation. In addition, ensuring an adequate consent may require repeating or supplementing the initial consent procedure.

15.2.10 Waiver of consent requirements

15.2.10.1 The HSREC may waive the requirement to obtain consent, or it may approve a consent process that does not include, or that alters, some or all of the required elements of consent. Waivers of consent or of consent elements can be granted only under certain conditions.

15.2.11 Where a relationship of dependence exists between participant and researcher (e.g. service provider/service recipient), consent should be obtained by an independent person.

15.2.12 Research studies that plan to involve any potentially vulnerable populations, including children, must have adequate procedures in place for assessing and ensuring each subject’s capacity, understanding, and informed consent and assent

15.2.13 For genetic research studies, the participant information and consent/assent document must be separate from the main consent form.

15.3 The Basic Elements of Informed Consent

15.3.1 In seeking informed consent, the following information must be provided to each prospective subject, unless the element is not applicable or an HSREC approves a waiver or alteration of the element. *Starred elements can be omitted if they are not applicable.

15.3.1.1 A statement that the study involves research.
15.3.1.2 An explanation of the purposes of the research.
15.3.1.3 An explanation of the expected duration of the subject's participation.
15.3.1.4 A description of the procedures to be followed.
15.3.1.5 A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
15.3.1.6 An explanation of whom to contact in the case of a research-related injury to the subject.
15.3.1.7 An explanation of how to contact the research team for questions, concerns, or complaints about the research.
15.3.1.8 An explanation of how to contact someone independent of the research team for questions, concerns or complaints about the research, questions about the subject's right to obtain information, or to offer input.
15.3.1.9 A statement that participation is voluntary.
15.3.1.10 A statement that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.
15.3.1.11 A statement that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
15.3.1.12 Any additional costs to the subject that may result from participation in the research.
15.3.1.13 A statement regarding whether the participant will be remunerated for their time and inconvenience and reimbursed for any expenses related to the research.
15.3.1.14 A statement that findings may be published.
15.3.1.15 The approximate number of subjects involved in the study.
15.3.1.16 A statement that the particular treatment or procedure may involve risks to the subject which are currently unforeseeable.*
15.3.1.17 A statement that if the subject is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus which are currently unforeseeable.*
15.3.1.18 Anticipated circumstances under which the subject's participation may be terminated by the researcher without regard to the subject's consent*.
15.3.1.19 The consequences of a subject's decision to withdraw from the research.*
15.3.1.20 The procedures for orderly termination of participation by the subject. *
15.3.1.21 A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation, will be provided to the subject. *
15.3.1.22 Identification of any procedures which are experimental.*
15.3.1.23 A description of any reasonably foreseeable risks or discomforts to the subject.*
15.3.1.24 A description of any benefits to the subject or to others which may reasonably be expected from the research.*
15.3.1.25 A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.*

15.3.2 Anonymous participation in a study:

15.3.2.1 Participation in a research study where no identifying details (name, file number, Id number, student number) of a participant is recorded by the researcher or participant him-/herself.
15.3.2.2 Anonymous participation means that there is no means of tracing or a link to a participant's name, e.g. where questionnaires are not numbered and upon completion are placed in a box. In summary, the researcher cannot link a completed questionnaire to a specific individual e.g. via a control list.
15.3.2.3 In cases of questionnaires where anonymous participation in a study is under discussion, the Informed Consent form must not be signed, but the following must be stated at the start of the questionnaire:

15.3.2.3.1 “You have been asked to participate in a research study. Please note that by completing this questionnaire you are voluntarily agreeing to participate in this research study. You will remain anonymous and your data will be treated confidentially at all times. You may withdraw from this study at any given moment during the completion of the questionnaire. The results of the study may be published.”

15.4 Procedures

15.4.1 HSREC Review and Approval

15.4.1.1 The consent process, the consent form, and any other materials that are part of the consent process must be reviewed and approved by the HSREC, in connection with the HSREC application for the research.

15.4.1.2 Advertising, announcements, social media postings, and other recruiting processes and materials are part of the consent process.

15.4.1.3 Clinical trial websites do not require HSREC review when the clinical trial listing is limited to basic descriptive information.

15.4.1.4 Basic descriptive information includes:

15.4.1.4.1 Study title

15.4.1.4.2 Purpose of the study

15.4.1.4.3 Protocol summary

15.4.1.4.4 Basic eligibility criteria

15.4.1.4.5 Study site location(s)

15.4.1.4.6 How to contact the study site for further information

15.4.1.5 Information exceeding “basic descriptive information” includes:

15.4.1.5.1 Descriptions of trial risks and potential benefits

15.4.1.5.2 Solicitation of identifiable information

15.4.1.6 Changes to approved consent and recruiting processes:

15.4.1.6.1 Changes to approved consent and recruiting processes and materials must be reviewed and approved by the HSREC, as amendments, before implementation.

15.4.1.6.2 Proposals to repeat or supplement the initial consent process must also be reviewed and approved by the HSREC before implementation, as amendments.

15.4.1.7 HSREC review and approval must be obtained prior to implementation of the recruiting and consent process and materials (or the changes to them). The consent process and documents are re-reviewed as part of the process of continuing review to ensure that they still meet the criteria for HSREC approval and do not require revision.

15.4.2 Criteria for HSREC approval

15.4.2.1 The HSREC approves the consent process when the HSREC determines that the consent requirements described above have been met. Particular attention is paid to the following issues and context:

15.4.2.1.1 Risk and potential benefit information: Is it accurate, fair, and balanced?

15.4.2.1.2 Other information: Does the information provide the potential subject with a sufficient and accurate picture of what participation involves?

15.4.2.1.3 Participation incentives (monetary and non-monetary): Are they age and culture-appropriate? Are they likely to create an undue influence on a potential subject’s decision about whether to participate in the research?

15.4.2.1.4 Undue influence or coercion: Do the circumstances of the consent process create the likelihood of undue influence or coercion about the decision to participate?

15.4.2.1.5 Time: Is there ample time and opportunity to consider the information and ask questions?

15.4.2.1.6 Comprehension: Are potential subjects likely to comprehend the information in the proposed circumstances and format?

15.4.2.1.7 Local context: Is the proposed consenting process and documentation appropriate for the subject population and culture?

15.5 Procedures: **Obtaining Consent**

15.5.1 Researchers are responsible for ensuring that:

15.5.1.1 Process of obtaining informed consent is sufficiently described in the HSREC application/protocol. Sufficiently described implies who would obtain consent, from whom the consent will be obtained interpreter used, when consent will be obtained and in what manner.

15.5.1.2 Informed consent is obtained through the HSREC-approved process, prior to initiating any research activities, including screening procedures.

15.5.1.3 All individuals who will obtain consent are qualified and appropriately trained to explain the research and to answer questions.

15.5.1.4 HSREC approval is obtained for any revisions to the consent process, before implementation.

15.5.1.5 Participants are sufficiently competent to give consent, and these procedures are described in the protocol.

15.5.2 HSREC Consent Form Templates

15.5.2.1 Though it is not an absolute requirement, researchers are encouraged to use one of the HSREC consent templates when drafting a consent form. Use of the templates ensures compliance with regulatory requirements. However, the HSREC recognizes that there are some circumstances where a significantly different form, organization, and/or approach may be more appropriate.

15.5.3 Secondary studies and additional specific procedures

15.5.3.1 Some studies have secondary ("sub") studies or procedures that are related to the main study but not required for it. Examples include: drawing an extra sample of blood and analysing it for a genetic marker; asking subjects to join a registry for being contacted about future studies; asking subjects for permission to put their data and/or specimens into a repository.

15.5.3.2 Consent for secondary studies and procedures can be documented in the following ways. The HSREC has the authority to require the method it believes is most appropriate.

15.5.3.3 A separate informed consent form

15.5.3.3.1 Using a separate informed consent form may be best if there is relatively little overlap with the main study, or if there is significant additional information (procedures, risks, etc.) to convey to the subjects.

15.5.3.3.2 Initials or signature on a section of the informed consent form

15.5.3.3.2.1 It may be most appropriate for the subject to document consent to secondary procedures by signing a sub-section of the study consent form. If this method is used, it must meet the following HSREC requirements:

15.5.3.3.2.1.1 The distinction between the main study and the secondary procedures is very clear and obvious – for example, the secondary procedures may be described within a labelled text box.

15.5.3.3.2.1.2 The consent process must be an "opt in" process, not an "opt out" process. That is, if the initial/signature line is left blank, it is assumed that the subject did not agree to the additional procedures.

15.5.4 Translation and interpretation

15.5.4.1 As part of each consent discussion, the researcher has an ethical and legal obligation to assess (informally or otherwise) the participant's understanding of the consent information to ensure that consent is truly informed. When the researcher and the participant do not speak the same language, the researcher must depend on the accuracy of the translated consent documents and/or the qualifications of an interpreter. In addition, the researcher's familiarity (or lack of it) with the participant's culture affects the communication.

15.5.4.2 Non-English-speaking participants

15.5.4.2.1 The consent process occurs in a language understandable to the participants.

15.5.4.2.2 Researchers (and the HSREC) should consider how likely it is that they will encounter participants whose language of choice is not English and how they will obtain consent from those individuals.

15.5.4.2.3 The consent presentation and discussion must occur in a language that is understandable to participants. Consent and information documents must be available in a language that is understandable to the participant. If necessary, an interpreter who is able to adequately obtain consent and answer questions in a consistent and reliable manner.

15.5.4.2.4 Translation of the participant informed consent document/information document/data collection tools:

15.5.4.2.4.1 In seeking informed consent, the information that is given to the participant shall be presented in a language, and format that optimally promotes understanding of the proposed research by the participant or the participant's legally authorized representative, where appropriate.

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

15.5.4.2.4.3 In the Free State participant related documents must be available in 3 languages: English, Afrikaans and Sesotho.

15.5.4.2.4.4 The HSREC would require translation into the languages inherent to the geographical area where the research is to be performed to ensure appropriate participation and representation of the population eligible for the research project.

15.5.4.2.4.5 Before approval of the proposed consent documentation, the HSREC will review the recruitment strategy provided in the protocol for adequate motivation and justification, based on the particular target participant population, of what would be the best language(s), and/or process(es), for informed consent in a particular context. If the research is to be conducted elsewhere in South Africa, other translation requirements may be applicable.

15.5.4.2.4.6 Participant information and informed consent documents (as well as other participant facing material) must be submitted for HSREC approval, in English, Afrikaans and Sesotho (as a minimum requirement for research performed in the Free State province).

15.5.4.2.4.7 The submission can be staggered, i.e., English information documents and informed consent documents may be submitted, reviewed and approved by the HSREC, and once approved these documents may be translated.

15.5.4.2.4.8 Only once the information document, and informed consent form (and other participant facing material) have been approved by the HSREC will “final HSREC approval” be granted, when the English documents have been submitted

15.5.4.2.4.9 “Modifications Required” status will be applied for any submission where the information document, and informed consent (and other participant facing material) have not been submitted in all the relevant languages.

15.5.4.2.4.10 In the case of contract and post-graduate research:

15.5.4.2.4.10.1 Once the original document is approved, it is the responsibility of the investigator to arrange for translations of the forms into appropriate languages. A professional translator service must be assigned

to this task. All translations should preferably be done 'back-to- back' i.e., English to Sesotho and back to English, by different translators.

15.5.4.2.4.10.2 Translations should be returned to the HSREC accompanied by either a certificate of translation and/or back-translation or letter from the principal investigator declaring that the translation is an accurate reflection of the approved English version. This should be submitted as a notification to the HSREC.

15.5.4.2.4.10.3 The HSREC will acknowledge receipt of translations.

15.5.4.2.4.11 The HSREC reserves the right to check translations and delay approval of the study, if the translations are deemed to be of poor quality.

15.5.4.2.4.12 Investigators and sponsors are encouraged to ensure that the informed consent process and the information that is given to the participant are presented in a language, and format, that optimally promotes understanding. This is also relevant for any other participant facing material.

15.5.4.2.5 Interpretation

15.5.4.2.5.1 While an interpreter may be helpful in facilitating the informed consent process, the HSREC does not promote the routine ad hoc translation of the information and informed consent documents by an interpreter. Verbal translation should not substitute a written translation of these documents.

15.5.4.2.5.2 If appropriate, researchers should have an ongoing arrangement for an interpreter, to convey the participants' questions and concerns throughout the study.

15.5.4.2.5.3 The HSREC application should describe who will serve as interpreter, and whether any conflict of interest applies to that interpreter.

15.5.4.2.6 In addition to providing in-person interactions and written documents in the language of the participants, researchers may consider additional methods of communication as well.

15.5.4.2.7 The HSREC has the authority to require revisions or additions to the consent process to ensure that non-English speaking participants are adequately informed and are providing truly voluntary informed consent.

15.5.5 Illiterate participants

15.5.5.1 Researchers sometimes rely on the consent form to communicate specific information about the research before initiating the consent discussion. This is not possible for illiterate and functionally illiterate participants.

15.5.5.2 The HSREC expects researchers to consider the literacy level and distribution in the study population and to make appropriate accommodations to the consent process so that all consent requirements are addressed.

15.5.5.3 It is HSREC policy to generally follow the following guidance:

15.5.5.3.1 The consent materials are read to the participant in the presence of an impartial witness who observes the entire consent process.

15.5.5.3.2 Sufficient time is allowed for questions to be asked and answered, to ensure that the participant comprehends the consent information.

15.5.5.3.3 Documentation is obtained:

15.5.5.3.3.1 If capable of doing so, the participant signs, or marks an X, to signify consent.

15.5.5.3.3.2 The witness signs and dates the consent form. By doing so, the witness attests that the consent information was accurately explained, that the participant apparently

understood the information, and informed consent was freely given.

15.5.5.3.3.3 The person obtaining consent signs and dates the consent form.

15.5.5.3.3.4 A signed copy of the informed consent form is provided to the participant.

15.5.5.3.3.5 The researcher considers using a video/audio recording of the consent discussion as part of the documentation of consent.

15.5.5.3.4 participants who can read but are physically unable to talk or write due to physical limitations

15.5.5.3.4.1 Participants with these characteristics may be able to participate in research if they are cognitively competent and able to indicate approval or disapproval by other means. The consent form should document the method used for communication with the participant and the specific means by which the participant communicated agreement to participate in the study. If the participant is unable to read, the method described above may be used, if approved by the HSREC. The manner in which the participant provided permission need to be recorded.

15.5.6 Legally blind participants

15.5.6.1 The preferred method of obtaining and documenting consent is to use Braille materials, if the participant is able to read Braille. However, the method described above may also be used, if approved by the HSREC.

15.5.7 Obtaining consent by telephone, Skype, social media, or interaction with a website

15.5.7.1 Consent obtained by these methods must still comply with all regulatory requirements about the process, the consent elements, and documentation of consent unless the requirements are waived by the HSREC.

15.5.7.2 The participant receives a copy of the consent form in advance. For example, it could be mailed, emailed, downloaded or posted on a website.

15.5.7.3 The researcher obtains consent over the phone or Skype. For website or social media interactions, the website may provide the researcher's contact information so that the potential participant can contact the researcher to set up a discussion by some method (phone or other, but it must provide the opportunity for a real-time or near real-time discussion.)

15.5.7.4 If the participant agrees to participate, s/he signs the consent form and returns it to the researcher for the researcher's signature, before any research procedures begin. This process may also be done electronically.

15.5.7.5 If the above procedures are not attainable, telephonic consent must be witnessed or recorded. This is disclosed to the participant.

15.5.8 Re-consenting

15.5.8.1 There are circumstances in which it may be appropriate to repeat or supplement the initial consent procedure for some or all of the participants.

15.5.8.2 Re-consenting may be appropriate, even if not required by consent regulations, when:

15.5.8.2.1 Significant new findings or information have been obtained during the course of the research that may relate to the participants' willingness to continue participation. Researchers are required by regulations to provide such information to participants, and it may be appropriate to repeat or supplement the consent process at the same time.

15.5.8.2.2 There are concerns about the circumstances under which consent is being obtained.

15.5.8.2.3 A significant period of time has elapsed between the time consent was obtained and the time when the participant begins the study.

15.5.8.2.4 The participants have been participating in a long-term longitudinal study. Periodic reiteration or affirmation of consent may be desirable, even if there have been no significant changes to the procedures, risks, or consent document.

15.5.8.2.5 Changes in the cognitive functioning, mental health, or physical health of the participants are likely to have occurred during the course of the research.

15.5.8.2.6 Research involving children must respect their evolving capacity to give consent. Minors who turn 18 years old during the course of a study should be approached at the time of their birthday to re-consent.

16 RESEARCH INVOLVING VULNERABLE RESEARCH PARTICIPANTS

16.1 Purpose

This section is intended to provide guidance to the HSREC regarding protecting the welfare of particularly vulnerable subjects, such as children, prisoners, pregnant women, capacity-impaired persons, or economically or educationally disadvantaged persons. The HSREC must also ensure that it has adequate representation to consider specific kinds of research involving these vulnerable populations in a satisfactory manner.

16.2 Policy

16.2.1 The HSREC must include review of the following elements for research involving vulnerable subjects:

16.2.1.1 Strategic issues include inclusion and exclusion criteria for selecting and recruiting participants, informed consent and willingness to volunteer; coercion and undue influence; and confidentiality of data.

16.2.1.2 The HSREC must carefully consider group characteristics, such as economic, social, physical, and environmental conditions, to ensure that the research incorporates additional safeguards for vulnerable subjects. The investigators must not over-select or exclude certain groups based on perceived limitations or complexities associated with those groups. For example, it is not appropriate to target prisoners as research subjects merely because they are a readily available captive population.

16.2.1.3 The HSREC must be knowledgeable about applicable laws that bear on the decision- making abilities of potentially vulnerable populations, such as issues relating to competency to consent for research, minors, legally authorized representatives, the age of majority for research consent, and the waiver of parental permission for research.

16.2.1.4 Just as in providing medical care, research studies that plan to involve any potentially vulnerable populations must have adequate procedures in place for assessing and ensuring each subject's capacity, understanding, and informed consent and assent. When weighing the decision of whether to approve or disapprove research involving vulnerable subjects, the HSREC must look to see that such procedures are part of the research plan. In certain instances, it may be possible for researchers to enhance understanding for potentially vulnerable subjects. Examples include requiring someone not involved in the research to obtain the consent, the inclusion of a consent monitor, a subject advocate, interpreter for hearing-impaired subjects, translation of participant related documents into languages the subjects understand, and reading the consent form to subjects slowly and ensuring their understanding paragraph by paragraph.

16.2.1.5 The HSREC may require additional safeguards to protect potentially vulnerable populations. For instance, the HSREC may require that the investigator submit each signed informed consent form to the HSREC, that someone from the HSREC oversee the consent process, or that a waiting period be established between initial contact and enrolment to allow time for family discussion and questions.

16.2.2 Definition of a child

16.2.2.1 A "child" is defined as someone younger than 18 years in the Bill of Rights of the Constitution of South Africa.

16.2.2.2 Research involving children must conform to ethical guidelines and the law. Research with children should comply with the Department of Health (2015). Ethics in Health Research: principles, processes and structures (2nd Edition). Department of Health: Pretoria, South Africa 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 the health needs of children.

16.2.3 Research involving children

16.2.3.1 Children are a "vulnerable population," because they are considered easily susceptible to coercion and undue influence and incapable of completely understanding the risks and benefits in making the decision to participate in

research. The respect for persons elaborated in the Belmont Report requires that the decision to participate in research be wholly informed and voluntary. The HSREC recognizes the importance of conducting scientifically sound research and ethically designed studies in this population. Excluding them from participating in the research is not an answer. Instead, special precautions should be incorporated into the design of the study to protect the rights and welfare of child participants.

16.2.3.2 The extent of protection of the child's rights and welfare considered by the HSREC depends on the risk of harm and its likelihood; the degree of the benefit to the child from involvement in the study; and the age range of the children who are asked to participate. This policy discusses these special considerations and protections.

16.2.3.3 For "Non-therapeutic" health research with minors, as part of the statutory requirements, Form A (NHREC Operational Guidelines for Ministerial Consent) must be completed and must accompany an application for ethics review. Non-therapeutic research is classified as research that includes interventions that do not hold the prospect of direct health-related benefit to the participant but may produce results that contribute to generalisable knowledge.

16.3 Requirements for the Submission of New Child Research

16.3.1 If a proposed research project involves children, the research applicant must indicate in the relevant sections of the HSREC Application form:

16.3.1.1 The age range of potential child participants;

16.3.1.2 Whether the research is therapeutic or non-therapeutic, with a brief justification;

16.3.1.3 Which risk category the research falls into, with a brief justification (see below);

16.3.1.4 That this is essential research for children.

16.3.2 The HSREC must categorise each project as therapeutic or non-therapeutic, with a brief justification.

16.3.2.1 Therapeutic research: Interventions hold out the prospect of direct health-related benefit for the child participant.

16.3.2.2 Non-therapeutic research: Interventions do not hold out the prospect of direct health-related benefit for the child participant but results may be produced that significantly contribute to generalisable knowledge about the participant's condition.

16.3.3 Research involving children should be determined by the HSREC as falling into one of the following risk categories:

16.3.3.1 The research poses no more than minimal risk to the child (that is, the risk commensurate with daily life or routine medical or psychological examinations – referred to as 'negligible risk' in some guidelines);

16.3.3.2 The research poses more than minimal risk but holds out the prospect of direct benefit for the child participant;

16.3.3.3 The research poses a minor increase over minimal risk, with no prospect of direct benefit to the child participant, but will likely yield generalisable knowledge about the condition under study;

16.3.3.4 The research does not meet the conditions for the risk categories above but the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.

16.3.4 Adequate provision should be made for obtaining assent from children and consent from their parents or legal guardians.

16.3.5 Research involving children must respect their evolving capacity to give consent and therefore the study must provide an opportunity to re-consent if the minor turns 18 years old during the course of the study.

16.3.6 Where parents and legal guardians are not available, the HSREC 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. Parental substitutes should be used in descending order as listed:

16.3.6.1 The minor chooses whether to participate and thus expresses his/her will after the parent gives assistance with understanding (in order for the minor to make an informed choice);

16.3.6.2 If no parent, then guardian, either court-appointed or as indicated by the parent in

a Will (section 27 Children's Act);

16.3.6.3 If no guardian, then foster parent (per order of Children's Court);

16.3.6.4 If no foster parent, then caregiver (section 1 Children's Act: defined as "any person other than a parent or guardian, who factually cares for a child and includes:

16.3.6.4.1 a foster parent;

16.3.6.4.2 a person who cares for the child with the implied or express consent of a parent or guardian of the child;

16.3.6.4.3 a person who cares for the child whilst the child is in temporary safe care;

16.3.6.4.4 the person at the head of a child and youth care centre where a child has been placed;

16.3.6.4.5 the person at the head of a shelter;

16.3.6.4.6 a child and youth care worker who cares for a child who is without appropriate family care in the community; or

16.3.6.4.7 the child at the head of a child-headed household.

16.3.6.5 If a minor is a caregiver in a child-headed household and no supervisory adult (section 137 Children's Act) is available, then a trusted adult nominated by the minor, including but not limited to social worker, community worker or teacher.

16.3.7 The HSREC provides a template informed assent form which should be used as a guide when drawing up informed assent forms for children.

16.3.8 The HSREC must indicate for each project:

16.3.8.1 Whether the research is therapeutic or non-therapeutic, with a brief justification.

16.3.8.1.1 The HSREC may exercise the Minister's delegated power in terms of the National Health Act in approving research with children that includes non-therapeutic components. The HSREC will ensure that their deliberations on these components are properly minuted and recorded;

16.3.8.1.2 The degree of risk of harm evaluated against the likelihood of benefit to the child participant as outlined in one of the risk categories above.

16.3.8.2 The HSREC will assess the documentation of assent and parental consent as well as the assent and parental consent process. If applicable, approval from the DoE needs to be obtained through the research information system and approval verified.

16.3.9 Paediatric Blood Volume:

16.3.9.1 Research involving blood draws from children must conform to the following guideline for the maximum allowable blood draw volumes:

16.3.9.1.1 It is important to take the child's clinical condition into account when determining what volume can be used for research purposes.

16.3.9.1.2 Blood volume should not exceed 5% of the total blood volume during a one-off sampling of total blood volume (including routine blood specimens for clinical care).

16.3.9.1.3 Blood volume should not exceed 5% of the total blood volume within 3-months (including routine blood specimens for clinical care). (US OHRP: 3 ml/kg or up to 50 ml total within 8 weeks).

16.3.9.1.4 If the blood volume necessary exceeds the above guideline, the research team need to submit additional motivation, which will be considered by the HSREC and may need expert opinion prior to final approval. If the blood volume necessary exceeds the above guideline, the research team must provide appropriate and adequate motivation, which will be considered by the HSREC.

16.3.9.2 The HSREC will assess the proposed research and clinical blood volumes for children during the research process.

16.3.9.3 Where there is an adequately motivated request by the principal investigator for a larger blood volume to be taken from a child participant, HSREC members reference the below guideline table: HSREC maximum allowable total (clinical and research) blood draw volumes.

HSREC Maximum allowable total (clinical and research) paediatric blood draw volumes

This guideline is to be used by HSREC members when there is an adequately motivated request by the principal investigator for a larger blood volume to be taken from a child participant. This guideline also takes into consideration the haemoglobin and is therefore a better guideline in the scenario dealing with impoverished communities and malnutrition.

Table 2: HSREC Maximum allowable total blood draw volumes (CLINICAL RESEARCH)

Body Wt (Kg)	Body Wt (lbs)	Total blood volume (mL)	Maximum allowable volume (mL) in one blood draw (= 2.5% of total blood volume)	Total volume (clinical + research) maximum volume (mL) drawn in a 30-day period	Minimum Hgb required at time of blood draw	Minimum Hgb required at time of blood draw if child has respiratory/CV compromise
1	2.2	100	2.5	5	7.0	9.0 -10.0
2	4.4	200	5	10	7.0	9.0-10.0
3	6.3	240	6	12	7.0	9.0-10.0
4	8.8	320	8	16	7.0	9.0-10.0
5	11	400	10	20	7.0	9.0-10.0
6	13.2	480	12	24	7.0	9.0-10.0
7	15.4	560	14	28	7.0	9.0-10.0
8	17.6	640	16	32	7.0	9.0-10.0
9	19.8	720	18	36	7.0	9.0-10.0
10	22	800	20	40	7.0	9.0-10.0
11-15	24-33	880-1200	22-30	44-60	7.0	9.0-10.0
16-20	35-44	1280-1600	32-40	64-80	7.0	9.0-10.0
21-25	46-55	1680-2000	42-50	64-100	7.0	9.0-10.0
26-30	57-66	2080-2400	52-60	104-120	7.0	9.0-10.0
31-35	68-77	2480-2800	62-70	124-140	7.0	9.0-10.0
36-40	79-88	2880-3200	72-80	144-160	7.0	9.0-10.0
41-45	90-99	3280-3600	82-90	164-180	7.0	9.0-10.0
46-50	101-110	3680-4000	92-100	184-200	7.0	9.0-10.0
51-55	112-121	4080-4400	102-110	204-220	7.0	9.0-10.0

56-60	123-132	4480-4800	112-120	224-240	7.0	9.0-10.0
61-65	134-143	4880-5200	122-130	244-260	7.0	9.0-10.0
68-70	145-154	5280-5600	132-140	264-280	7.0	9.0-10.0
71-75	156-185	5680-6000	142-150	284-300	7.0	9.0-10.0
76-80	167-176	6080-6400	152-160	304-360	7.0	9.0-10.0
81-85	178-187	6480-6800	162-170	324-340	7.0	9.0-10.0
86-90	189-198	6880-7200	172-180	344-360	7.0	9.0-10.0
91-95	200-209	7280-7600	182-190	364-380	7.0	9.0-10.0
96-100	211-220	7680-8000	192-200	384-400	7.0	9.0-10.0

Based on blood volume of:		
kg	**mL/kg**	
1-2	100	Pre-term infant
> 2	80	Term infant - adult

This information is similar to that used by the Committee on Clinical Investigations, Children's Hospital in Los Angeles, CA; Baylor College of Medicine, Dallas, TX; and Cincinnati Children's Hospital Institutional Review Board, OH. These charts were adapted by: Rhona Jack, Ph.D. Children's Hospital and Regional Medical Center Laboratory, Seattle, WA in August 2001.

16.4 Community Research

16.4.1 The HSREC must ensure that, particularly with regard to research involving communities, those communities' traditions and values are respected. This applies particularly with regards to obtaining consent to participate in 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.

16.5 Prison-Based Studies

16.5.1 When reviewing studies involving prisoners, the HSREC must ensure that:

16.5.1.1 at least one member of the HSREC 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 a voting member of the HSREC, unless the study has also been reviewed by another accredited REC on which a prisoner representative was present,

16.5.1.2 at least one member present shall be a non-scientist,

16.5.1.3 the majority of the HSREC members, other than the member described above,

shall have no association with the prison(s) involved, apart from their membership of the HSREC,

16.5.2 Studies on prisoners should only be conducted on prisoners if the researcher satisfies the HSREC that the research cannot be carried out equally well on non-prisoners and the research question cannot be answered with non-prisoners. The purpose of the research must be to obtain knowledge relevant to prisoners' health and well-being needs.

16.6 Research with Adult Participants with Diminished Functional Abilities Related to Capacity to Consent

16.6.1 ICH GCP and SA GCP 2020 guidelines define those individuals who are incapable of giving consent as vulnerable, and outline procedures for the consent process, including when consent is provided by a legally acceptable representative of the participant.

16.6.2 When reviewing studies involving such adults:

16.6.2.1 The HSREC must ensure that the research should only be approved when it cannot reasonably be conducted without their participation. Their participation in research should never be justified based simply on their availability or the convenience of the researcher.

16.6.2.2 The HSREC must determine that the risks to the participants are reasonable in relation to the importance of the knowledge that may reasonably be expected to result.

16.6.2.3 The HSREC application should include details as to whether the participant recruitment plan includes individuals who have a condition of a type or severity likely to lead to impairment to functional abilities to the extent that it might affect capacity to consent. These include, but are not limited to:

16.6.2.3.1 Acute medical conditions,
16.6.2.3.2 Psychiatric disorders,
16.6.2.3.3 Neurological disorders,
16.6.2.3.4 Developmental disorders, and
16.6.2.3.5 Behavioural disorders.

16.6.2.4 Researchers and HSREC members should be aware that some conditions might cause functional abilities to fluctuate over time, or to decrease gradually over the course of the study. When the participant recruitment plan includes individuals likely to experience fluctuating functional abilities or functional abilities that will decrease over time, the HSREC members might consider whether provisions should be included for the event that participants' capacity to consent changes over the course of the study, including whether:

16.6.2.4.1 Procedures have been described for re-evaluating participants' capacity to consent over the course of the study;
16.6.2.4.2 Such participants are asked to designate an individual to serve as a legally acceptable representative, if necessary;
16.6.2.4.3 Individuals identified as potential legally acceptable representatives are involved in the consent process;
16.6.2.4.4 Such participants are asked to document their wishes regarding participation in the study.

17 COLLECTION AND STORAGE OF DATA OR BIOLOGICAL SPECIMENS FOR RESEARCH PURPOSES

17.1 Purpose

The purpose of this section is to outline specific ethical issues and regulations, including informed consent requirements, in research which involves the collection and storage of data and biological specimens.

17.2 Policy

17.2.1 Research involving the collection of data and/or biological specimens may need added protections, for instance:

17.2.1.1 Genetic studies where findings may carry psychological, social or economic risks for an individual, a family or a community will require a detailed plan of how confidentiality would be protected.

17.2.1.2 In studies using anonymous specimens and perceived risks are lower, the protocol would need to state what measures will be taken to de-identify samples to render them anonymous.

17.2.2 Use of existing or archived specimens collected for clinical or diagnostic purposes, including waste and left-over samples, requires HSREC review. The Chair or designee must determine whether consent was obtained at the time of collection and the nature of that consent. If subsequent use falls within the scope of the original informed consent, then additional informed consent is not required. Researchers wishing to use information or specimens for research that differs in any way from that described in the original informed consent form must submit a new or amended consent document for approval before initiating the new activity.

17.2.3 If blood or tissue specimens are to be stored for future analysis and such analysis is planned to take place outside the University of the Free State (UFS), the specimens must be stored in a repository located within the Free State (or as otherwise specified and approved by HSREC) and released only with HSREC approval and approval from a local Research Ethics Committee at the proposed site of the analysis (unless otherwise specified and approved by HSREC).

17.2.3.1 Only HSREC approved analyses may be done.

17.2.3.2 The HSREC must be provided with details of provisions made to protect the privacy of the donors and the maintenance of the confidentiality of the data.

17.2.3.3 Specimens may not be shared with any party unless approved by the HSREC in advance.

17.2.3.4 Where tissue samples are to be exported, a valid current export permit is required.

17.2.3.5 A separate consent form or section of the informed consent form, for storage of additional or residual samples is required.

17.2.3.6 A separate consent form for genetic testing is required.

17.2.3.7 A signed Material Transfer Agreement (MTA) must be in place before samples are transferred to other sites. A copy must be submitted to the HSREC for record purposes.

17.2.4 As a general principle, written informed consent is not needed if:

17.2.4.1 Samples will be used anonymously and the results will not place an individual, family or community at social, psychological or economic risk.

17.2.4.2 If the link to identifiers exists but is not provided to the research team and the results will not place an individual, family or community at social, psychological or economic risk. The investigator holding the code or link must sign a written agreement that he or she will not release the identifiers to the research team. This written confirmation must be included in the submission to the HSREC.

17.2.5 Removal or Withdrawal of Biological Samples from living persons

17.2.5.1 A competent person may not remove any biological material from the body of another living person for purposes of genetic testing, genetic training, genetic health research or therapeutics, unless it is done with written informed consent of the person or legal proxy of the person from whom such biological material is removed.

17.2.6 Removal of Biological Samples from Deceased Persons

17.2.6.1 Any organisation or institution or person that intends to use tissue from a deceased person for purposes of genetic testing, health research and therapeutics, where no

consent had been given by the deceased person before her or his death and where there is no evidence that the removal of the tissue or cells would be contrary to a directive given by the deceased before his or her death, must take steps to locate the spouse, partner, major child, parent, guardian, major brother or major sister of a deceased person, in the specific order mentioned, in order to obtain consent.

17.2.7 Research Utilising Embryonic Stem Cells and Umbilical Cord Blood Stem Cells

17.2.7.1 Excess embryos obtained from in vitro fertilisation may be used to produce embryonic stem cell lines for the purpose of research, provided that the competent person obtains written informed consent from the embryo donor or cord blood donor.

17.3 Definitions

17.3.1 Biological material is 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.

17.3.2 A donor is 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.

17.3.3 Proband is a person serving as the starting point for the genetic study of a family.

17.3.4 Anonymous samples/data are data or biological specimens obtained by a researcher without any identifying information and without a link to a specific participant or donor.

17.3.5 Identifiable samples/data are data or biological specimens obtained by the researcher with identifying details such as name, folder number or address.

17.3.6 Identifiers are information that could be associated with a specific research participant such as name, address, medical folder number, phone or fax number or biometric identifier (e.g. finger print).

17.3.7 Coded data/samples are identifiers that have been replaced with a number, symbol or a letter and a key exists to decipher the code, allowing linkage of the code to a specific individual.

17.3.8 Broad consent refers to a process by which individuals donate their samples for a broad range of future studies, subject to specific restrictions such as approval by a human research ethics committee.

17.3.9 Blanket consent refers to a process by which individuals donate their samples without any restrictions. This standard operating procedure does not support blanket consent for future storage of samples.

17.3.10 A retrospective study is a study which uses specimens that already exist when HSREC approval is requested. This includes tissue collected for diagnostic purposes and then stored; for example, pathology samples or the secondary use of specimens previously collected for another research proposal and subsequently stored in a tissue bank.

17.4 Procedures

17.4.1 An authorised institution that keeps or discloses genetic material records or other individually identifiable or related health information in any form must ensure the:

17.4.1.1 Information is used for the purpose for which it was originally intended.

17.4.1.2 Written informed consent of the user or donor is obtained for long term storage of genetic material, stem cells or research findings.

17.4.1.3 The records are destroyed after the purpose for which they were created, had been served.

17.4.1.4 The information is treated as anonymous if used for research purposes.

17.4.2 Considerations for research involving genetic and/ or genomic material:

17.4.2.1 Depending on the scope or nature of the research, complex ethical issues may arise when conducting studies involving genetic material and/or genetic testing:

17.4.2.1.1 Participating in research using genetic material may involve psychosocial risks to individual participants, their families and communities. For example, social risks may include a breach of confidentiality which could affect family relationships, lead to stigmatisation or loss of insurability; and psychological risks may include the impact of learning a genetic diagnosis, and the impact if no effective therapy exists.

17.4.2.1.2 On the other hand, where genetic research is conducted using anonymous samples, there may be minimal risk of psychosocial harm

to individuals or groups from whom samples are acquired, for instance, anonymous samples of tumour cells analysed for specific genetic information.

17.4.2.2 For studies which carry distinct psychosocial risks, investigators need to consider the following ethical issues in their protocols:

17.4.2.2.1 Are clear guidelines in place for disclosure of information to participants, including interim or inconclusive research results?

17.4.2.2.2 Will participants be protected against disclosure of medical or other personal information about themselves to other family members?

17.4.2.2.3 Will participants be given the option not to receive information about themselves?

17.4.2.2.4 Will limits on such protections be clearly communicated to participants, including obtaining advance consent should such disclosures need to be made, for example, when family members will be warned about risks to their health?

17.4.2.2.5 Will participants receive counselling as part of the process of communicating test or other findings to participants?

17.4.2.2.6 Will participants be told about possible incidental findings such as paternity, a disease or condition other than the one under study?

17.4.2.2.7 Will the data be protected from disclosure to third parties such as employers and insurance companies?

17.4.2.2.8 Will participants be informed of potential risks of a third party becoming aware of the study findings?

17.4.2.2.9 Will data be stored in a secure manner? Describe measures.

17.4.2.2.10 Will data be coded to protect each participants' identity? Describe measures.

17.4.2.2.11 Are there adequate provisions for protecting against misuse of tissue samples, for example, obtaining consent for any use other than specified in the study?

17.4.2.2.12 Have participants consented to future use of stored specimens in new studies?

17.4.2.2.13 Are there adequate provisions to manage data or specimens if a participant withdraws from the study?

17.4.2.2.14 Does the researcher plan to disclose research findings to a participant's personal physician for clinical purposes? Is this appropriate? Will participants have an option to refuse?

17.4.2.2.15 In the event of publication, will participants' privacy be protected? Have participants been informed about how findings might be published?

17.4.2.2.16 If research involves family members, has the appropriateness of different strategies for recruitment been evaluated? If a researcher wishes to contact relatives of an index case, the index case or proband must be asked whether this contact is acceptable. If the index case declines to allow contact of relatives, the study may not proceed. If consent is given, the following recruitment strategies are recommended:

17.4.2.2.16.1 The researcher may provide the proband with a packet of information about the study and ask that he or she distributes the information to eligible relatives. The packet should include instructions about how to contact the researchers if the relative has further questions. Researchers can include postcards for relatives to return indicating their interest in being contacted about the study.

17.4.2.2.16.2 The researcher may ask the proband to provide limited contact information (name, address, phone number) for relatives who are eligible for the study. Researchers may send information to the named relatives about whom to contact for further information if they are interested in taking part.

17.4.2.2.16.3 The researcher could ask the proband which option he or she feels is the more appropriate.

17.4.2.2.17 If a researcher wants to collect information about relatives from the proband, the researcher must collect the least identifiable information necessary to meet the scientific goals of the study. If the researcher plans to collect personal information about family members, strong confidentiality protections need to be in place. Alternatively, the researcher should obtain HSREC approval to recruit family members into the study and collect information from them directly with informed consent.

17.4.2.2.17.1 The informed consent form should explain the following:

17.4.2.2.17.1.1 The kind of information researchers will feedback to participants (e.g., only information the researcher feels is reliable, or no genetic information will be disclosed), a justification for either decision, and at what point in the study they will receive that information.

17.4.2.2.17.1.2 The risks associated with taking part in genetic/genomic research.

17.4.2.2.17.1.3 Participants may learn things about themselves or their family that they did not really want to know, or that they may be uncomfortable knowing.

17.4.2.2.17.1.4 If participants want information, precautions must be in place to minimise the potential harm of receiving bad news and to preserve the confidentiality of the results. Ideally, genetic findings should be communicated in a clinical rather than a research relationship with the participant.

17.4.2.2.17.1.5 Information about participants may be learned by others in their family.

17.4.2.2.17.1.6 The extent to which findings will and are able to be kept confidential.

17.4.2.3 Guidelines for the information document for storage and future use of biological samples

17.4.2.3.1 The information sheet and consent form for future storage of genetic and/ or genomic information should not be longer than two pages and must be separate from the informed consent form (ICF) for the main study.

17.4.2.3.2 Explain that the researcher is seeking permission to store participants' unused samples for possible future use in either his or her own research or for someone else's research.

17.4.2.3.3 Explain that participants need to decide about the future use of their blood, tissue, sperm or sputum sample because they have given consent only for the study, they are presently taking part in.

17.4.2.3.4 Explain that sometimes people do not want their samples used for research into areas they do not agree with, for example research into birth control. Use lay terms to explain different research possibilities.

17.4.2.3.5 State that participants can choose if they don't want their sample used at all.

17.4.2.3.6 If genetic and/ or genomic research is a possibility, explain what this is and any implications for participants or their families.

17.4.2.3.7 Inform the participant that at present, the researchers can trace which blood, tissue, sperm or sputum sample belongs to the participant. Participants must choose whether they want to let researchers keep the sample but remove the identifiers, or whether they would not mind

if the researchers know whose sample it is. Explain the risks and benefits of each option.

17.4.2.3.8 Inform the participant of a researcher's obligations in cases where the sample remains linked; for example, an obligation to inform a participant of results which have immediate clinical relevance such multi-drug resistant tuberculosis.

17.4.2.3.9 Explain that any research which uses participants' samples must be approved by the HSREC.

17.4.2.3.10 Explain that the participant may refuse to allow samples to be stored with no loss of benefits and that participation in the current study will not be affected in any way.

17.4.2.3.11 Inform participants that they may withdraw permission at any time and provide the necessary contact details of the researcher or institution.

17.4.2.3.12 Explain how confidentiality will be maintained including any limitations.

17.4.2.3.13 Inform participants of no direct benefit, if applicable; inform of other potential benefits as appropriate: advancement of knowledge, clinical relevance to individual, family or society as a whole and long-term benefit if researcher plans to re-contact participants to disclose clinically relevant information.

17.4.3 HSREC requirements for a research protocol that includes genetic analysis:

17.4.3.1 Steps to protect 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.

17.4.3.2 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.

17.4.3.3 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.

17.4.3.4 A researcher must not transfer genetic material and related information to another research group unless:

17.4.3.4.1 There is a formal collaboration that has been approved by the HSREC and a Material Transfer Agreement has been signed by the appropriate authorities;

17.4.3.4.2 The genetic material and information are transferred in a form that ensures participants cannot be identified. (*Prima facie* principle).

17.4.4 Request for waiver of individual consent for genetic analysis:

17.4.4.1 The HSREC adheres to the *prima facie* principle in 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.

17.4.4.2 Before granting a waiver of consent the HSREC must determine:

17.4.4.2.1 The nature of any existing consent i.e., reviews of the original consent documents.

17.4.4.2.2 The justification presented for the waiver including how difficult it would be to obtain consent.

17.4.4.2.3 Arrangements with respect to protecting privacy and confidentiality, including de-identifying the information.

17.4.4.2.4 Extent to which the proposed research poses a risk to the privacy and well-being of the participant.

17.4.4.2.5 Whether the research proposal is an extension or closely related to the original research.

17.4.4.2.6 The possibility of commercial exploitation of derivatives of the sample and relevant statutory provisions.

18 PHOTOGRAPHS IN RESEARCH

18.1 Purpose

This section describes the policies and procedures for using photographs as a research tool/aid in research with human subjects.

18.2 Policy

18.2.1 Photographs as a research tool/aid should be used if the researcher believes that the photographs will contribute something positive, significant, meaningful, and/or substantive to the research question; or that they may, through highlighting visually, promote the rights of a particular group.

18.2.2 Researchers should develop a standardised protocol for taking photos during fieldwork and how to ethically manage photos.

18.3 Procedure

18.3.1 There must be specific and fully informed consent (IC) to photography before the photography takes place. It would be preferable to get informed consent before but in cases where this may alter the "real" nature of the photo, it is permissible to request nominal consent after the photo is taken and before the photo is used.

18.3.1.1 The informed consent document should contain a separate section, which explains:

18.3.1.1.1 the need for and contribution the photograph(s) will make to the study aim;

18.3.1.1.2 a description of how the photograph(s) may be used e.g. report writing, presentations, conferences, meetings, journal; and a description of how the photograph(s) will be kept stored to protect confidentiality.

18.3.1.2 The researcher must offer the participant a copy of the photograph. Include a statement in the informed consent form, “I have been asked whether I want the photograph sent to me and where to send it.”

18.3.1.3 In the case of child research, the researcher must obtain informed assent from the child and informed consent from the child’s parent, legal guardian, or someone with a genuine emotional attachment to the child.

18.3.1.4 Before seeking consent researchers have a responsibility to provide information about the research, including its wider implications and the consequences of participant involvement, in a format that is accessible and understandable to potential participants.

18.3.1.5 Informed consent should be for each use of the image.

18.3.1.6 The consent may be withdrawn at any time, however if the photograph had already been published, it is too late.

18.3.2 The photographer must at all times respect the rights and dignity of the research participant in the handling of photos.

18.3.3 The researcher must endeavour to protect participant privacy and confidentiality. All images must be stored in a safe and regulated environment with controlled access. The applicant should describe measures in detail in the protocol.

18.3.4 Complete anonymity is not always possible and the minimum area of the body, or minimal identifiable features necessary should be photographed. Only in those cases where the face is essential to the image should this area be photographed.

18.3.5 Avoid signs, or other readily identifiable objects, in the immediate environment, in pictures that will deny individuals anonymity and inadvertently allow others to locate them in the community.

18.3.6 Allow confirmation from the participant of accurate/appropriate re-presentation before the photograph is published.

19 DATABASES, REGISTRIES AND REPOSITORIES

19.1 Purpose

The purpose of this section is to outline ethical requirements for establishing databases, registries and repositories for research purposes.

19.2 Definitions

19.2.1 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. Examples of databases include:

- 19.2.1.1 A set of observations (i.e., data) from a research study;
- 19.2.1.2 An electronic file of a clinic's patients;
- 19.2.1.3 A collection of diagnosis, treatment and follow-up information on a sub-set of hospital patients, for example patients with diabetes or admissions to an intensive care unit;
- 19.2.1.4 A file of outcomes information compiled for quality assurance activities;
- 19.2.1.5 Names, diagnosis and contact information of potential research participants in specific research fields; for example, HIV prevention research.

19.2.2 Registries are collections of information or databases whose organisers:

- 19.2.2.1 Receive information from multiple sources;
- 19.2.2.2 Maintain the information over time;
- 19.2.2.3 Control access to and use of the information by multiple users or for multiple purposes which may change over time.
- 19.2.2.4 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.

19.2.3 Repositories collect, store and distribute human materials for research purposes. Human biological material may include any material collected from a human. Examples include, but are not limited to, blood, urine, faeces, bone marrow, embryos 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. The Human Heredity and Health in Africa (H3Africa) Initiative of the National Institutes of Health is an example of an international repository initiative.

19.3 Policy

19.3.1 Databases, registries and repositories (tissue banks) all involve the collection of information and/or biological specimens over time.

19.3.2 Databases, registries and repositories may be created for research, diagnostic or clinical/operational purposes or any combination of the above-mentioned.

19.3.3 With advances in molecular techniques and information technology, data and tissue banks constitute a valuable resource for researchers to address questions extending far beyond those envisaged when the data and/or specimens were first collected.

19.3.4 Data management: To ensure that participants' privacy and confidentiality are protected, databases, registries and repositories must develop procedural mechanisms for secure collection, receipt, storage and sharing of information and specimens.

19.3.5 Material transfer Agreements: When information and/or specimens are provided to researchers outside the UFS Faculty of Health Sciences and its affiliates, use of the data and/or specimens must comply with any additional requirements of the recipient institution and its Institutional Review Board. Likewise, the recipient institution must agree to comply with all terms stipulated by the donor institution. These inter-institutional agreements should be confirmed in writing. If the institution with which information and/or specimens are being shared is in another country, the regulations of the countries concerned, as well as regulations about the international transport of human material, must also be adhered to.

19.3.6 Researchers with existing databases, registries and repositories needs to register these with the HSREC and develop procedural mechanisms for secure collection, receipt, storage and sharing of information and specimens to enable future research

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19.3.7 All research, including that undertaken for further qualifications, using registered databases, registries and repositories, requires submission as a new study. The study will receive its own HSREC number that will be linked to the main database, registry or repository.

19.4 Procedures

19.4.1 HSREC Oversight of Databases, Registries or Repositories

19.4.1.1 The role of the HSREC varies with the intent and use of a database, registry or repository:

19.4.1.1.1 Committee approval and oversight are not required for database, registry or repositories created and used for operational purposes. Such purposes may include diagnosis, treatment, billing, quality assurance and quality improvement, and public health surveillance. These data cannot be used for research unless the database, registry or repository is registered with the HSREC, in addition separate ethics approval is required prospectively on a study-by-study basis.

19.4.1.2 Information to be supplied by an applicant:

19.4.1.2.1 Stipulate type of application: database, registry or tissue repository;

19.4.1.2.2 Name of Database, Registry or Repository.
(Please provide a descriptive name that indicates the nature of the contents);

19.4.1.2.3 The names and professional registration of co-investigators;

19.4.1.2.4 Site of Database, Registry or Repository;

19.4.1.2.5 Type of data/specimens (including description of identifying details, whether routine clinical data or data collected specifically for a specific research project, whether data is collected retrospectively or whether it is known at time of data collection that data will be included in a research database);

19.4.1.2.6 A data sheet including all data point to be collected

19.4.1.2.7 Data management:

19.4.1.2.7.1 The name and proof of current professional registration of the person that will maintain the database, registry or repository. This person must seek further approval from the HSREC for any research originating from this database, registry or repository.

19.4.1.2.7.2 The physical process (flow chart) by which items will be accepted into the database, registry or repository and released from it;

19.4.1.2.7.3 The procedural mechanisms (receipt, storage, information handling) to protect privacy and confidentiality;

19.4.1.2.7.4 A description of the conditions under which data/ specimens may be shared with or released to researchers;

19.4.1.2.7.5 The period that data/specimens will be maintained in the database, registry or repository;

19.4.1.2.7.6 A description of how the data/specimens will be destroyed;

19.4.1.2.7.7 If participants will be able to withdraw their data/specimens;

19.4.1.2.8 Material or Data Transfer agreement:

19.4.1.2.8.1 The name of the person that will be responsible for ensuring that any requests for sharing information meet the database, registry or repository's specifications;

19.4.1.2.8.2 An example of an application form to be completed by researchers who request access to biological material or data;

19.4.1.2.8.3 A draft Material or data transfer agreement is required where biological material or data will be transferred to or received from another location.

19.4.2 **Informed Consent**

19.4.2.1 Since a database, registry or 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 at a reading level appropriate to the study population:

19.4.2.1.1 Name and purpose of specific database, registry or repository for which consent is requested.

19.4.2.1.2 What a database, registry or repository entails.

19.4.2.1.3 Types of research the database, registry or repository supports. The HSREC does not support blanket approval by the patients for any future research. The informed consent form must stipulate the broad theme of the database, registry or repository's research.

19.4.2.1.4 Conditions and requirements under which data/specimens will be shared with researchers.

19.4.2.1.5 How participants' privacy and confidentiality will be protected.

19.4.2.1.6 Specific risks related to use and storage of data/specimens, particularly if personal identifiers are retained.

19.4.2.1.7 When human genetic research is anticipated, refer to SOP 17 for all requirements for such an informed consent.

19.4.2.1.8 Potential benefits, if any:

19.4.2.1.8.1 Inform participants if there is no direct benefit.

19.4.2.1.8.2 Include other potential benefits such as societal benefit through the advancement of knowledge.

19.4.2.1.9 Where applicable, the fact that specimens may be:

19.4.2.1.9.1 Used for future research not yet identified. The procedure that will be followed to obtain consent, if a patient's sample is to be used for research not related to the main theme of the database, registry or repository, needs to be described.

19.4.2.1.9.2 Shared with or transferred to other institutions. The assurance must be given that HSREC approval will be obtained before any such sharing or transfer.

19.4.2.1.10 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 in line with the Informed Consent SOP in this document.

19.4.2.1.11 Information about the duration of storage.

19.4.2.1.12 Whether consent to use information or specimens will expire.

19.4.2.1.13 Information about possible secondary use of stored tissue or the possible creation of an immortalised cell line based on the specimen. Refer to SOP 17 for use of genetic material.

19.4.2.2 Waiver of Informed consent: Obtaining informed consent to use data or specimens stored in a database, registry or repository created for operational purposes may be problematic since research was not intended at the time of collection. Where feasible, the HSREC may require a researcher to obtain informed consent. However, the HSREC may approve a waiver of consent if the following conditions are met:

19.4.2.2.1.1 The research involves no more than minimal risk (6.1.4.1 e.g., anonymous use of samples); and

19.4.2.2.1.2 The waiver will not adversely affect participants' rights and welfare; and

19.4.2.2.1.3 If a clear motivation is provided why the research could not practically be carried out without the waiver.

20 PARTICIPANT INSURANCE

20.1 Purpose

To ensure that research participants are adequately insured in the event of a research injury.

20.2 Policy

The South African Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa (2nd edition – 2006, also known as the SA GCP 2006) stipulate that the sponsor of a trial must ensure that the participants of a clinical trial are covered by comprehensive insurance in the event of physical (bodily) harm or injury, including death. Guideline 4.11 of the SA GCP 2006 states that the sponsor of a study should pay the costs for the medical treatment of any bodily injury without the participant having to prove that the sponsor was at fault.

20.3 Procedure

20.3.1 In accordance with SA GCP 2006 guidelines, the sponsor's insurance company will compensate a participant for medical expenses which may have resulted directly from their participation in a particular clinical trial (either from using the medicine in question or participating in the required procedures).

20.3.2 These costs must be reasonable and do not include costs for, for example, a loss of income, compensation for pain or emotional suffering. This was confirmed in the decision by the Western Cape High Court in the matter of Venter v Roche.

20.3.3 The sponsor will, however, not have to pay these costs if the injury or harm was caused by:

- 20.3.3.1 the use of unauthorised medicine or substances during the study;
- 20.3.3.2 an injury that results from the participant not following the protocol requirements or the instructions that the study doctor had provided;
- 20.3.3.3 an injury that arises from any action or lack of action to deal adequately with a side effect or reaction to the study medication on the part of the participant [This point must be very carefully checked in each case – it is unacceptable to impose a burden on participants who may not recognize symptoms or have the ready means to take action];
- 20.3.3.4 an injury that results from any other negligence on the part of the participant.

20.3.4 It is important to explain to the participant that:

- 20.3.4.1 By agreeing to participate in this study, he/she agrees that there is a risk that the study medicine or procedures may cause him/her harm. If it does, the sponsor will reimburse him/her for his/her medical expenses.
- 20.3.4.2 The participant may, however, still claim for emotional pain and suffering but if he/she so chooses. In this event, he/she will have to prove that the sponsor was negligent and did not take all reasonable and foreseeable steps to prevent the injury or emotional trauma. This will be a separate legal matter.

20.3.5 Guideline 4.11 of the SA GCP 2006 states that the participant will normally be asked to accept that any payment made under the Guidelines will be in full settlement of the claim.

20.3.6 Insurance taken out for this clinical trial does not replace a clinician's malpractice insurance.

21 RECRUITMENT AND PAYMENT OF HUMAN RESEARCH PARTICIPANTS

21.1 Purpose

The purpose of this section is to describe the policy and procedure to be followed in research approved by the HSREC for the recruitment of human research participants and to provide guidance for recruitment, especially when advertising.

21.2 Policy

21.2.1 The HSREC is required to review all documents and activities related to recruitment that bears on the rights and welfare of the participants of proposed research; this includes the recruitment process.

21.2.2 Any payment or other incentive offered to prospective research participants to take part in the research study must also be reviewed and approved by the HSREC.

21.2.3 The Investigator must obtain HSREC approval for all television, radio, video recorded or print advertisements, e-mail solicitations, internet websites, and other recruitment methods and materials intended for the recruitment of prospective research participants. All methods of advertisement require approval from the HSREC prior to their use.

21.2.4 The HSREC considers advertising or soliciting for study participants to be the start of the informed consent process and subject selection process. Advertisements must be reviewed and approved by the HSREC as part of the package for initial review. When the Investigator decides after the initial approval to advertise for participants or to change the advertisement, the advertising is considered an amendment to the ongoing study.

21.2.5 Blanket approvals are evaluated on a case-by-case basis.

21.3 Definitions

21.3.1 Direct advertising or recruitment materials refers to any form of solicitation for prospective research subjects including, but not limited to using social network ads, banner ads, paid search ads, fliers, posters, brochures, screening tools (i.e. scripts or questionnaires), recruitment letters, postcards, clinical trial web sites, or communications intended to be seen or heard by health care professionals such as “dear doctor” letters and doctor-to-doctor letters (unless not soliciting for study subjects), or oral communications by an investigator or his staff.

21.3.2 Clinical trial web sites mean any clinical trial web site that lists clinical trials being conducted. An internet advertisement is not automatically a clinical trial web site. The HSREC does not assume oversight of a “public” clinical trial web site.

21.3.3 Recruitment letter means any letter, postcard, or other personal communication sent to potential subjects that solicits research participation.

21.3.4 Social media is defined as an interactive platform for electronic communications, used by groups of people to create, share, and exchange information. Typically, these platforms are internet-based and allow users to interact with other users through a website or web application. Although the forums and types of social media are distinct, the HSREC’s review is based on the same fundamental principles and regulatory requirements. Examples of social media usage in the context of clinical trials include, but are not limited to:

21.3.4.1 Facebook and Twitter advertising campaigns to recruit participants;

21.3.4.2 A phone application (i.e., iPhone, iPad, or an Android platform-based phone) that users download on their phone and use as an electronic diary;

21.3.4.3 A Pinterest board where a clinical trial site can “pin” news articles, blog postings, and enrol clinical trials; or,

21.3.4.4 A Facebook “fan” page for the study.

21.4 Guidelines

21.4.1 When advertising is to be used, the HSREC must review the information contained in the advertisement and the mode of its communication, to determine that the procedure for recruiting participants is not coercive and does not state or imply a certainty of favourable outcome or other benefits beyond what is outlined in the consent document and the protocol. This is especially critical when a study may involve participants who are likely to be vulnerable to undue influence. The HSREC must review the final version of advertisements to evaluate the relative size of type used and other visual effects. When advertisements are to be recorded for broadcast, the HSREC must review and approve the final wording of the advertisement prior to broadcasting.

21.4.2 Any advertisement to recruit participants should be limited to the information the prospective participants need to determine their eligibility and interest.

21.4.3 Advertisements should include:

21.4.3.1 The purpose of the research;

21.4.3.2 A statement that the solicitation is for research participation;

21.4.3.3 In summary form, the criteria that will be used to determine eligibility for the study;

21.4.3.4 The time or other commitment required of the participants; and

21.4.3.5 The location of the research, facility or institution, and the person or office to contact for further information.

21.4.4 Advertising materials should not:

21.4.4.1 State or imply a certainty of a favourable outcome or other benefits beyond what was outlined in the consent document and the protocol;

21.4.4.2 Use catchy words like “free” or “exciting”;

21.4.4.3 Emphasize the payment or the amount to be paid, by such means as larger type.

21.4.5 Receptionist scripts

21.4.5.1 The first contact prospective study participants make is often with a receptionist who follows a script to determine basic eligibility for the specific study. The HSREC must review the procedures to assure that they adequately protect the rights and welfare of the prospective participants. The HSREC must have assurance that any information collected about prospective participants will be appropriately handled.

21.4.6 Internet recruitment, including social media recruitment.

21.4.6.1 For Internet recruitment sites, HSREC review and approval are required to ensure that the information does not promise or imply a certainty of cure or other benefit beyond what is outlined in the protocol and the informed consent document.

21.4.7 Data base/Primary care physician recruitment

21.4.7.1 Investigators may request to use search methods of particular databases looking for potential participants that may be eligible for their research projects (e.g., disease, age, sex, etc.), or they request to contact primary care providers for access to potential participants from the primary care providers’ patient population. These recruitment methods require HSREC approval prior to initiation.

21.4.8 Finder’s Fees and bonus payments.

21.4.8.1 Finder’s fees and bonus payments are compensation of any type (cash, office or medical supplies, educational stipends, gift certificates, priority in authorship listings, travel reimbursement, or anything else of value) to a professional (i.e., health professional, teacher, faculty member, study coordinator) made in exchange for referral or recruitment of a participant to a research study. The HSREC does not permit the payment of finder’s fees (monetary or in kind) in any form, due to the potential that such a practice could be perceived as coercive and bordering on unethical research subject recruitment.

21.4.9 Referral fees

21.4.9.1 Research participants may be offered a nominal fee to assist with participant recruitment efforts (i.e., respondent-driven sampling). Researchers must include information in the HSREC protocol, such as the value of the fee and the circumstances under which fees will be paid. The HSREC must ensure that there is no coercion on referred individuals to participate, and no coercion on current participants to provide referrals.

21.4.10 Payment of research participants

21.4.10.1 The HSREC must review the amount and method of payment to research participants in accordance with the provisions of the National Health Research Ethics Council (NHREC).

21.4.10.2 Neither the amount nor method of payment for research participants must present the potential for undue influence.

21.4.10.3 Compensation to participants must be prorated and not wholly contingent on completion of the study by the participant.

21.4.10.4 The amount and method of payment to research participants should reflect the following three components:

21.4.10.4.1 Compensation for time:

21.4.10.4.1.1 Time payments should be made at rates commensurate with unskilled labour rates. This acknowledges that trial participation (while valuable) does not necessarily

require special skills and training, but does entail expending effort.

21.4.10.4.1.2 The above recommendation recognises that payment is being made for what the 'work' of research participation is worth, and not what the participants' actual time is worth.

21.4.10.4.1.3 Even if participants are not formally employed, it could be considered that participation in research may compete with efforts to find other similar economic opportunities and that participants forgo other opportunities while they are engaged in research, therefore participants should be compensated for their time.

21.4.10.4.2 Compensation for inconvenience:

21.4.10.4.2.1 In some studies participants will be required to undergo certain procedures that may cause inconvenience or discomfort. Consideration should be given to compensating participants for this inconvenience, over and above time payments.

21.4.10.4.2.2 Payment amounts for inconvenient procedures should reasonably reflect the extent of such inconvenience. For example: the inconvenience attached to answering a simple and unobtrusive questionnaire may be lower than a blood draw.

21.4.10.4.3 Reimbursement of expenses:

21.4.10.4.3.1 The costs of participation should be established in consultation with community representatives who may be familiar with expenses for, for example, travel, parking, meals or child-care. The cost for participants of being away from their individual place of work should not be considered.

21.5 Procedure

21.5.1 A copy of the final version of the advertisement must be submitted with the Initial application, or as an amendment at least 7 working days prior to the scheduled meeting in order to be included in the agenda of that meeting.

21.5.2 If submitted as an amendment, a cover letter must accompany the advertisement with the following information:

21.5.2.1 Project title (if applicable);
21.5.2.2 HSREC reference number (if applicable);
21.5.2.3 Name of principal investigator (if applicable);
21.5.2.4 Motivation for the inclusion of the advertisement in the application/amendment.

21.5.3 The following information must be included in the advertisement where applicable:

21.5.3.1 Advertisement in its final form (logo etc.);
21.5.3.2 Description of condition in layman's terms;
21.5.3.3 The category of participants (age, etc.);
21.5.3.4 Which method will be used, e.g., questionnaires;
21.5.3.5 Remuneration for transport and inconvenience;
21.5.3.6 Any costs payable by participant;
21.5.3.7 Contact person's name and number for further enquiries (also note office hours, if applicable);
21.5.3.8 Mention that participation is voluntary and the participant may withdraw at any time;
21.5.3.9 Patients currently on treatment will participate in the research study in conjunction with the treating physician; and
21.5.3.10 Time duration of study.

22 RESEARCHER AND HSREC MEMBER CONFLICT OF INTEREST

22.1 Purpose

This section describes the process for identifying and managing any conflict of interest that HSREC members as well as investigators may have with respect to review and determinations about a research project.

22.2 Policy

22.2.1 HSREC members and HSREC Administration do not participate in the following activities related to a research project when they have a potential conflict of interest related to the project:

- 22.2.1.1 pre-review;
- 22.2.1.2 initial review;
- 22.2.1.3 expedited review;
- 22.2.1.4 voting in an HSREC meeting; or
- 22.2.1.5 making determinations (however, they may provide information to the HSREC upon request).

22.2.2 A conflict of interest 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.

22.2.3 Conflict of interest policy for investigators:

22.2.3.1 Investigators are expected to declare to the HSREC any potential or existing conflict of interest that may pose a threat to the scientific integrity and ethical conduct of the study. This declaration is an integral part of the application process. Investigators should disclose financial and other conflicts of interest that could compromise the trustworthiness of their work in research proposals, publications and public communications as well as in all review activities. Investigator conflicts of interests are of particular importance when an unacknowledged or undisclosed interest, financial or otherwise, may negatively affect the wellbeing of research participants. It is this aspect of conflicts of interests that is of concern and relevance to the HSREC.

22.2.3.2 Appropriate disclosure of affiliation with, or financial involvement in any organisation or entity with a direct interest in the subject matter or materials of researchers must be made. These procedures must cover the full range of potential interest, including:

- 22.2.3.2.1 Equity or stock holding in a sponsor company;
- 22.2.3.2.2 Proprietary interests in product- patent holding, intellectual property rights, trademark, and licensing agreements;
- 22.2.3.2.3 Grants paid, speaking arrangements, retainers for ongoing consultations, sitting on "Pharmaceutical Advisory Boards" etc.;
- 22.2.3.2.4 Travel/conference sponsorship;
- 22.2.3.2.5 Recruitment fees or other personal payments that are linked to study outcome, in any way;
- 22.2.3.2.6 Co-authorship of articles, where the co-author's input has been minimal;
- 22.2.3.2.7 Funding for additional staff and facilities, especially if not directly linked to the research project;
- 22.2.3.2.8 Equipment for use in a study that will then belong to the department;
- 22.2.3.2.9 Donation of equipment unrelated to study;
- 22.2.3.2.10 Contributions to a departmental budget not directly related to project expenses.

22.2.4 Conflict of interest policy for HSREC members:

22.2.4.1 Members of the HSREC are bound by the Confidentiality and Conflict of Interest clause relating to the HSREC meetings.

22.2.4.2 The confidentiality clause states: "I further undertake to declare to the HSREC any interest I may have in any research project discussed by the HSREC and to excuse myself from the meeting for the duration of the discussion of such project".

22.2.4.3 Members of the HSREC are expected to make decisions and conduct their oversight responsibilities in an independent manner, free from bias and undue influence. HSREC members (and members of their immediate families) may be involved in activities that could be perceived as conflicting with their HSREC responsibility. The integrity of the HSREC review process could be compromised if such conflicts of interests are not disclosed and should, where necessary, be avoided.

22.2.4.4 HSREC members should disclose information that may lead to perceptions of conflict of interest –including the following:

22.2.4.4.1 Personal relationship. The HSREC member has a personal relationship with the principal investigator or key personnel of a research protocol under review by the HSREC;

22.2.4.4.2 Relationship to the research study: The HSREC member (his/her spouse or immediate family member) is the principal investigator or co-investigator of the research protocol under review by the HSREC;

22.2.4.4.3 Business relationship or affiliation: The HSREC 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 the HSREC;

22.2.4.4.4 Financial interest: The HSREC member has a financial interest that could be affected by the outcome of the research protocol under review by the HSREC. 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. In the event that the conflict of interest involves the Chair, he or she will appoint the Vice-Chair, or another member as acting Chair (with approval of the HSREC). The acting Chair will conduct the meeting, for the remainder of the discussion of the item in question.

22.2.4.5 HSREC members with a conflict of interest may not take part in the discussion or decision-making and this should be recorded in the minutes of the meeting. These members should recuse themselves when the protocol in question is discussed. Members must also withdraw from the HSREC when discussion on their own projects are taken and must not use their membership on the HSREC to gain a favourable advantage. The outcome of the HSREC 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.

22.3 Definitions

22.3.1 HSREC member: In this document, the term is used for convenience to refer to all HSREC members and HSREC Administration and their immediate families, except where indicated.

22.3.2 Immediate family includes: Spouse, domestic partner, or other similar type of partner, parents, children, siblings, household members

22.3.3 Recusal: Conflicted HSREC members leave the HSREC meeting before the discussion and vote on the item with which they have a conflict. When this occurs, the member does not count towards the quorum for the vote. The member's absence under these circumstances is called a recusal.

22.3.4 Conflict of interest: Types of conflict of interest include:

22.3.4.1 Significant involvement in the preparation of the materials submitted to the HSREC for review or determination: HSREC members occasionally are significantly involved in the preparation and writing of materials submitted to the HSREC. It is considered a conflict of interest when this has occurred for:

22.3.4.1.1 An initial application for HSREC approval;

22.3.4.1.2 A continuing review application;

22.3.4.1.3 A modification that involves new risk information, decreased benefits, or a significant change in research procedures;

22.3.4.1.4 Participation on the research team: The HSREC member is listed as an investigator on the HSREC application, or is otherwise a member of the research team;

22.3.5 Research supervision of the investigator: This refers to any situation in which the investigator is currently under the research supervision of the HSREC member.

22.3.6 Supervision of the HSREC member by a member of the research team: This means that the investigator on the HSREC application has a supervisory or other official authority role with regard to the HSREC member.

22.3.7 Other potentially conflicting relationship with the research sponsor: Examples include serving on a non-governmental sponsor's board of directors, advisory board, scientific board, or safety board.

22.3.8 Personal relationship with the investigator: This is defined as having an immediate family relationship or other close personal relationship with the investigator, or with co-investigators who have a significant role in the research.

22.3.9 Competitive relationship with the investigator: This means the HSREC member is in direct competition with the investigator for limited resources (e.g., funding, sponsorship, space, equipment, research subjects), or the HSREC member is considered a personal or professional adversary of the investigator for reasons not related to the HSREC. Whether this situation creates a conflict of interest for the HSREC member should be determined by the HSREC Chair.

22.3.10 Other: The HSREC member may have other interests that the HSREC member believes conflicts with his or her ability to objectively review the research. For example, the HSREC member may be a participant in a study; such participation may be a conflict of interest for participating in the review of a Status Report, modification, or study problem.

22.4 Procedures

22.4.1 Identification: A conflict is most likely to be identified when incoming materials are assigned to an HSREC member for review.

22.4.2 Disclosure:

22.4.2.1 Voluntary disclosure: It is the responsibility of the HSREC member to disclose all, certain or potential conflicts of interest prior to engaging in any HSREC review or determination activities.

22.4.2.2 Query at HSREC meetings: At the beginning of each meeting, the HSREC Chair asks the members to disclose any conflict of interest concerning any of the items on the agenda. During the meeting, any conflicted HSREC member discloses the existence of the conflict just before the review of the relevant item begins.

22.4.3 Determination when not clear: When it is not clear whether a conflict of interest exists, the individuals listed below make a determination. The determination is based on gathering as much information as necessary from relevant sources.

22.4.3.1 Conflicted HSREC member: HSREC Chair;

22.4.3.2 Conflicted HSREC Chair: HSREC members.

22.4.4 Management of conflict of interest

22.4.4.1 HSREC members:

22.4.4.1.1 As reviewers

22.4.4.1.1.1 Do not serve as primary or expedited reviewers. If the conflict is disclosed after review assignment, the review is re-assigned to another HSREC member.

22.4.4.1.2 At HSREC meetings

22.4.4.1.2.1 The conflict is disclosed at the beginning of an HSREC meeting and just prior to the review of the relevant item. The HSREC member does not participate in the discussion except to provide information at the HSREC's request.

22.4.4.2 The HSREC member is recused before the discussion and decision of the project.

22.4.4.3 The meeting minutes note that the member (by name) was recused.

23 RECORD KEEPING

23.1 Purpose

The purpose of this section is to describe the policy and procedure to be followed in the retention of documents and record keeping of the HSREC.

23.2 Policy

Legal and ethical requirements regarding human research participant protection require that records be retained in an orderly and easily accessible manner for future reference and for audit purposes. SA GCP 2006 requires retention of records for a minimum of 15 years post-clinical trial. The HSREC retains all research study records for 15 years in accordance with GCP requirements.

23.3 Procedure

23.3.1 Research projects

23.3.1.1 An HSREC reference number is allocated to all new applications. This number is recorded on all correspondence and additional attachments/amendments.

23.3.1.2 A research ethics data base is used to capture project information such as names of investigators, titles of projects etc.

23.3.1.3 Copies of all research study related documents and correspondence are filed according to their reference numbers.

23.3.1.4 Records of all communication between investigators and the HSREC office are recorded and filed using this reference number.

23.3.2 Records kept by the HSREC include the following:

23.3.2.1 Protocols or research plans;
23.3.2.2 Investigator brochure (if any);
23.3.2.3 Scientific evaluations, when provided by an entity other than the HSREC;
23.3.2.4 Recruitment materials;
23.3.2.5 Informed consent documents;
23.3.2.6 Continuation reports submitted by researchers;
23.3.2.7 Reports of injuries to participants;
23.3.2.8 Records of continuing review activities;
23.3.2.9 Data and safety monitoring reports;
23.3.2.10 Modifications to previously approved research;
23.3.2.11 Unanticipated problems involving risks to participants;
23.3.2.12 Documentation of non-compliance;
23.3.2.13 Significant new findings;
23.3.2.14 Additionally, the HSREC will also keep records for expedited review procedures including the following:

23.3.2.14.1 The justification for using the expedited/exempt review procedure;
23.3.2.14.2 Actions taken by the reviewer.

23.3.3 Meetings

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

23.3.3.1.1 Show attendance at the meetings;
23.3.3.1.2 All actions taken by the HSREC;
23.3.3.1.3 Whether or not decision was reached by consensus or voting. Decisions are made by consensus unless otherwise indicated;
23.3.3.1.4 If by vote, then the number voting for, against and abstaining;
23.3.3.1.5 The basis for requiring changes to, or disapproval of research;
23.3.3.1.6 A written summary of the discussion of controversial issues and their resolution;
23.3.3.1.7 The approval of minimal risk reviews by the Chair or designee;
23.3.3.1.8 The approval of required protocol modifications must be documented in the minutes of the first HSREC meeting that takes place after the date of the approval;

23.3.3.2 The meeting minutes must also document committee members' attendance with respect to the following:

23.3.3.2.1 Attendance at the meeting;
23.3.3.2.2 Member's absence from discussion, deliberation, and vote on specific protocols because of financial or non-financial conflict of interest;
23.3.3.2.3 The presence of a quorum;

23.3.3.2.4 The name of the HSREC members who recused themselves due to conflict of interest;

23.3.4 Record of membership

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

24 GUIDELINE FOR CONDUCTING SITE AUDITS

24.1 Purpose

This section describes the policy and procedure for the HSREC when conducting site audits.

24.2 Policy

24.2.1 According to the Department of Health's Ethics Guidelines for Research "a 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."

24.2.2 Monitoring routinely involves the regular review of study continuation reports, but sometimes more in-depth monitoring of a project in the form of a site audit may be necessary.

24.2.3 The main objective of a site audit is to ensure compliance with both the protocol and GCP guidelines, where applicable.

24.2.4 The HSREC has the authority to conduct audits on any active research activities involving human participants.

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

24.2.6 Parties generally involved in the process include the investigator, the research team, the HSREC, the HSREC Chair, the auditor/audit team and the Vice-Rector: Research.

24.2.7 The HSREC has the authority to audit any research site. However, as site audits are costly and time consuming, the following sites will be prioritised:

- 24.2.7.1 Routine audits (group A), which include but are not limited to:
  - 24.2.7.1.1 Inexperienced sites;
  - 24.2.7.1.2 High-recruiting sites;
  - 24.2.7.1.3 Sites recruiting vulnerable patients; and
  - 24.2.7.1.4 Research that is more "risky".
- 24.2.7.2 For cause audits (group B), which include but are not limited to:
  - 24.2.7.2.1 Sites from which complaints have been received (whether by a participant, sponsor or some other third party);
  - 24.2.7.2.2 Sites, at which it is suspected that the procedures approved by the HSREC are not being followed, based on evidence provided in continuation reports or in sponsor monitoring notes.

24.3 Procedure

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

24.3.2 Implementation of an audit and notification:

- 24.3.2.1 Sites from Group A will be selected randomly by the HSREC.
- 24.3.2.2 Sites from group B will be selected on an ad-hoc basis as necessary, either after discussion by the HSREC, or on the specific instructions of the Senate Research Ethics Committee or the Vice-Rector: Research.

24.3.3 A notification of sites for proposed audits will be tabled at the next HSREC meeting.

24.3.4 The principal investigator(s) will be given at least 2 weeks' notice that an audit will be performed, so as to ensure their active participation and to protect their right to due process.

24.3.5 The audit:

- 24.3.5.1 The audit team will examine the structure of the principal investigator'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 participants.
- 24.3.5.2 In the case of audits in response to a complaint, the audit team will be supplied with an audit brief, which may outline the complaint and indicate specific focus areas for the audit.
- 24.3.5.3 In the case of random audits, the audit team reviews records maintained by the principal investigator, including site-monitoring notes where applicable, for the duration of the study.
- 24.3.5.4 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.

24.3.5.5 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. (Important: Some of the documents listed here may not be applicable)

24.3.5.5.1 INVESTIGATOR'S STUDY FILE

24.3.5.5.1.1 Confirmation of Regulatory Approval;
24.3.5.5.1.2 Signed funding agreement and copies of receipts or financial correspondence (where applicable);
24.3.5.5.1.3 Signed copy of the final protocol and any amendments;
24.3.5.5.1.4 Example of diary card, questionnaires, etc.;
24.3.5.5.1.5 Dated, signed CVs of all study site personnel;
24.3.5.5.1.6 Copy of signatures of site staff;
24.3.5.5.1.7 Responsibilities list;
24.3.5.5.1.8 Correspondence and communication with funders, and other authorities e.g., provincial government authority;
24.3.5.5.1.9 Records relating to equipment loan during the study;
24.3.5.5.1.10 Equipment calibration logs;
24.3.5.5.1.11 Laboratory certification (including updates);
24.3.5.5.1.12 Laboratory normal reference ranges (including updates).

24.3.5.5.2 HSREC COMPLIANCE

24.3.5.5.2.1 Any correspondence with the HSREC;
24.3.5.5.2.2 List of Committee members;
24.3.5.5.2.3 Letter of HSREC approval and approval of any protocol amendments or other changes;
24.3.5.5.2.4 6-monthly/annual continuation report to the HSREC;
24.3.5.5.2.5 Annual re-approval from the HSREC;
24.3.5.5.2.6 Notification of end of study;
24.3.5.5.2.7 Insurance statement (if applicable);
24.3.5.5.2.8 Signed indemnity letter (if applicable);
24.3.5.5.2.9 Any advertisement used for participant recruitment;
24.3.5.5.2.10 Example of participant information consent forms;
24.3.5.5.2.11 Signed consent forms;
24.3.5.5.2.12 Participant screening list;
24.3.5.5.2.13 Participant recruitment log;
24.3.5.5.2.14 Participant identification record;
24.3.5.5.2.15 Copies of serious adverse events.

24.3.5.5.3 PHARMACY AND DRUG RECORDS (IF APPLICABLE)

24.3.5.5.3.1 Dispensing dates match up with visit date;
24.3.5.5.3.2 Drug logs are complete;
24.3.5.5.3.3 Tablet counts are recorded;
24.3.5.5.3.4 All drug returns are counted;
24.3.5.5.3.5 Boxes containing drugs for return are labelled for return;
24.3.5.5.3.6 Drug storage is appropriately recorded.

24.3.5.5.4 CASE RECORD FORMS

24.3.5.5.4.1 All CRFs are as complete as possible;
24.3.5.5.4.2 All amendments are made correctly;
24.3.5.5.4.3 Date of patient visits match recruitment logs;
24.3.5.5.4.4 Laboratory result, x-ray results, etc.;
24.3.5.5.4.5 All trial details filed in appropriate place.

24.3.5.5.5 TRANSPORT LOGS

24.3.6 Additional points of note:

24.3.6.1 Interviews may be conducted with the principal investigator and site personnel.
24.3.6.2 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.

24.3.7 Reporting of Audit and Follow-up:

24.3.7.1 The audit team will compile an audit report, which is submitted to the Chair of the HSREC and/or the Vice-Rector: Research if appropriate, and to the principal investigator.

24.3.7.2 The principal investigator will be requested to respond formally in writing to the audit report and address each point. The principal investigator‘s report should also include a corrective action plan, if appropriate.

24.3.7.3 The audit team or the HSREC 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.

24.3.7.4 The auditor/team may arrange a formal meeting between the principal investigator, audit team, representatives from the HSREC and the Vice-Rector: Research or Senate Research Ethics Committee, 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.

24.3.7.5 The Audit Report, principal investigator‘s written response and minutes of the follow-up meeting are confidential and will usually be tabled at a forthcoming HSREC meeting.

24.3.7.6 The HSREC Chair and Vice-Rector: Research may jointly, in certain circumstances, decide not to table the full audit report. However, this decision should not compromise the institutional independence of the HSREC.

24.3.8 HSREC deliberations and decisions:

24.3.8.1 The full HSREC reviews the audit team’s summary report, the principal investigator‘s written response and the minutes of the follow up meeting report, where applicable.

24.3.8.2 The HSREC will decide either by consensus or by vote to:

24.3.8.2.1 Accept the audit findings and principal investigator’s written response as acceptable with no cause for further action. A final letter will be sent to the principal investigator, briefly summarising the outcome and declaring the matter satisfactorily resolved.

24.3.8.2.2 Request the principal investigator 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.

24.3.8.2.3 Withdraw study approval; and/or

24.3.8.2.4 Refer the matter to line management, the Vice-Rector: Research or the Senate Research Ethics Committee for further investigation and action where appropriate.

24.3.9 All correspondence between the HSREC, auditor and principal investigator 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 by the Vice-Rector: Research after discussion with the Chair of the HSREC and other relevant stakeholders.

24.3.10 Important note: When an audit is initiated in response to a third-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 and the involvement or not, of line and faculty management, including the Vice-Rector: Research, the Dean of the Faculty of Health Sciences or the Senate Research Ethics committee.

25 RESEARCH PARTICIPANTS' REQUESTS OR COMPLAINTS

25.1 Purpose

This section describes the procedures followed by the HSREC for dealing with study participants' requests or complaints.

25.2 Policy

25.2.1 The primary role of the HSREC is to protect the interests (rights, safety and welfare) of the research participants who volunteer to take part in scientifically sound research and maintains exemplary standards in research activities.

25.2.2 At all times, human participants involved in research have the right to voice a concern, complaint, or question. Researchers, the HSREC, and the UFS are all responsible for addressing complaints in a timely and suitable manner. Proper precautionary measures must be identified to protect the rights, safety and welfare of research participants.

25.2.3 A participant may voice a concern or complaint directly, or a representative of the participant may voice the concern or complaint on behalf of the participant by phone, in writing or in person. When addressing participant complaints, appropriate privacy and confidentiality protections must be in place throughout the process to ensure protection of the participant.

25.2.4 Research participants have the right to forward complaints to the NHREC (National Health Research Ethics Council).

25.3 Definitions

25.3.1 Unexpected problem: An unexpected problem is any incident, experience or outcome that meets the following three criteria:

25.3.1.1 Unexpected in terms of its nature, severity or frequency, or the research population being studied; or if anticipated it is not fully addressed or specified in information provided to the HSREC or to participants such as in initial protocol applications, any amendments, investigator's brochures, scientific literature, product labelling, package inserts and HSREC-approved informed consent documents or any existing documentation regarding the research conducted to date under the protocol;

25.3.1.2 Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research) such as psychological, economic, or social harm other than was previously known or recognized;

25.3.1.3 Examples of unexpected problems include, but are not limited to, the following:

25.3.1.3.1 Loss of a laptop computer containing confidential information about participants or others;

25.3.1.3.2 Any person with a lack of agency in a personal relationship who experiences abuse partner for taking part in the study;

25.3.1.3.3 Publication in the literature or a Data and Safety Monitoring Report that indicates an unexpected change in the balance of risks and benefits in the study;

25.3.1.3.4 Finding that laboratory reports on blood or other samples were in error.

25.3.1.3.5 Accidental unblinding of the investigator and/or the study team.

25.4 Responsibilities

25.4.1 The principal investigator is responsible for ensuring the HSREC-approved consent documents contain accurate information for contacting the principal investigator should the participant have questions or research-related problems and contact information for the HSREC, should the participant have questions about the participant's rights as a research participant or to report research-related problems.

25.4.2 The HSREC responsibilities are described below.

25.5 Procedures

25.5.1 Complaints received by the principal investigator or study team:

25.5.1.1 If the principal investigator or the study team receives a complaint, the research team must address and resolve the matter as soon as possible. Complaints must be reported to the HSREC as appropriate, according to the following guidelines:

25.5.1.1.1 If the complaint meets the definition of an unexpected problem, the principal investigator must report the complaint to the HSREC within 15 days.

25.5.1.1.2 If the complaint involves possible non-compliance or research misconduct, the report will be reviewed according to HSREC policy.

25.5.1.1.3 If a complaint does not meet the definition of an unexpected problem but the investigator is unable to resolve the complaint satisfactorily with the research participant, the complaint should be referred to the HSREC for additional action. This report should be submitted as soon as it is determined that the issue cannot be resolved without assistance from the HSREC or the institution.

25.5.1.2 If the complaint does not meet any of the three criteria above and the investigator was able to satisfactorily resolve the complaint, the investigator should report the complaint at the time of continuing review. The principal investigator must provide a summary of the complaint, how it was resolved, and why it did not meet criteria for prompt reporting as an unexpected problem or non-compliance.

25.5.1.3 If a complaint results in the need to change the HSREC approved study, an amendment should be submitted to the HSREC for review and approval as soon as the complaint is resolved. The report of the complaint must be included in the amendment submission.

25.5.2 Complaints received by the HSREC:

25.5.2.1 If a research participant complaint is received by the HSREC, the HSREC will take the necessary steps to address the complaint.

25.5.2.2 When receiving notification of a complaint via phone, in writing or via email HSREC Administration may record the following information

25.5.2.2.1 Personal information is not required if the person wishes to remain anonymous, but the individual will be informed that without this information, direct follow-up will not occur.

25.5.2.2.2 The HSREC project number and name of the principal investigator, if available.

25.5.2.2.3 The person's relationship to the study (present or past participant or representative of present or past participant).

25.5.2.2.4 A detailed explanation of the complaint/concern/question.

25.5.2.2.5 Who the person has contacted previously regarding the complaint/concern/question, when the contact was made, and the resolution of the contact.

25.5.2.2.6 A proposed resolution from the individual, if offered.

25.5.2.3 HSREC Administration will communicate to the research participant that an inquiry will be made into the circumstances associated with the complaint/concern/question.

25.5.2.4 After consultation with the principal investigator and research team, if the complaint was previously raised with the investigator, the HSREC will request submission of the complaint formally either immediately or within 7 calendar days. The investigator should report the complaint formally through to document receipt of the complaint as well as the process used to address the complaint in collaboration with the HSREC. The HSREC will review the complaint report, as appropriate.

25.5.3 HSREC Review Procedures:

25.5.3.1 Upon receipt of a complaint/concern, the HSREC will determine whether it may constitute an unexpected problem, non-compliance, or other reportable matter, and if so, proceed with appropriate reporting procedures. The HSREC may consult with the HSREC legal member to seek assistance in the handling of any complaint or concern.

25.5.3.2 After a complaint report is provided to the HSREC, the HSREC Chair or designee will review the report to determine if it involves potential risks to participants or others or a change in the risk/benefit ration associated with the study.

25.5.3.3 If the HSREC determines that the complaint/concern/question does not involve potential risk to participants or others or changes the risk to benefit ratio associated with the study, the HSREC may accept the report and provide written acknowledgement of receipt and review. The report and acknowledgement of the report will be included in the project file.

25.5.3.4 If the HSREC determines that the complaint/concern/question does involve potential risk to participants or others or changes in the risk to benefit ratio associated with the study, the following may occur:

25.5.3.4.1 HSREC Administration places the report and response on the next meeting agenda for full HSREC review and it is minuted.

25.5.3.4.2 If an immediate effect to participants is expected, the HSREC may contact the principal investigator to request establishment of immediate procedures for the protection of participants until review can be completed by the HSREC.

25.5.3.4.3 The HSREC may require amendment to the protocol, recruitment materials, and/or consent materials as appropriate to protect future participants.

25.5.3.4.4 The HSREC may suspend or request termination of the research.

26 RESEARCHER APPEALS AND COMPLAINTS

26.1 Purpose

This document describes the procedures for appealing a determination by the HSREC.

26.2 Policy

26.2.1 The HSREC may determine that some or all of a proposed research activity cannot be approved, or the HSREC may require the researcher to make changes to the research in order to obtain HSREC approval. HSREC requirements and disapprovals that are consistent with regulations and policies may not be reversed by any official or agency, including another HSREC.

26.2.2 A researcher may appeal to the HSREC to do a formal re-review of a decision. The only grounds for requesting an appeal are when:

- 26.2.2.1 There have been multiple unsuccessful efforts by the researcher and the HSREC to resolve a disagreement; and
- 26.2.2.2 the researcher believes that the HSREC's decision is due to:
  - 26.2.2.2.1 Inadequate or inaccurate information;
  - 26.2.2.2.2 HSREC non-compliance with HSREC policy, national and/or international regulations.

26.2.3 The HSREC Chair has the authority to determine whether an appeal request will be accepted.

26.2.4 Only one appeal will be allowed on a given matter. The concluding determination made by the HSREC regarding the appeal is final and not subject to further appeal.

26.2.5 Complaints about HSREC-related business must be directed to the HSREC in the first instance. If the matter remains unresolved, it may be escalated to an appeal committee appointed by the Management of the Faculty of Health Sciences for a decision and then to the National Health Research Ethics Council (NHREC) for further adjudication.

26.3 Procedures

26.3.1 The appeal must be requested by the researcher within 30 calendar days of the date of the most recent HSREC review letter to the researcher concerning the decision that is being appealed.

26.3.2 The appeal request consists of sending the following to HSREC Administration:

- 26.3.2.1 A cover letter outlining the basis for the appeal.
- 26.3.2.2 Any supplemental documentation that supports the appeal.
- 26.3.2.3 Within three business days of receipt, the HSREC Administration:
  - 26.3.2.3.1 Provides the HSREC Chair with a copy of the materials; and
  - 26.3.2.3.2 Sends the researcher an acknowledgment of receipt of the appeal request.

26.3.3 The HSREC Chair reviews the appeal request to determine whether an appeal is appropriate, as defined above. This may include consultation with the researcher, HSREC Administration, the initial HSREC reviewer(s) and others, as needed.

26.3.4 HSREC Administration informs the researcher by email if the appeal request has been accepted.

26.3.5 The appeal is heard at an HSREC meeting. This may be a regularly scheduled HSREC meeting, or it may be a meeting convened specifically for this purpose.

26.3.6 The researcher is required to attend the HSREC meeting and to present the appeal to the HSREC members. HSREC Administration works with the HSREC and the researcher to schedule a mutually-acceptable review date as soon as possible.

26.3.7 HSREC Administration follows standard procedures to identify the HSREC member who will be the primary reviewer of the appeal (usually the initial primary reviewer), and to provide all relevant materials (including those provided by the researcher) to all attendees at the meeting.

26.3.8 During the HSREC meeting:

- 26.3.8.1 The HSREC Chair may hold a closed session without the researcher and colleagues, prior to the appeal portion of the meeting, to establish the key issues and questions to consider.
- 26.3.8.2 The researcher is invited to present information and rationale to the HSREC.
- 26.3.8.3 The researcher's colleagues (if present) are invited to present.
- 26.3.8.4 There is a question-and-answer session with the researcher and colleagues.

26.3.8.5 The researcher and colleagues leave the meeting room.
26.3.8.6 The HSREC members and other meeting attendees discuss the appeal.
26.3.8.7 The HSREC moves and then votes whether to take one of the following actions:
26.3.8.7.1 Approve the appeal and modify the original decision;
26.3.8.7.2 Disapprove the appeal and uphold the original determination; or
26.3.8.7.3 Defer the appeal and obtain additional information or consultation in order to make a final decision.

26.3.9 HSREC Administration communicates the HSREC's appeal determination, and any considerations or requirements associated with it, to the researcher in a letter within 7 business days of the HSREC's determination. If appropriate, the determination may also be communicated by email or telephone call with follow-up email, by the HSREC Chair.
26.3.9.1 All HSREC correspondence must be addressed to the principal investigator or delegated signatory unless dictated by particular circumstances.
26.3.9.2 HSREC Administration works with the HSREC Chair and/or the primary reviewer to draft the letter.

27 REPORTING RESEARCH MISCONDUCT AND FRAUD (WHISTLE-BLOWER POLICY)

27.1 Purpose

27.1.1 This section describes the policy and procedures the HSREC follows when research misconduct is reported. The purpose of this procedure is to:

27.1.1.1 Enable individuals to raise legitimate concerns relating to research misconduct.

27.1.1.2 Make clear to individuals that allegations of research misconduct are taken seriously by the HSREC.

27.1.1.3 Provide the opportunity for an individual who has inadvertently breached good practice to declare the problem openly, allowing the process to occur in a fair and transparent manner.

27.1.1.4 Provide a process for concerns to be raised, investigated and, where appropriate, acted upon in a fair and transparent manner and in confidence.

27.1.1.5 Act as a deterrent to potential perpetrators of research misconduct.

27.1.1.6 Strengthen the confidence of all parties (e.g., research funders, the individual making an allegation) that the HSREC maintains the highest standards of research conduct.

27.2 Policy

27.2.1 Researchers should report evidence of fraud and other crimes or scientific misconduct in research to the HSREC.

27.2.2 The HSREC expects all approved research to be conducted observing the highest standards of research practice.

27.2.3 Sources are encouraged to put their name to any allegation they make since part of the purpose of this procedure is to promote openness and discourage a fear of reprisals. Allegations made anonymously are far less capable of being addressed effectively but may be considered after taking into account the seriousness of the issue, the credibility of the allegation, the likelihood of being able to investigate the matter and confirm the allegation from alternative sources, and fairness to any individual mentioned in the allegation.

27.2.4 The identity of the person raising the matter will, if required, be kept confidential for as long as possible provided that this is compatible with an effective investigation. The investigation process may however at some stage have to reveal the source of the information and the individual making the allegation may need to make a statement as part of the evidence required. All allegations made under this procedure will be treated in a confidential and sensitive manner.

27.2.5 Named individuals will be informed of the allegation(s) made against them and the supporting evidence and this will be confirmed in writing, taking all aspects of confidentiality into consideration. The point at which this occurs will depend upon the specific nature of the case.

27.2.6 The named individual will be given an opportunity to respond and if they so wish can be accompanied by a work colleague or staff representative of his/her choice.

27.2.7 The named individual will, in all circumstances where a case has been established and where formal action is to be taken, have the opportunity to put their case forward and respond to the allegations in accordance with agreed ethics committee procedures.

27.2.8 Individuals making an allegation, which is found by subsequent investigation to be malicious, may be subject to disciplinary or other appropriate action. Suspicions reported in confidence and in good faith which are not confirmed by subsequent investigation will not lead to any action against the person making the allegation.

27.2.9 Investigations will be conducted as speedily as possible, having regard to the nature and complexity of the allegation.

27.2.10 The outcomes of the process will be made known to relevant persons involved, including the person making the allegation and the person against whom the allegation has been made, whilst also maintaining confidentiality wherever possible.

27.3 Definitions

27.3.1 Research misconduct and fraud based on guidance issued by the Wellcome Trust:

27.3.1.1 “The fabrication, falsification plagiarism or deception in proposing, carrying out or reporting results of research or deliberate, dangerous or negligent deviations from accepted practices in carrying out research. It includes failure to follow established

protocols or adhere to established ethical principles if this failure results in unreasonable harm to human beings, other living organisms or the environment and facilitating of misconduct in research by collusion in, or concealment of, such action by others. It includes intentional, unauthorised use, disclosure or removal of, or damage to, research-related property of another, including apparatus, materials, writings, data hardware or software or any other substance or devices used in or produced by the conduct of research. It also includes any plan or conspiracy or attempt to do any of the above."

27.3.2 It does not include honest error or honest differences in the design, execution, interpretation or judgment in evaluating research methods or results or misconduct unrelated to the research process. Similarly, it does not include poor research unless this encompasses the intention to deceive.

27.4 Responsibilities

27.4.1 Researchers have a duty to report any incident of misconduct, whether this has been witnessed or whether it is suspected.

27.4.2 The HSREC responsibilities are described below.

27.5 Procedures

27.5.1 Allegations should be made in writing to the HSREC Chair.

27.5.2 Any individual wishing to make a disclosure, or to give further details as the matter is investigated, may be accompanied by a work colleague or staff representative of his/her choice.

27.5.3 The HSREC Chair shall appoint a sub-committee to lead an initial investigation.

27.5.4 Since the person conducting the investigation should not be the person who would ultimately take decisions based upon the outcomes of the investigation, the Chair will not personally conduct the investigation and will remain separate from it, in order to maintain impartiality and fairness in the investigative process.

27.5.5 The HSREC Chair shall:

27.5.5.1 Decide how an investigation should take place and what form it should take.

27.5.5.2 Appoint (a) relevant person/s to investigate the allegation;

27.5.5.3 Decide whether there are grounds for proceeding further.

27.5.6 The process of the investigation will be recorded and filed according to the HSREC Record Keeping policy.

27.5.7 Outcome of initial investigation:

27.5.7.1 The HSREC Chair will, when the matter has been investigated, decide whether the matter should be taken further and, if so, how it should be handled. Reporting of the allegations or findings of any investigation will depend on the nature of the allegation.

28 CASE REPORTS/SERIES

28.1.1 **Case studies/series**

28.1.1.1 In general, informed consent should be obtained from each patient before publishing or presenting a case report or case series. Case reports can sometimes reveal very personal information of patients and may even possibly lead to their recognition by readers of the report, particularly if photographs or other visual media are used.

28.1.1.2 HSREC Administration accepts new case report and case series applications on an ongoing basis.

28.1.1.3 The application for HSREC review of a case report or case series should include:

28.1.1.3.1 An application in InfoEd RIMS on the appropriate e-form

28.1.1.3.2 Cover letter for the case study/series

28.1.1.3.3 A title of the case study/series

28.1.1.3.4 A grade 8 reading level summary describing the case and a brief rationale for publishing this case report/series. Explain all medical and technical terms

28.1.1.3.5 The medium of presentation: Article/presentation/both

28.1.1.3.6 Copies of all images, videos, drawings or any other media, and all potentially identifying data that will be included in the publication/presentation.

28.1.1.3.7 Signed consent from each patient or their legally appointed representative. If informed consent was not available, a clear and adequately motivated justification for a waiver of informed consent, for HSREC consideration. This should include what measures the researcher has explored to obtain consent.
28.1.1.3.8 Method of de-identifying all potentially identifying data/images/media.
28.1.1.3.9 The case report/series or draft article/presentation that will be submitted.
28.1.1.3.10 Name and contact details of the applicant.
28.1.1.3.11 Name, contact details and role of all collaborators/co-investigators
28.1.1.3.12 Signed investigator declaration.
28.1.1.3.13 HPCSA registration for all investigators
28.1.1.3.14 Abbreviated curriculum vitae of all investigators
28.1.1.3.15 Letters of approval from:
28.1.1.3.15.1 Head of department
28.1.1.3.15.2 Free State Department of Health (in the case of public patients)
28.1.1.3.15.3 Other relevant documentation as described in the HSREC Preparation Guide.

29 PROTECTION OF PERSONAL INFORMATION ACT

29.1 Definitions

29.1.1 **POPIA:** The "Protection of Personal Information Act". This SOP is based on Act No. 4 of 2013.
29.1.2 **Data subject:** A person whose information is collected, processed, and stored in a research trial.
29.1.3 **Participant:** An identifiable, living, natural person participating in a research trial or information of an identifiable, living, natural person processed in a research trial.
29.1.4 **Participant identification code list:** The Participant Identification Code List is a document where the researcher keeps a confidential list of all participants allocated to coded trial numbers upon enrollment. This document allows the researcher to link the coded trial number with the identity of any participant for the purpose of participant safety, audits and inspections. Auditors and inspectors also keep the information confidential. A participant identification code list is important in clinical trials, interventional trials, or any other clinical trial where a natural person is included.
29.1.5 **Responsible party**: A public or private body, Principal Investigator, or any other person which, alone or in conjunction with others, determines the purpose of and means for processing personal information. In the context of research, the responsible party is the **researcher**.
29.1.6 **Principal investigator:** A South African scientist (researcher) that is responsible for the trial design, conduct, delegation of responsibilities, data collection, analysis of data, and the reporting the trial outcome. In clinical, medical devices, and clinical interventional trials, the Principal Investigator must be a medical doctor or dentists (within their scope of practice).1
29.1.7 **Information officer**: The designated individual within an institution that takes responsibility for the institution to ensure that the institution is compliant with POPIA. This may be:
29.1.7.1 public body means an information officer or deputy information officer as contemplated in terms of section 1 or 17 of the Promotion of Access to Information Act; or
29.1.7.2 private body means the head of the private body as contemplated in section 1 of the Promotion of Access to Information Act.
29.1.8 **Information regulator:** An independent, juristic body that is empowered to monitor and enforce the compliance by private and public entities with the provisions stated by POPIA.2
29.1.9 **Health Sciences Research Ethics Committee (HSREC):** A National Health Research Ethics Council accredited research ethics committee for review of trials in humans and of human data.

[1] ICH GCP R2 (2014) and SA GCP V2 (2006)
[2] https://www.justice.gov.za/inforeg/index.html

29.2 Abbreviations:

29.2.1 ASSAf: Academy of Science of South Africa
29.2.2 HSREC: Health Sciences Research Ethics Committee
29.2.3 ICF: Informed Consent Form
29.2.4 IR: Information Regulator
29.2.5 NHREC: National Health Research Ethics Committee
29.2.6 PI: Principal Investigator
29.2.7 POPIA : Protection of Personal Information Act

29.3 The importance of the Protection of Personal Information Act (POPIA)

29.3.1 POPIA aims to give effect to the constitutional right to privacy by protecting personal information, regulating the way in which personal information may be processed, providing rights and remedies available to persons and by establishing certain compulsory measures to ensure respect and to promote, enforce and fulfil privacy rights. POPIA is not applicable to data available in the public domain. This means that POPIA is legally binding and as such, non-compliance may lead to civil or even criminal liability.

29.4 What POPIA addresses:

29.4.1 How the eight (8) conditions for processing personal information are understood for research
29.4.2 How the exemptions (from the information regulator), exceptions and exclusions (de-identified) are to be interpreted for research
29.4.3 Use of social media data in research
29.4.4 Information matching programmes in research
29.4.5 Processing of genetic data
29.4.6 Cross-border data transfers
29.4.7 Security safeguards
29.4.8 Prior authorisations
29.4.9 Governance and review of the Code

29.5 What is personal information?

29.5.1 **Personal information** means information relating to an identifiable, living, natural person (data subject), and where it is applicable, an identifiable, existing juristic person, including, but not limited to:

29.5.1.1 information relating to the race, gender, sex, pregnancy, marital status, national, ethnic or social origin, colour, sexual orientation, age, physical or mental health, well-being, disability, religion, conscience, belief, culture, language and birth of the data subject
29.5.1.2 information relating to the education or the medical, financial, criminal or employment history of the data subject
29.5.1.3 any identifying number, symbol, e-mail address, physical address, telephone number, location information, online identifier, or other assignment to the data subject
29.5.1.4 the biometric information of the data subject
29.5.1.5 the personal opinions, views, or preferences of the data subject;
29.5.1.6 correspondence sent by the data subject that is implicitly or explicitly of a private or confidential nature or further correspondence that would reveal the contents of the original correspondence
29.5.1.7 the views or opinions of another individual about the data subject; and
29.5.1.8 the name of the person if it appears with other personal information relating to the person or if the disclosure of the name itself would reveal information about the data subject

29.5.2 **Special personal information** means personal information as referred to in section 26; A responsible party may, subject to section 26 not process special personal information **without specific informed consent and appropriate deidentification of the information** concerning—

29.5.2.1 the religious or philosophical beliefs, race or ethnic origin, trade union membership, political persuasion, health, sex life or biometric information of a data subject; or
29.5.2.2 the criminal behaviour of a data subject to the extent that such information relates to—

29.5.2.2.1 the alleged commission by a data subject of any offence; or
29.5.2.2.2 any proceedings in respect of any offence allegedly committed by a data subject or the disposal of such proceedings.

29.5.3 **Responsible party for information processing**

29.5.3.1 **Responsible party** means a public or private body or any other person which, alone or in conjunction with others, determines the purpose of and means for processing personal information. In the context of research, the responsible party is the **researcher**. This party is responsible for lawful processing of information, which entails:

29.5.3.1.1 Providing the HSREC with the relevant information to allow adequate review, outlining the **process** of:

29.5.3.1.1.1 Data management

29.5.3.1.1.2 Risk assessment and management

29.5.4 **Risk assessment and management**

29.5.4.1 The following information should be considered by the **responsible party** when performing a personal information risk assessment:

29.5.4.1.1 What type of personal information is being processed, e.g., is high risk information being collected?

29.5.4.1.2 Transfer of data outside of South Africa

29.5.4.1.3 Informed consent

29.5.4.1.4 Appropriate safeguards for data protection

29.5.4.1.5 Level of de-identification and de-identifiability

29.5.4.1.6 Use of information matching programmes (Risk of re-identification)

29.5.5 **The procedure for de-identification of data subjects (participants)**

29.5.5.1 **De-identify**, in relation to personal information of a data subject, means to delete any information that—

29.5.5.1.1 identifies the data subject;

29.5.5.1.2 can be used or manipulated by a reasonably foreseeable method to identify the data subject; or

29.5.5.1.3 can be linked by a reasonably foreseeable method to other information that identifies the data subject,

29.5.5.2 The process of participant de-identification should be described in detail in the protocol. There are various methods that can be used. The European General Data Protection Regulation (GDPR) divides de-identification into anonymisation and pseudonymisation. Anonymisation involves removing data and altering data to protect identities.

29.5.5.3 The commonest form of de-identification is called pseudoanonymisation. The data is divided into two components. Only if the two are combined can a subject be identified. One component contains identifiable personal data of the subjects, as well as the unique research study numbers of each subject. It is often called a participant identification code list. The other component contains the participants' unique research study number as well as the actual research data. The security issue with pseudoanonymisation is how the two data components are kept apart.

29.5.5.4 The responsible party must describe in the protocol how data (and the participant identification code list) are protected so that a motivated intruder could not easily find and combine both of separate data sets.

29.6 The rights of a data subject (participant)

29.6.1 Data protection rights:

29.6.1.1 The participant in any research study has the following rights vis-à-vis protection of personal information:

29.6.1.1.1 *Right of access:* Right to ask for copies of personal information. There are exceptions to this right, and not all information processed may be given to participants.

29.6.1.1.2 *Right to rectification:* Right to ask for information that is considered inaccurate to be rectified, and the right to request incomplete information to be completed.

29.6.1.1.3 *Right to erasure:* Under certain circumstances, the participant has the right to request erasure of personal information.

29.6.1.1.4 *Right to restriction of processing:* A participant may make a request (written or verbal), with motivation for an organisation to restrict the use of personal information. This is usually related to unlawfully processed data, inaccurate data, or data that is no longer required for the purpose that it was initially processed for.

29.6.1.1.5 *Right to object to processing:* Participants have the right to object to processing of personal information that is used for:

29.6.1.1.5.1 A task carried out in the public interest

29.6.1.1.5.2 The exercise of official authority

29.6.1.1.5.3 Their legitimate interests

29.6.1.1.5.4 Scientific or historical research, or statistical purposes

29.6.1.1.5.5 Direct marketing purposes

29.6.1.1.6 *Right to data portability:* The participant has the right to request that personal information is transferred to one organization to another, or to the participant him/herself. Applies to information obtained from a participant.

29.6.2 **Informed consent document (ICF)**

29.6.2.1 Specific information needed in the ICF:

29.6.2.1.1 Exactly what data is being collected and for what purpose (how will data be used)

29.6.2.1.2 How data is collected

29.6.2.1.3 How data is stored

29.6.2.1.4 Whether, and how the information will be de-identified and protected

29.6.2.1.5 Whether data will be shared with third parties

29.6.2.1.6 Details of the responsible party (data management), researcher and HSREC

29.6.2.1.7 Information about right to object to processing of information

29.6.2.1.7.1 The informed consent form (ICF) should address the management of data, and whether data can be amended/destroyed or deleted.

29.6.2.1.7.2 A request to amend/destroy or delete data may be made, but this may not always be possible. However, the request and the outcome of the request should be documented.

29.6.2.2 Information about reporting direct complaints regarding the protection of participant information

29.6.2.2.1 Direction of POPIA relevant complaints:

29.6.2.2.1.1 To the researcher, however at times the HSREC may be the first point of call

29.6.2.2.1.2 If unresolved -> HSREC

29.6.2.2.1.3 If unresolved -> NHREC

29.6.2.2.1.4 If unresolved -> to ASSaF

29.6.2.2.1.5 If unresolved -> Information Regulator

29.6.3 **What are data protection rights?**

29.6.3.1 **Other rights of data subjects (participants)**

29.6.3.1.1 Apart from informed consent, data subjects are entitled to:

29.6.3.1.1.1 Notifications that their personal information is collected

29.6.3.1.1.2 Notified if their information is accessed by an unauthorised person

29.6.3.1.1.3 Request that their information is corrected/amended, destroyed or deleted completely

29.6.3.1.1.4 Reasonable objection to the processing of their information

29.6.3.1.1.5 An enquiry about handling of their information or complain about data handling

29.6.3.1.1.6 Re-consent if their data is now processed for another purpose than what the participant initially consented to.

29.7 How information may be recorded and secured

29.7.1 Recording measures

29.7.1.1 **Record** means any recorded information—

29.7.1.1.1 regardless of form or medium, including any of the following:

29.7.1.1.1.1 writing on any material

29.7.1.1.1.2 information produced, collected, recorded, transmitted or stored by means of any audio recording, computer equipment, whether hardware or software or both, or other device, and any material subsequently derived from information so produced, recorded or stored

29.7.1.1.1.3 label, marking or other writing that identifies or describes anything of which the record forms part, or to which it is attached by any means

29.7.1.1.1.4 book, map, plan, graph or drawing

29.7.1.1.1.5 photograph, film, negative, tape or other device in which one or more visual images are embodied so as to be capable, with or without the aid of some other equipment, of being reproduced

29.7.1.1.1.6 broadcast over any social media platform

29.7.1.1.2 in the possession or under the control of a responsible party

29.7.1.1.3 whether or not it was created by a responsible party

29.7.1.1.4 regardless of when it came into existence

29.7.2 Data security measures

29.7.2.1 All data security measures should be appropriate and modelled according to the level of risk. The following are *examples* of data security measures (safeguards for personal information):

29.7.2.1.1 Policies and procedures for authorised access to personal information, including physical access, computational infrastructure access and network access

29.7.2.1.2 Physical security safeguards, such as locks, barriers and anti-theft systems

29.7.2.1.3 Use of hardware and /or software to protect personal information

29.7.2.1.4 Policies to ensure employee training and review of information access privileges

29.7.2.1.5 Automatic updates of anti-virus and anti-malware software on all personal information storage devices

29.7.2.1.6 Encryption of storage and transmission mechanisms (including email) and secure applications for decryption

29.7.2.1.7 The level of security measures applied should be appropriate to the level of risk

29.7.2.1.8 Policies for access to personal information when working off-site, particularly on less secure networks, logs to trace system activity of a specific user accessing personal information, and to prevent storage of personal information on mobile computing devices

29.7.2.1.9 Policies and procedures to ensure correct disposal of paper and/or electronic personal information, redundancy and backups, as well as disaster recovery safeguards

29.7.2.1.10 Technical safeguards such as firewalls, virus scanners, monitoring operating system logs, version control and encryption methods.

29.7.2.2 **Security breach:**

29.7.2.2.1 There must be a system in place to notify participants of any intentional or unintentional breach in data security.

29.7.2.2.2 The participant must be informed of the breach, what information was unlawfully accessed, what has been done to correct the situation, mitigate risk and prevent further security breaches.

29.7.2.2.3 The security breach should be reported to the HSREC as well as the information officer.

29.8 What is lawful processing of information?

29.8.1 *Principle 1: Accountability*

29.8.1.1 The organisation must appoint a party (Information Officer) who will be responsible for ensuring that the information protection principles within **POPIA** and the controls that are in place to enforce them are complied with

29.8.2 *Principle 2: Processing Limitation*

29.8.2.1 The second principle deals with the lawfulness of processing, minimality of information collected, consent, justification and objection, and the collection of personal information directly from the data subject.

29.8.2.1.1 Minimality means that no more information should be collected than necessary to meet the aims and objectives of the research

29.8.2.1.2 Informed consent must be obtained for collection and processing of information

29.8.2.1.3 Justification means that all data should be justified according to the aims and objectives of the research project

29.8.2.1.4 Objection means that participants may lodge their objection against the collection and processing of their information

29.8.3 *Principle 3: Purpose Specification*

29.8.3.1 Personal information must be collected for a specific purpose and the data subject from whom the personal information is collected must be made aware of the purpose for which the personal information was collected

29.8.4 *Principle 4: Further processing limitation*

29.8.4.1 If a responsible party further processes personal information, such processing must be compatible with the purpose for which the information was collected in principle 3.

29.8.5 *Principle 5: Information quality*

29.8.5.1 The fifth principle provides that the responsible party must take reasonable steps to ensure that the personal information that has been collected is complete, accurate, not misleading, relevant and up to date.

29.8.6 *Principle 6: Openness*

29.8.6.1 The responsible party must be open about the collection of personal information by notifying the HSREC if it is going to process personal information and, if personal information is going to be collected, the responsible party must take "reasonably practicable steps" to ensure that the data subject has been made aware that his or her personal information is going to be collected. The responsible party should for example, take reasonable steps to make the data subject aware of its name and address, and the purpose for which the personal information being collected.

29.8.6.2 The regulator in this instance is the HSREC, the institutional gatekeepers and the information officer at the study site and any other relevant statutory body.

29.8.7 *Principle 7: Security Safeguards*

29.8.7.1 The responsible party must ensure that the integrity of the personal information in its control is secured through technical and organisational measures.

29.8.8 *Principle 8: Data Subject Participation*

29.8.8.1 The data subjects have the right to request that a responsible party confirm (free of charge) whether it holds personal information about the data subject, and he or she may also request a description of such information.

29.9 Example of a data privacy notice (PDN)

[Title of research protocol]
Purpose of the project [Lay term summary of protocol]

This document will explain how this research will use personal data that we collect when you participate in this study.

What data do we collect?

- [Here the researcher should specify all personal information (refer to SOP section "What is personal information")]

- [Also mention all other data that will be collected]

How do we collect your data?

- Your personal information is collected during the research process. [Explain to the participant which stages of the research process involve collection of personal information.]
- [Explain to the participant of all sources of personal information (e.g., University records etc.)]
- [If online data collection is performed does the website have cookies. If cookies are used explain to the participant what cookies are, what type of cookies are used, what the purpose of cookies is in the research process, how to manage cookies.]

How we will use your data?

- [Explain to the participants what the data is needed for.]
- [Will e-mail addresses and phone numbers be used to make contact with research participants? Who will use this information?]
- [With whom will this information be shared?
    - List all organisations who will receive data
    - Why this information is shared with other organisations.]

How do we store your data?

- The researcher securely stores your data at [enter the location and describe the security precautions taken to protect data]
- Your data may be/will not be stored on a cloud-based system called [enter name]. The following persons will have access to that data [name persons] and the data is used for [explain the purpose].
- The researcher will keep your data for [insert time period]. Once this time period has expired, we will delete your data by [enter how participant data will be destroyed].

Will your personal information be de-identified?

- [insert a statement of de-identification plan]
- [insert a statement on how information will be de-identified}
- [insert a statement on the purpose of re-identifying data and how coding lists work]

Will your personal information be shared?

- As a research participant, your personal information may be shared with third parties
- [explain exactly which third party's personal information will be shared, why it needs to be shared, and what processes are in place to protect shared personal information]

Use of personal information for marketing

- If you agree, your personal information (like phone number or e-mail address) may be used for marketing purposes (e.g., to invite you to participate in future research).
- This information will be available to [list name all people and organisations who will have access to the personal information for marketing purposes]
- [insert a specific section where the participant signs for this in the informed consent document].
- You have the right to stop researchers from contacting you for marketing purposes, or giving your data to other researchers, even if you previously agreed to this. If you no longer want to be contacted to participate in research, please [describe the process]

What are your data protection rights?

- As researchers we would like to make sure that you are fully aware of all your data protection rights. You have the following rights:
    - **Right to access** – you have the right to ask the researcher for copies of your personal data. We may charge you a small fee for this service.
    - **Right to rectification** – you have the right to request that the researchers correct any personal information that you believe is inaccurate. You also have the right to request that the researcher completes any personal information that you believe is incomplete.
    - **Right to erasure** – you have the right to request that the researcher erases you personal information, under certain conditions. [explain to the participant when this will and will not be possible]

- **Right to object to processing** – you have the right to object to the researcher processing your personal information, under certain conditions. [explain to the participant what these conditions are]
- **Right to portability (transferring personal information)** – you have the right to request that the researchers transfer the personal information collected on you to another organization or directly to you, under certain conditions. [explain to the participant what these conditions are]

What if there are changes to our personal information policy?

- Participants in research have a right to know if there are changes in our personal information policy. We will notify you of such changes [specify how] if your data is still stored with us.

Who is responsible for your personal information?

- [insert PI's name] is the principal investigator (researcher) on this project and is responsible for how information is collected, processed and used.
- [insert data manager's name] is the person who is responsible for the personal information that we may collect on you in this research.

How to contact the researchers?

- If you make a request regarding your protection of personal information, the researchers have one month to respond to you.
- If you would like to exercise any of these rights, please contact:
  - The **researchers** at:
    - Telephone
    - Email:
  - The **data manager** at:
    - Telephone
    - Email:

How to contact the research organisation?

- If you have any questions of the [University of the Free State's or research organisation, or researcher's] protection of personal information policy, please visit the website [give address] or contact us at:
  - Telephone
  - Email

How to contact the Health Sciences Research Ethics Committee (HSREC)?

- Should you wish to report a complaint or if you feel that the data managers or researchers have not addressed your concern in a satisfactory manner, you may contact the Health Sciences Research Ethics Committee (HSREC) of the University of the Free State at:
  - Telephone
  - Email

30 REFERENCES AND SOURCE DOCUMENTS

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Other

- US Food and Drug Administration. IRB Information Sheets: A Self Evaluation Checklist for IRB's. Available at: www.fda.gov/oc/ohrt/irbs/irbchecklist.html
- AAHPP Tip Sheet 7: Evaluation of IRB Chairs, Vice-Chairs, IRB Members and IRB Staff. Available at: https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_7_Evaluation_of_IRB_Chairs,_Vice-Chairs,_IRB_Members_and_IRB_Staff.PDF
- Fred Hutchinson Cancer Research Centre and the University of Washington. Institutional Review Board IRB "Conflict of Interest Procedure.
- Policies, Procedures and Guidance for the Office of Research, University of Washington

- Standard Operating Procedures (SOPs) and Guidelines. Health Research Ethics Committee, Stellenbosch University.

Genetic Research

- Prof Jacqui Greenberg, Div Human Genetics, UCT. *IRENSA* Lecture Series. 2003.
- South African Medical Research Council (2003). Guidelines on Ethics for Medical Research: Reproductive Biology and Genetic Research (4th Edition). SAMRC.
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Appendix 1: Ethical Principles

The primary role of the Research Ethics Committee (REC) is to protect the interest (rights and welfare) of the research participants who volunteer to take part in scientifically sound research.

The key criteria and guiding principles according to NHREC specification are outlined and discussed here.

- **Ethical principles: The broad ethical principles are**

    - **Beneficence and non-maleficence**
      This refers to the ethical obligation to maximize benefit and to minimize harm, and requires that the risks of harm posed by the research must be reasonable in light of anticipated benefits; that research design must be sound, and that researchers must be competent to carry out the proposed research activities. Beneficence prohibits deliberate infliction of harm on persons; sometimes expressed as a separate principle: non-maleficence (do no harm). Research that involves human participants should seek to improve the human condition. If research cannot do this, then it is unlikely to be ethical.

    - **Distributive justice (equality**
      This means that there should be a fair balance of risks and benefits amongst all role-players involved in Research, including participants, participating communities and the broader South African society. In this way the principle of equality is expressed in the research context. 'No segment of the population should be unduly burdened by the harms of research or denied the benefits of knowledge derived from it.' There should be a reasonable likelihood that the population from which participants are drawn will benefit from the research results, if not immediately, then in the future.

    - **Respect for persons (dignity and autonomy)**
      This principle requires that persons capable of deliberation about their choices must be treated with respect and permitted to exercise self-determination. Further, persons who lack capacity or who have diminished capacity for deliberation about their choices must be protected against harm from irresponsible choices. Respect for persons recognises that dignity, well-being and safety interests of all research participants are the primary concern in research that involves human participants. Respect for persons includes 'the dual moral obligations to respect autonomy and to protect those with developing, impaired or diminished autonomy'. Autonomy includes the ability to deliberate about a decision and to act on that decision. Interests of participants should usually outweigh the interests of science and society. Consequently, involvement of persons or particular categories of people in the research should be justified in research proposals. Respect for persons means also that the interests of researchers must be considered. These include welfare and safety interests, authorship and intellectual property interests, and collegial and professional interests.

Persons who conduct research in South Africa are expected to adhere to these nationally and internationally recognised principles which underscore responsible and ethical research conduct.

1. **Relevance and value**
   How does the research: a) contribute to knowledge generation? b) Contribute to the improvement of the living standards or the well-being of the community?
   However, researchers may not exploit their participants in the name of knowledge generation and communal benefit.
   Relevance and value of a study/research is usually outlined in the 'Impact of Research' section of a research proposal or ethical application form.

2. **Scientific Integrity**
   This is not an ethical issue on its own. However, a poorly designed method could be detrimental to the researcher and the participant.

Research methods should not expose participants to unnecessary risks. The scientific integrity of a study will be outlined by how data collection methods are designed.

3. Role-player engagement

Researchers should engage key role-players within the community at various stages and, where possible, offset power differentials. This means (where necessary) it is the responsibility of the researcher to seek knowledge of their desired group of participants.

a) Indicate if the desired population is communal or individualistic - meaning - (Can the researcher approach participants without consulting elder/gatekeepers/authority figures?)
b) In the event where a gatekeeper must be approached, the researcher must be forthcoming with information regarding the research and how the researcher intends to share finding of the study/research.

The researcher must be cognisant of power differentials between researcher and participants and must strive towards not being authoritarian with participants.

Where necessary, the researcher must debrief participants as soon as the study/research has been concluded.

Engagement efforts may comprise of various activities, including awareness-raising initiatives for role players, including but not limited to participating communities.

4. Fair selection of participants

Persons should not be excluded or specifically targeted unreasonably or unfairly based on any prohibited grounds for discrimination: race, age, sex, sexual orientation, disability, education, religious belief, pregnancy, marital status, ethnic or social origin, conscience, belief or language.

5. Fair balance of risks and benefits

The potential risk of harm to a participant should be outweighed by the likelihood of obtaining benefits.

Usually, participant who might face undue risk of harm should not be included even if they represent a category of person that may benefit from the research. However, research with such persons may nevertheless be approved after careful review and acceptable justification that demonstrates the anticipated importance and value of the research for society.

6. Informed consent

Participation in research should be voluntary and based on informed choices. Participants must be informed on the nature of their participation and possible risks they may be exposed to, before the research commences. Informed consent forms/ letters/ information sheets should unequivocally state that participants may withdraw from the study without fear of any consequence.

7. Ongoing respect for participants, including privacy and confidentiality

Privacy (who has access to personal information) and confidentiality (measures that prevent the disclosure of information that might identify the participant directly or indirectly). “Dignity is the right of a person to be valued and respected for their own sake, and to be treated ethically.

'Confidentiality' is also about ensuring the appropriate measures will be implemented to prevent disclosure of information that might identify the participant (inadvertently or not) either during the course of the research or afterwards.

The Protection of Personal Information Act 4 of 2013, has increased the need to ensure computer safety, locked record storage facilities and careful gate keeping about access to raw data including completed informed consent documents.

8. Researcher competence and expertise

The Principal Investigator carries the primary responsibility of the research/study and to ensure the well-being of research participants.

Researchers must be suitably qualified and technically competent to carry out the proposed research.
Questions to ask:

a) Is the researcher conducting the study/research in a discipline they are knowledgeable in?
b) Does the researcher have any knowledge of ethics or training in ethics?

Principal Investigators must disseminate research results or findings and have the responsibility to report back to the participants or participant communities where appropriate. (In accordance to the norm of role player engagement and collaboration).