WALTER SISULU UNIVERSITY

FACULTY OF MEDICINE & HEALTH SCIENCES

HEALTH RESEACRH ETHICS COMMITTEE

MANUAL OF STANDARD OPERATING PROCEDURES

Last Edited 23 April 2023 (Under review)

WSU
Walter Sisulu University
In pursuit of excellence

Contents

1. TERMS OF REFERENCE

1.1. The Walter Sisulu University Health Research Ethics Committee (hereafter referred to as HREC) is mandated to fulfil its function by the Senate of Walter Sisulu University through the Faculty of Health Sciences Board to which HREC will report annually in writing.

1.2. The essential purpose of HREC is to protect the dignity, rights, safety, and well-being of all human participants in health-related research. HREC 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.

1.3. The definition of health research used by REC is in accordance with the South African National Health Act No 61. 2003.

1.4. HREC may, accept for review research protocols involving human participants in the Eastern Cape province submitted to it by researchers from other institutions who are not WSU staff members, students or affiliates.

1.5. WSU HREC functions in compliance with, but not limited to, the following documents and guidelines:

- The SA National Health Act. No. 61 of 2003.
- The SA Department of Health (2015) Ethics in health research: Principles, Processes and Structures (2nd ed). Department of Health: Pretoria, South Africa; The SA Department of Health (2020) South African Clinical Trial Guidelines: Good Practice for clinical trials with human participants (3rd ed). Department of Health: Pretoria, South Africa.
- Declaration of Helsinki.
- The Belmont Report.
- The US Office of Human Research Protections 45 CFR 461 (for non-exempt research with human participants conducted or supported by the US Department of Health and Human Services.

1.6. The HREC will not consider research for approval if it has already been conducted. Ethical approval must be obtained before a study commences.

1.7. The HREC, when necessary, will appoint a standing or ad hoc subcommittee to investigate or finalize certain matters under its jurisdiction, in compliance with applicable rules and regulations of conducting research with human participants.

1.8. The HREC will continue to register with NHREC and meet all the necessary compliance and auditory requirements.

2. APPOINTMENT AND MEMBERSHIP

2.1 Appointment

2.1.1. Appointment to HREC will be by nomination by academic departments and co-option in consultation with the people concerned. The total number of members on HREC must be no less than 15.

2.1.2. In the HREC, at least one (1) community member, one (1) religious representative and one (1) legal representative should be members in the committee.

2.1.3. HREC members are appointed, with an appointment letter signed by the Executive Dean of the Faculty of Medicine & Health Sciences, Walter Sisulu University.

2.1.4. On appointment HREC members shall sign a member agreement that stipulates the Code of Conduct for all HREC members.

2.1.5. The Chairperson and the Deputy Chairperson shall be elected by HREC members in a session chaired by the Dean of the Faculty of Medicine & Health Sciences.

2.1.6. Walter Sisulu University has a professional liability and indemnity insurance to cover affiliated and non- affiliated HREC members when carrying out professional duties on behalf of the HREC.

2.2. Membership

2.2.1. The HREC shall:

2.2.1.1. Be constituted of members that collectively possess qualifications and experience to review and evaluate the scientific, psychosocial, legal, medical and ethical aspects of proposed research applications.

2.2.1.2. Have members of good standing, credible with a good understanding and working knowledge of research ethics guidelines and codes.

2.2.1.3. Be representative of communities that it serves.

2.2.1.4. Consider gender equity in terms of membership.

2.2.1.5. Have a Chairperson and two Deputy Chairpersons – Clinical and Basic Sciences. The Chairperson and the Deputy Chairperson will constitute the Executive Committee (Exco) of the HREC.

2.2.1.6. Ensure that members are adequately informed on all matters of research proposals and protocols, including its scientific and statistical validity, ethical relevance that are critical when deciding on approving or not approving approved research.

2.2.1.7. Include at least a member trained and with experience in quantitative and qualitative research methodologies.

2.2.1.8. Consider a quorum of 33.3% of members attending a meeting including at least one non-affiliated member and one non- scientific member (this could be one and the same person).

2.2.1.9. Members not attending three (3) consecutive meetings and not submitting their reviews with no valid reason risk termination of their membership.

2.2.1.10. Have its members serve a term of four (4) years, renewable for two consecutive periods.

2.2.1.11. The HREC may co-opt expert members and other representatives including researchers and students, however, their attendance should be confirmed or approved by the HREC in advance on a case-to-case basis.

2.2.1.12. Ensure that members are empowered continuously to address all considerations arising from research categories likely to be submitted applying for ethics approval.
2.2.1.13. The membership and composition of the HREC will be reflected on the attendance register of the committee.

2.3. Conflict of interest

2.3.1. HREC members shall declare prior interest and/ or relationship in any matter being discussed by the committee to avoid conflict of interest in the HREC decision making, including reviewing proposals/ protocols. This includes business relationship or affiliation, personal involvement to the research or financial interest.

2.3.2. HREC members should make disclosure to the Chairperson before the research protocols get to be discussed.

2.3.3. HREC members who have conflict of interest related to any research up for discussion need to excuse themselves from the meeting. S/he will be called in for clarification.

2.3.4. The decision made in the absence of members who have recused themselves upon their return is not open for further debate.

2.3.5. All HREC members will sign conflict of interest declaration to safeguard the quality and credibility of decisions made about research protocols. During online meetings members having conflict of interest will not participate in the discussions by leaving the meeting and being called after the discussion of the proposals they are conflicted with.

2.4. Confidentiality

2.4.1. Confidential information shall mean certain proprietary, personal, clinical or protocol-specific information, discussions and decisions of the committee. Such information includes protocols relating to research with human participants and associated documentation. The confidential information may be conveyed in written, graphic, oral or physical form including (but not limited to) scientific knowledge, skills, processes, inventions, techniques, formulae, products, business operations, patient requirements, biological materials, designs, sketches, photographs, drawings, specifications, reports, studies, findings, data, plans or other records, and/or software.

2.4.2. All HREC members and support staff shall sign a standard confidentiality and non-disclosure agreement on appointment to HREC.

2.5. Training, education, and continuous professional development

2.5.1. Training of HREC members and staff is essential for the committee to fulfil its mandate to protect the rights and wellbeing of research participants in studies conducted by the institution.

2.5.2. The HREC members and staff responsible for reviewing, approving and overseeing research involving human participants must receive annual training in the guidelines, regulations, ethics, policies and laws applicable to such research. The training must be fully funded by the management of HREC. WSU will be responsible to provide funding.

2.5.3. The HREC chairperson and/or HREC administrator will provide new HREC members and staff with a general overview of relevant institutional, national and international policies and SOPs pertinent to HREC functions and responsibilities.

2.5.4. New HREC members will receive an orientation package. Before beginning their formal duties on the HREC, members are expected to read and familiarise themselves with the information in the orientation package.

2.5.5. The orientation package will include the following at the very least:

2.5.5.1. All SOPs and terms of reference (TOR) outlining the procedures and functions of the HREC.

2.5.5.2. Department of Health 2015. Ethics in Health Research (2015, DOH South Africa);

2.5.5.3. Letter of appointment

2.5.5.4. Member agreement form

2.5.5.5. Reviewer checklist template

2.5.6. All members will go through an orientation session on appointment to the HREC.

2.5.7. All members are required to undergo and complete the TRREE online ethics training course within six (6) months of joining the HREC and for continued development.

2.5.8. All members should be kept updated with recent developments in the area of research ethics and science, members are assisted through the HREC office for continued GCP training and other research ethics courses as per availability of resources. HREC chair and administrators keep records.

2.5.9. Management level staff and members of the HREC involved in overseeing experimental work and research involving human participants will receive initial and ongoing training regarding responsible review and oversight of research and the policies and procedures that accompany such activities.

2.5.10. The HREC chairperson and administrator, in consultation with the REC members and Faculty Dean, should establish the educational and training requirements for REC members who evaluate and review biomedical and behavioural research. Initial and ongoing training must be provided and documented by the REC administrator.

2.5.11. All HREC members are to participate in the initial and ongoing training and education in areas critical to their areas of responsibility.

2.5.12. HREC chair and administrator will receive additional training and education in areas germane to their additional responsibilities.

2.5.13. HREC members and staff are encouraged to attend workshops and other educational opportunities focused on HREC functions. The Faculty of Health Sciences and Walter Sisulu University should support such activities to the extent possible at all times.

2.5.14. **Conferences.** HREC members and staff are encouraged to attend national and international conferences focusing on human participant research protection and biosafety such as the International Conference on Ethics Education, the PRIM & R Advancing Ethical Research Conference, and the Annual Biological Safety Conference.

2.5.15. **Workshops and Seminars.** HREC members are encouraged to attend, either in person or via webinars, other relevant local and international workshops and educational sessions pertinent to their role as research ethics and biosafety reviewers and evaluators.

2.5.16. Conferences, workshops and seminar attendance may be funded by the HREC depending on the availability of funding. Members who receive sponsorship from HREC are required to attend any of the above educational events and will be required to give a presentation to HREC members and staff at the next HREC meeting.

2.5.17. All evidence of training and continuing education of HREC members and staff should be documented and stored in the HREC document repository.

3. APPLICATION AND ADMINISTRATIVE REQUIREMENTS

3.1. Procedure for HREC application: new research

3.1.1. Application forms and guidelines can be accessed from the Research Development and Support Office, Administration Building, Faculty of Health Sciences, Medical School, Sisson Street Fort Gale Mthatha.

3.1.2. Forms, templates and guides are available on the website of Walter Sisulu University and the link is: https://www.wsu.ac.za/index.php/health-sciences-research-ethics-biosafety-committee

3.1.3. Applications for HREC approval of research can be submitted on a rolling basis by email.

3.1.4. The dates of meetings are available from the Research Development and Support office from the administrative team and on the WSU website (link mentioned above).

3.1.5. On submission the application form must be signed by the applicant, supervisor and head of department accompanied by a full proposal/ protocol, participant information document, informed consent document, all translated into a local language as per requirements of the study, a short CV of the principal investigator, budget and financial contract, and investigator declaration of all investigators.

3.1.6. The application must also be accompanied by a risk assessment checklist accessible from the WSU HREC link on the WSU website.

3.1.7. For clinical trials the following documents should be attached to the protocol:

3.1.5.1. Cover letter

3.1.5.2. Flow chart

3.1.5.3. A description of the study site, including the available infrastructure and the roles and responsibilities of study staff
3.1.5.4. South African Health Products Regulatory Authority (SAHPRA) approval or proof of application (if applicable)
3.1.5.5. NHREC approval or proof of application
3.1.5.6. Proof of insurance for participants
3.1.5.7. Material for distribution to patients, including diary cards,
3.1.5.8. Recruitment material and advertisements (if applicable)
3.1.5.9. Proof of GCP training
3.1.5.10. SA approved package insert(s) of registered comparators of the drug under investigation
3.1.5.11. Investigator's brochure
3.1.5.12. Evidence of registration with HPCSA under investigation

3.2. HREC Review Fees

3.2.1. The HREC has a graded administrative fee structure in place, which is revised annually.
3.2.2. The HREC needs funding to cover the following:
3.2.3.1. Administration of the secretariat including remuneration of the secretarial staff and purchase of consumables.
3.2.3.2. Monitoring of studies particularly clinical trials including conducting of study site visits.
3.2.3.3. Transport allowance to HREC members representing the community.
3.2.3.4. Organization of courses, seminars and workshops for members and the larger University community.
3.2.3. The HREC has a review fee structure that gets to be revised on an annual basis.
3.2.4. Exempted from paying review fees are:
3.2.4.1. Non- sponsored student research for degree purposes.
3.2.5. A current fee structure is available at the Research Development & Support office.
3.2.6. The HREC reserves the right to not review a proposal/ protocol or withhold an ethics clearance certificate when a review fee has not been settled.
3.2.7. The investigator needs to submit a completed and signed payment instruction form with the application for a new project, progress report, amendments etc.
3.2.8. You/your sponsor will receive a HREC invoice.
3.2.9. Proof of payment should be submitted with all applications.
3.2.10. HREC fees for funded research projects will be decided on an annual basis and charged according to the type of the proposed research:
3.2.10.1. Clinical trials
3.2.10.2. Funded not for degree purposes research projects.
3.2.10.3. PhD

3.2.10.4. Masters
3.2.10.5. Honours and postgraduate research
3.2.10.6. Undergraduate research
3.2.11. Fees for unfunded research will be wavered.

3.3 Review Process: New research

3.3.1. The HREC will receive applications after they have undergone scientific review by the Research Innovation and Higher Degrees Committee and certified as scientifically sound.
3.3.2. The following documents should be submitted as part of the application:
3.3.2.1. Human ethics application form.
3.3.2.2. Copy of the research proposal or research protocol.
3.3.2.3. Short CV of the investigator/s
3.3.2.4. Investigators' declarations
3.3.2.5. Source of funding for the project
3.3.2.6. Participant information document (translated where necessary)
3.3.2.7. Consent document (translated where necessary)
3.3.2.8. Proof of insurance (if necessary)
3.3.2.9. Recruitment material and advertisements (if to be used)
3.3.2.10. Itemised budget for research project
3.3.2.11. Action plan for the project
3.3.3. Application must be submitted prior to the agenda closure date. These dates are available at research ethics office.
3.3.4. Documents will be checked for completeness by the administrative team.
3.3.5. The HREC will review all applications within a reasonable time.
3.3.6. All protocols for full review must be submitted to the HREC offices during the first 10 days of each month to be discussed in the following meeting to be held on the last Wednesday of each month.
3.3.7. All protocols for full review will be allocated to two HREC members for ethics review.
3.3.8. Each protocol will be discussed at a convened quorate HREC meeting at which a majority of the members of HREC are present, including at least one member whose primary concerns are in non-scientific areas.
3.3.9. For all non-expedited reviews, all committee members will receive copies of the HREC application form and the review comments form to be ready for the meeting's deliberations.
3.3.10. At the HREC meeting the primary reviewer will give a synopsis as well as the positive and negative aspects of the proposed research and make a recommendation thereof.
3.3.11. The committee attempts to reach a decision by consensus. If a consensus is not reached, then the HREC will vote on a proposal as summarised by the chairperson:
3.3.11.1. Approval with no changes

3.3.11.2. Provisional approval (project can be finalised without having to serve before the HREC again).
3.3.11.3. Deferred (to be reconsidered after changes at a full HREC sitting).
3.3.11.4. Rejected
3.3.12. The secretary records all the decision in the minutes and the methods by which they were made.
3.3.13. Minutes of all discussion points, issues of controversy and all decisions are recorded by secretary, also document any member leaving or entering during the meeting, in order to record ensure that a quorum is always present.
3.3.14. The chairperson closes the meeting.
3.3.15. Post meeting decision taken at the HREC meeting with respect to each new research application are communicated in writing to the applicant. It is not unusual for the committee to request some changes to the project, or information and consent form, or clarification of certain issues. Only once these requirements are fulfilled, will a formal letter of ethical approval be issued.
3.3.16. Minutes will be recorded and written up by the secretary and usually given to the research ethics manager or chairperson to check.
3.3.17. The secretary will send feedback letters to all principal investigator/s or applicant detailing the committee's decision regarding the research study and also detailing any request for alterations to be made.
3.3.18. Investigators can address any queries to the HREC administrator or research ethics manager or, who will attempt to resolve problems and liaise with the chairperson when necessary.
3.3.19. It is the responsibility of the investigator to comply with all requests and return the requested documentation with a covering letter, to the HREC as soon as possible but not later than 3 months from the date of issue. The application will be cancelled if no feedback is received by 6 months (with a reminder in between).
3.3.20. All queries should be addressed in a letter. All requested protocol and informed consent form (ICF) changes must be clearly marked. The tracked changes facility on your word processor should be used.
3.3.21. The primary evaluator (or another HREC member, if requested to do so by the primary evaluator of chairperson) will carefully check all amended documentation, including patient information and consent forms.
3.3.22. If correct, the said documentation will be forwarded to the chairperson for final approval.
3.3.23. If not corrected the primary reviewer or HREC administrator/s will liaise with the investigator and attempt to assist in the process of finalising the application as soon as possible.

3.4. Expedited Review

3.4.1. A review of a protocol with minimal risk to the human participants.

3.4.2. Criteria for approval by expedited review are the same as those of the full committee and the expedited review should be as substantive and rigorous as that of the convened meeting.

3.4.3. The Chairperson or Deputy has the final responsibility for which new protocols, continuing reviews and amendments are eligible for expedited review and has the authority to designated one or more experienced committee members to perform an expedited review.

3.4.4. No member with a conflict of interest may serve as a reviewer for any expedited item.

3.4.5. A monthly report of all research approved through an expedited procedure is distributed to members before the full committee meeting.

3.4.6. Types of research that may undergo expedited review include:

3.4.8.1. Research classified as no greater than minimal risk, depending on the details of the study.

3.4.8.2. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinary encountered in daily life or during the performance of routine physical or psychological examinations.

3.4.8.3. Annual renewals of studies that initially qualified for expedited review or were determined to be minimal risk at a convened committee meeting, provided no serious adverse events or ethical problems have occurred.

3.4.8.4. Amendments to previously approved research where changes to the study protocol or consent document do not results in significantly increased risk to participants.

3.4.8.5. When, in the chairperson's opinion, using an expedited procedure would be in the public interest.

3.4.8.6. Studies deemed as minimal risk include undergraduate and honours studies with minimum risk as defined in 3.4.8. will follow that category.

3.4.7. Applications for expedited reviews may be accompanied by a motivation letter justifying requesting minimal risk review.

3.4.8. The HREC does not consider clinical trials, multi-centre and international grant funded research as qualifying for expedited reviews.

3.5. Review Process: Continuing Review

3.5.1. Routine continued review (progress reports)

3.5.1.1 International and local guidelines and regulations [Dept. of Health, ICH GCP, SA GCP, SAHPRA and 45 (United States of America Code of Federal Regulations) CCFR 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.

3.5.1.2 The HREC will conduct continuing reviews of each ongoing study at intervals appropriate to its risk level to human participants. This has to be at least once a year.

3.5.1.3 Ethics clearance is valid for a period of a year and has to be renewed at least two months before it expires.

3.5.2 Progress reports:

3.5.2.1 All clinical trials falling under the jurisdiction of the SAHPRA must submit a progress report to the SAHPRA six monthly. Copies of these SAHPRA progress reports should accompany the annual progress report submitted to the HREC. Please do not submit your 6 monthly MCC progress report outside of this annual reporting to our HREC, unless necessary for safety reasons.

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

3.5.2.3 The progress report should contain sufficient information to allow the reviewer to conduct a substantive and meaningful review of the progress of the project, including any challenges or problems encountered.

3.5.2.4 An updated complete protocol, incorporating all approved amendments should be submitted approximately every three years unless there have been no, or minimal changes to the project.

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

3.5.2.6 Information that must be included in the progress report:

- For multi-site studies: For each of the reporting requirements listed below, the PI must report specifically for the local site(s), while putting these local reports into perspective by reporting them relative to the larger study:
- the number of participants recruited.
- a summary of any unanticipated problems and available information regarding adverse events
- a summary of any withdrawal of participants from the research since the last HREC review.
- a summary of any complaints about the research since the last HREC 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 HREC review.
- any relevant multi-centre trial reports.
- any other relevant information, especially information about risks associated with the research.
- A copy of the current informed consent document and any newly proposed consent document.

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

3.5.2.8 Progress reports must be submitted to the HREC annually until such time as the investigator submits a final study report (this includes the premature completion of the study) and/or a notice of termination of the study.

3.5.2.9 If a research project was eligible for expedited review when initially approved, the continuing review may occur via an expedited process.

3.5.2.10 If the researcher does not provide continuing review information to the HREC or the HREC has not approved a protocol by the expiration date, approval will lapse and the investigator will have to provide a reason for such delay and suspend all activities till such time that the study's ethics clearance has been extended.

3.6. Protocol Amendments

3.6.1 In line with local and international prescripts and guidelines, amendments to an approved protocol may become necessary as the research project continues.

3.6.2 The HREC must review and approve all proposed protocol amendments before the amendment is implemented in the study.

3.6.3 Amendments can be defined as planned changes to an approved study protocol, made in advance.

3.6.4 Amendments may be classified as minor or major. Minor amendments do not change the risk profile of the study in any way. These include additional Investigators or study sites, small changes in the Informed Consent, Change in background information or update of literature review, Extension of period of study, administrative changes as well as more stringent inclusion or exclusion criteria.

3.6.5 Major amendments require a change(s) to the study methodology or procedure that may result in an alteration of the risk benefit profile of the study. Major amendments include: Change in study aims, objectives or design, Additional study procedures, as well as less stringent inclusion or exclusion criteria.

3.6.6 HREC will decide whether any significant new findings that arise from the review process related to participants' willingness to continue participation are provided to participants. Applications must be accompanied by an informed consent form.

3.7. Protocol deviations

3.7.1 A protocol deviation is a "once off" instance when, for some reason, the protocol is not followed e.g. the protocol states that only people over the age of 18 will be enrolled. However, a participant, aged 17 years and 6 months meets all admission criteria and is deliberately enrolled in this study.

3.7.2 Protocol deviations can also happen when errors are made e.g. the wrong follow up date is given and thus follow up occurs outside of a specified time frame.

3.7.3 Protocol deviations can be classified into major and minor deviations.

3.7.3.1 Major deviations are those that affect safety, condition and status of the research participant; affecting the scientific integrity and/or validity of the study data; pose a significant risk of harm to the research participant; changing the balance of risks and benefits of the research; a wilful breach of ethical and/or regulatory policies; and/or involving a serious and/or continuing non-compliance with institutional, ethical and/or regulatory policies.

3.7.3.2 Minor deviations may include patient visits outside a protocol window period, study procedure missed or conducted out of sequence as well as missing pages of a completed informed consent form.

3.7.4 If the deviation is planned, submission to the HREC must be done for review and approval or not before the deviation gets to be implemented.

3.7.5 For an unplanned deviation, as soon as it is identified in the study, it must be reviewed, documented and categorized as major or minor by the investigator.

3.8. Unanticipated problems involving risks to research participants/ others including adverse events

3.8.1 The REC needs guidance on the requirements and timelines for reporting on Adverse Drug Reactions (ADR) and Serious Adverse Events (SAE) in research with human participants. These can be defined as follows:

3.8.1.1 Adverse Drug Reaction (ADR): In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reaction(s). The phrase," responses to a medicinal product "means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function.

3.8.1.2 Adverse Event (AE): Any untoward or unfavourable medical or psychological occurrence in a clinical trial participant or clinical investigation participant administered a pharmaceutical product and which does not necessarily have a causal relationship with the treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product or any other intervention, whether or not related to the medicinal (investigational) product or any other intervention.

3.8.1.3 Unexpected adverse event: Is an event whereby the specificity or severity is not consistent with the current Investigator's Brochure or package insert, is inconsistent with the risk information in the current protocol application and the event is occurring more frequently than anticipated.

3.8.1.4 Serious Adverse Event (SAE): An event in research that is associated with death, admission to hospital, prolongation of a hospital stay, requires medical or surgical intervention to prevent permanent impairment or damage, inadvertent disclosure of confidential information if this presents immediate risk to a participant, persistent or significant disability or incapacity, or is otherwise life-threatening, in connection with the clinical trial but not related to the investigation product.

3.8.2 Serious Adverse Drug Reaction (SADR): refers to any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation

of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

3.8.3 Reporting:

3.8.3.1. Serious Unexpected adverse events: Principal Investigator/s must report to the HREC immediately followed by documentation within **seven days** of the site knowing of the event(s). Unexpected non- fatal Adverse Drug Reactions: Principal Investigators must report to the HREC within fifteen days of the occurrence of the non-fatal adverse drug reaction.

3.8.3.2. Expected Adverse Drug Reactions: Principal Investigators must report to the HREC within fifteen days of the occurrence of the expected adverse drug reaction.

3.8.3.3. Adverse drug Reaction: The sponsor should expedite the reporting to all concerned investigator(s)/institution, to the HREC where required, and to the regulatory authority(ies) of all adverse drug reactions (ADRs) that are both serous and unexpected.

3.8.3.4. 3.8.8.4. Such expedited reports should comply with the applicable regulatory requirement(s) and with the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.
The sponsor should submit to the REC and other regulatory authorities all safety updates and periodic reports, as required by applicable regulatory requirement(s).
3.8.8.5. Serious Adverse Events or Drug reaction expected or unexpected: The principal investigator must inform the REC and the sponsor, within the time specified in the protocol, of any serious or unexpected adverse events occurring during the study.

3.8.8.6. The initial serious adverse event or drug reaction report form and any relevant follow-up information should be sent to the sponsor, who in turn should forward the relevant information to the HREC and the SAHPRA within 15 days.
3.8.8.7. The timeframes and format for reporting of serious adverse events, adverse events and drug reactions are described in the SAHPRA guidelines and should be strictly adhered to.

3.8.8.8. Investigator to report to the sponsor, HREC and participants immediately for Serious Adverse Drug Reaction and Serious Unexpected events using the appropriate SAHPRA form for reporting. The sponsor should expedite the reporting of all adverse drug reactions (ADRs) that are both serous and unexpected to all concerned, including investigator(s)/institution(s), BRE and SAHPRA.

3.8.8.9. The expedited reporting should occur within the timeframe and format specified by the SAHPRA. Serious unexpected adverse events suspected to be related to the investigational product/s or investigation procedures should be reported to the REC as soon as possible, and in line with the requirements of the SAHPRA adverse events reporting guideline.
3.8.8.10. If the study is multi-centred, the sponsor should ensure that all serious and

unexpected adverse drug events that occur in other study sites are also reported without delay on a six-monthly basis to all appropriate parties including, investigator(s), RECs, and to the SAHPRA. The sponsor is responsible for the ongoing safety evaluation of the investigational product(s). The sponsor should promptly notify, in writing all concerned investigator(s) and the SAHPRA and HREC of findings that could affect adversely the safety of participants, impact the conduct of the trial, or alter the ethics committee's approval/favourable opinion to continue the trial. Study participants should also be informed of any new information that could adversely affect their safety. (ICH E6 GCP guidelines subsection 4.11 Safety Reporting)

3.8.8.11. All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify participants by unique code numbers assigned to the trial participants rather than by the participants' names, personal identification numbers, and/or addresses.

3.8.8.12. The investigator should also comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority(ies) and the HREC.

3.8.8.13. Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor and the HREC according to the reporting requirements and within the time periods specified by the sponsor in the protocol. For reported deaths, the investigator should supply the sponsor and the HREC with any additional requested information (e.g., autopsy reports and terminal medical reports).

3.8.8.14. HREC will collaborate with SAHPRA and other relevant regulatory bodies for the course of action to take, depending on the outcome of the investigations. These may include but not limited to:

a) Revise the protocol.
b) Modify exclusion and inclusion criteria to investigate the newly identified risk.
c) Suspend enrolment of new participants
d) Suspend procedures in the currently enrolled participants.
e) Modify informed consent documents to include description of newly identified risks
f) Provide details about newly identified risks to previously enrolled participants.
g) Suspension of HREC approval
h) Terminate HREC approval.

3.9. Communication of Review decisions

3.9.1 The HREC has to ensure that investigators are appropriately informed about HREC review decisions.

3.9.2 Decisions taken at an HREC meeting, or via a minimal risk review process, are communicated in writing to the applicant.

3.9.3 Investigators can address any queries to the HREC office, which will attempt to resolve problems and liaise with the Chairperson when necessary.

3.9.4 The average turnaround times for notifying research applicants of the review outcome are 5-6 weeks for full committee review after the HREC submission deadline.

3.9.5 For expedited reviews the turnaround time is 3-4 weeks after the REC submission deadline. NB: *These expected turnaround times apply to research applications that are scientifically and ethically sound*.

3.9.6 All HREC approval letters are issued manually and signed by the HREC Chairperson.

4. INFORMED CONSENT

4.5 The ethical principle of respect for persons requires that participants be given the opportunity to choose what may or may not happen to them. In the research context, the REC views the informed consent process between the researcher and the potential participant as the primary mechanism for securing a participant's consent. For the informed consent process to be valid, participants must receive sufficient and relevant information about the research; must understand this information and must voluntarily choose whether to take part or not. Documentation must be written in layperson's language.

4.6 Except as provided elsewhere in this document, no investigator may involve a human being as a participant in research covered by this policy unless the investigator has obtained the legally effective informed consent of the participant or the participant's legally authorized representative, where appropriate. Written informed consent should always be obtained unless an alternative process is adequately justified and approved in advance by HREC (WSU Health Research Committee). The alternative could always be stated in the proposal e.g., thumb print. The process of recruitment and documentation of informed consent must be described clearly and in detail in the study protocol.

4.7 Elements of Informed Consent include:

4.7.1 A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the participant's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

4.7.2 A description of any benefits and/ or risks to the participant or to others which may reasonably be expected from the research.

4.7.3 A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant.

4.7.4 A statement describing the extent to which confidentiality of records identifying the participant will be maintained.

4.7.5 For research involving more than minimal risk, a statement that the researcher and/or sponsor will adhere to the South African Good Clinical Practice Guidelines (SAGCP Section 4.11: Compensation to participants); an explanation that there is a risk that the study medicine(s) or procedure(s) may cause harm and if so. How this risk will be managed and reported to HREC (See Adverse events SOP, mentioned in 3.8.).

4.7.6 Explanation of how participant will be compensated for their time and inconvenience and reimbursed for any expenses related to the research if it involves any other additional costs for participants.

4.7.7 An explanation of whom to contact for answers to pertinent questions about the research and research participants' rights, and whom to contact in the event of research-related injury to the participant (See Adverse events SOP). Contact person- Chairperson of Ethics committee.

4.7.8 When the participants want to know more about the research, they should consult the principal investigator.

4.7.9 A statement that participation is voluntary and that refusal to participate will involve no penalty or loss of benefits or reduction in the level of care to which the participant is otherwise entitled.

4.7.10 A statement that the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.

4.8 Additional Elements of Informed Consent

4.8.1 Research Ethics Clearance number.

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

4.8.2.1 A statement that the particular treatment or procedure may involve risks to the participant (or to the embryo or foetus, if the participant is or may become pregnant) which are currently unforeseeable.

4.8.2.2 Anticipated circumstances under which the participant's participation may be terminated by the investigator without regard to the participant's consent.

4.8.2.3 The consequences of a participant's decision to withdraw from the research and procedures for voluntary termination of participation by the participant.

4.8.2.4 The approximate number of participants involved in the study.

4.9. Obtaining informed consent

4.9.1 Those obtaining informed consent must be appropriately trained and authorised to do so by the Principal Investigator (PI). Questions from participants should be answered as relevant to the team member’s qualification and noted in research information sheet. Information may be given in a group however consent should be obtained in a private place so that participants can voice questions and concerns in confidence.

4.9.2 The participant (and impartial witness in cases of illiteracy) should be given provided information in his/her choice of language.

4.9.3 Should consent be given, the investigator and the participant (or witness) sign and date an original consent form together. Illiterate participants may also mark in place of a signature. This document is filed in the investigator's file with a copy (or further original) provided to the participant and another placed in the medical records. Should the participant not have medical records or refuse his/her consent documents it will be stored in the investigator file with a note to that effect.

4.10. Consent requiring additional attention.

4.10.1 Vulnerable groups:
- 4.10.1.1 Children
- 4.10.1.2 Mentally incapacitated or substance-abuse disorders
- 4.10.1.3 Highly dependent on medical care (e.g., intensive or emergency care)
- 4.10.1.4 Incarcerated (Prison)
- 4.10.1.5 Refugees

4.10.2 Any adaptations should be fully documented.

4.11. Documentation of Informed Consent

4.11.1 Informed consent must be documented using a written consent form approved by HREC and signed by the participant or the participant's legally authorized representative. In addition, the researcher must document the informed consent process in the research information sheet.

4.11.2 Once the participant has agreed to participate, the original signed informed consent form must be kept at the investigator site. This information sheet must be left with the participant.

4.11.3 Clinical trials and Novel therapies (Innovative) require SAHPRA registration, REC approval certificate and EC DOH certificate to conduct study, however, other research do not need SAHPRA registration.

4.12. Translation of the participant informed consent document

4.12.1 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.
- 4.12.1.1 Format: visual cards, braille, audio
- 4.12.1.2 Language: isiXhosa, Afrikaans, etc.

4.12.2 In the Eastern Cape informed consent should generally be available in 2 languages: English and translated to a local language.

4.12.3 Before approval of the proposed consent documentation, HREC 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.

4.12.4 Consent documents may be submitted for HREC approval, in either English and/or local language. Once the original document is approved it is the responsibility of the investigator to arrange for translations of the forms into other languages, where appropriate. A proficient translator must be assigned to this task. Local language translations should preferably be done 'back-to- back' i.e., English to local language and back to English, by different translators. If the research is to be conducted elsewhere in South Africa, other translation requirements may be applicable.

4.12.5 To ensure a content focused quality instrument that is trusted to offer accurate information, three steps for translation are recommended:

4.12.5.1 **Forward translation**: this involves translation from language of research to local language by a translator whose first language is the local language.

4.12.5.2 **Back translation**: this involves translation from local language back to language of research and preferably to be done by a different translator.

4.12.5.3 **Reconciliation**: this will involve comparison of the two versions of translated documents to ensure discrepancies are minimised.

4.12.6 Where the tools have technical language used in specific disciplines, translator who has a sector-specific knowledge with the researched topic (preferably a professional in that field) must be used for translation. High risk (invasive procedures, clinical trials, etc) research studies need an expert translator with forward and back translation certificates provided. Medium to low risk (questionnaire based) does not require an expert translator.

4.13. Variation of Consent Procedures (Expedited consent)

4.13.1 HREC may approve a consent procedure especially research involving *undergraduate students* which does not include, or which alters some or all, the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided HREC finds and documents that:

4.13.1.1 The research involves no more than minimal risk to the participants.

4.13.1.2 The waiver or alteration will not adversely affect the rights and welfare of the participants; (Waiver of consent- Retrospective record review or pathology results does not require consent.)

4.13.1.3 Waiver of consent must be justified. Even when a research project is eligible for a waiver of informed consent, the waiver must normally be given by the HREC. Researchers may not decide by themselves that their projects fulfil the criteria for a waiver. Researchers should explain why a waiver is justified to the satisfaction of the HREC.

4.13.1.4 The research could not practicably be carried out without the waiver or alteration; and

4.13.1.5 Whenever appropriate, the participants will be provided with additional pertinent information after participation.

4.14 **Biobank**: Secondary use of biological material e.g., Biobanking store for future use:

4.14.1 For research on human materials and personal information, researchers should ensure that the samples and data are anonymized, or coded, so that the source persons cannot be identified, even when the biobanks or databases are linked to other ones.

4.14.2 If anonymization is not possible (e.g., for DNA samples), then researchers must ensure their confidentiality of the samples, to protect both the source persons and their genetic communities (who can be harmed by stigmatization based on genetic characteristics and susceptibilities).

4.14.3 As with any other type of research, informed consent is a normal requirement for research on identifiable human material or personal data. As the 2008 Declaration of Helsinki, paragraph 25, states: "For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse."

4.14.4 It is preferable that potential research participants be informed in advance about any possible future uses of their materials or data so that it will not be necessary to re-contact them when another such use is proposed.

4.14.5 This is especially important when the materials will be stored in a biobank, or the personal health information in a database, that can be accessed at any time in the future.

4.14.6 When the materials in biobanks and the information in databases are anonymized and aggregated, it is often impossible to identify the source persons from whom to ask informed consent for new uses.

4.14.7 This is especially true for biobanks and databases that were established in the past when informed consent for future uses was not sought.

4.14.8 HREC may decide to enforce the informed consent requirement strictly and refuse to approve any research for which informed consent is not possible.

4.15. Verbal consent

4.15.1 When is it Used? Obtaining verbal consent in place of written consent may be the only feasible method to obtain consent from participants in some instances. For example, this method may be helpful when recruiting participants and completing screening surveys over the phone. In order to use verbal consent in place of written consent, your study must meet one of the criteria for a waiver of written consent (Ref. 4.1.3).

4.15.2 What is Required if Using Verbal Consent: When this method is used, the REC must approve a written summary (i.e., information sheet) of what is to be said to the participant or the representative. The researcher obtaining verbal consent must sign and date the information sheet to document each participant's consent. Note: the information sheet should include the required elements found in a consent document. View the Consent Form Checklist to review the required elements.

4.15.3 If verbal consent is the only method for obtaining consent for a particular study (i.e., study will not obtain written consent from participants at a later date), there must be a witness to the oral presentation and verbal consent. Both the witness and researcher obtaining verbal consent must sign and date the written summary (i.e., information sheet) to document each participant's consent.

4.15.4 Research team and participants cannot witness.

5. Compliance

5.5 Definition: Adherence to all the trial-related requirements, protocol and SOPs or applicable regulatory requirements (National Health Authority).

5.6 Compliance with protocol

5.6.1 The investigator/institution should conduct the trial in compliance with the protocol approved/agreed upon by sponsor and REC and as required by regulatory authority(ies). The investigator/institution and sponsor should review and sign the protocol before submission to HREC, or contract to stipulate and confirm commitment to adhere to submitted protocol.

5.6.2 The investigator/institution should not implement any deviation from, or changes to the protocol without agreement by the sponsor(s) and prior review and documented approval from REC of an amendment, except where necessary to eliminate an immediate hazard(s) to trial participants, or when changes involve only logistical/administrative aspect of the trial e.g., changes to telephone numbers, or to monitors.

5.6.3 The investigator or person designated by the investigator must document and explain any deviation from the approved protocol.

5.6.4 Investigator(s) may implement a deviation from, or a change of the protocol to eliminate an immediate hazard(s) to trial participants without prior REC approval. Such implemented deviation, the reason for the deviation and if appropriate the proposed protocol amendment(s) should be submitted within 2 weeks of incidence to:

a) HREC for review and approval
b) Sponsor(s) for agreement if required.
c) The regulatory authority(ies)

5.7. Noncompliance

5.7.1 Any persistent intentional/ unintentional deviation from protocol that may /may not affect the participants' rights, safety or welfare; and/or on the integrity of the data.

5.7.2 Noncompliance with the protocol, SOPs, GCP, and/or applicable regulatory requirement(s) by an investigator/institution, or by member(s) of the sponsor's staff should lead to prompt action by the sponsor/ REC to secure compliance.

5.7.3 If noncompliance that significantly affects or has the potential to significantly affect human participant protection or reliability of trial results is discovered, the sponsor should perform a root cause analysis and implement appropriate corrective and preventive actions.

5.7.4 If the monitoring and/or auditing identifies serious and/or persistent noncompliance on the part of an investigator/ institution, the sponsor should terminate the investigator's/ institution's participation in the trial. When an investigator's/ institution's participation is terminated because of noncompliance, the sponsor should notify promptly the regulatory authority(ies) and HREC.

6. MONITORING THE PROGRESS OF STUDIES THAT HAVE BEEN GRANTED ETHICS APPROVAL

6.1 Monitoring progress of studies granted ethics approval by the HREC as well as getting timely safety reports on the participants of the study is very important. This is also a mechanism of granting researchers permission/ clearance to continue with their research for a further year.

6.2 After the investigator has fulfilled all the requirements for ethics approval, the WSU HREC will issue the investigator(s) with the Ethics Approval certificate. This certificate will allow the investigator(s) to proceed and seek permission to conduct the study from relevant authorities.

6.3 Before commencement of the study, the investigator(s) must present to the WSU HREC a copy or copies of permission to conduct the study from relevant authorities such as the National

Department of Health (NDOH), the Eastern Cape Department of Health (ECDOH), and the South African Clinical Trial Register (SACTR) where applicable with their first study progress reports to the HREC. This information will be communicated to the investigator (s) when the HREC sends them their ethics clearance certificate.

6.4 The HREC will remind all investigators two months before the due date to submit their progress (6-monthly and/or annual) report. When the reminder is sent to the investigators, a copy of the progress report template will be attached.

6.5 Undergraduate and Honours research projects may be exempted from submitting final research reports to the HREC.

6.6 Passive monitoring that involves submission of a monitoring report to the HREC as set out as terms during the approval process of the protocol will apply as follows:

6.6.1 Minimal risk studies will submit annual/ final reports.

6.6.2 Medium and high-risk studies will submit six- monthly reports.

6.7 Active monitoring applies mainly to high-risk and/ or clinical trials as follows:

6.7.1 Random study site visits for inspection of the approved research documents and processes, recorded individual interviews/ focus group proceedings, and verification that approved informed consent documents and data collection tools are used appropriately.

6.7.2 Verification that experiments and other procedures are conducted as per approved procedures.

6.7.3 To verify that study records are filed as required and according to study SOPs.

6.8 For all randomized controlled trials (RCT) involving medications and other therapeutic agents, the researcher(s) is (are) required to attach the certificate of approval of the therapeutic agent from the SAHPRA at the time of submission of the project to the HREC for Ethical approval.

6.9 The HREC may appoint a monitoring committee for site visits to check compliance with ethical conduct of the research as outlined in sections 6.12 and 7.12 of the South African Department of Health Good clinical practice guidelines of 2019 Third Edition and the National Health Act, 2003 (Act No.61 of 2003).

6.10 The essence with randomised clinical trials is to monitor compliance with approved protocols and SOPS and provide a written report to HREC focusing on the following:

6.10.1 The investigators and sub-investigators

6.10.2 The participants

6.10.3 The investigational product

6.10.4 Communications between study site and HREC, sponsors, SAHPRA.

6.10.5 Documentation

6.10.6 Report of monitoring visit

6.11 Monitor investigators and sub-investigators:

6.11.1 Check that only approved investigators as contained in the trial protocols and SOPS are conducting the study.

6.11.2 Check for current and valid GCP certificate for investigators, sub-investigators and other staff directly involved in the trial.

6.11.3 Check that investigators, sub-investigators and other staff directly involved in the trial are only performing functions allocated to them as per approved protocols and SOP.

6.12 Monitor participants:

6.12.1 Check subject screening forms for compliance with inclusion and exclusion criteria.
6.12.2 Confirm that only eligible participants are enrolled into the study.
6.12.3 Check that randomization is documented.
6.12.4 Check documentation of withdrawals and dropouts and the reasons.
6.12.5 Check for clear and complete documentations of adverse events.

6.13 Monitor for investigational product [IP]
6.13.1 Check that someone is in-charge of the IP.
6.13.2 Check that the IP is available, adequate, not expired and properly stored.
6.13.3 Check that eligible subjects receive the IP as per protocol specified doses.
6.13.4 Check that subjects are provided with the necessary instruction on using, storing and returning unused IP where applicable.
6.13.5 Check that there is documentation of receipt, use and return of the IP.
6.13.6 Check that disposal of the IP at trial sites follows regulatory requirements.

6.14 Monitor communications between study site and REC, sponsors, SAHPRA:
6.14.1 Check that investigators provide regular reports to REC, sponsors, SAHPRA as per contained in protocol.
6.14.2 Check that all adverse events are reported to REC, sponsor, SAHPRA with outcomes and actions taken by the investigator.
6.14.3 Check that all protocol deviations are clearly recorded with explanations and are reported to HREC, sponsor, SAHPRA.

6.15 Monitor documentation:
6.15.1 Peruse the following documents:
6.15.2 All versions of protocols inclusive of amended versions.
6.15.3 Current Ethics certificate.
6.15.4 Current GCP certificate of all site investigators and staff involved in the trial.
6.15.5 Participant information sheets
6.15.6 Screening forms.
6.15.7 Signed consent forms.
6.15.8 Completed source documents.
6.15.9 Completed case report forms.
6.15.10 Investigational product brochure.
6.15.11 SAPHRA approval for IP.
6.15.12 Proof of malpractice insurance cover
6.15.13 Confirm that all changes made to any documents are crossed out with a single stroke that allows clear legibility of what is crossed out and that it is signed and dated.
6.15.14 Copies of the report by the monitor appointed by the Sponsor.

6.16 The monitoring committee will be expected to provide written reports to REC and the study PI on items listed above with findings and recommendations after the site visit.

6.17 For all randomized controlled trials (RCT) involving medications and other therapeutic agents, the researcher(s) is (are) required to provide evidence of compliance with SAHPRA guidelines at intervals that will be determined by the HREC depending on the potential risk to the study participants as mentioned in 6.6.2.

6.18 The investigator(s) will be required to provide the HREC with copies of all study audit reports.

6.19 The investigator(s) must provide the HREC with copies of all publications or dissemination at conferences or other forums accruing from the study that was granted Ethical approval.

6.20 Studies involving secondary data analysis: A research that is carried out as secondary data analysis once granted ethical approval will not be required to submit any progress reports. However, a final report must be submitted at the end of the research.

7. RISK COVER

7.1 While acknowledging the voluntary acceptance of risk of possible harm necessitated by participating in the study or undergoing procedures as outlined in the consent documentation, research participants should not have to bear the financial cost of managing harms that occur as a result of the study. The researcher(s), or sponsors must ensure that they have covered the participants for medical costs necessitated as a result of a research-related injury.

7.2 The purpose of this policy is to ensure appropriate and optimal care of research related bodily injury (RRBI), and to encourage legal protection of the investigator(s).

7.3 Whilst non-interventional studies generate risks that may be mitigated, most interventional studies pose potential risks to study participants that may be a threat to their general well-being or life. Furthermore, medical litigation is increasingly common whether well-founded or not. Thus, malpractice cover is essential.

7.4 Research-related bodily injury (RRBI)- Any injury to the body integrity of the study participant that may be directly or indirectly ascribed to the study itself. This excludes any complication of an already existing ailment. For example, a need for a limb amputation in a diabetic participant who is a participant in a lung study.

7.5 Malpractice: This occurs when the investigator has conducted himself/ herself in a manner not in keeping with the fundamental principles of primum non nocere, respect for the dignity of persons, beneficence and non-maleficence, and justice. The technical incompetence of the investigator forms part of this principle.

7.6 Medical practice insurance: Insurance cover that is specifically designed to cover the investigator pertaining to his/ her skills.

7.7 RRBI insurance: This is a medical insurance cover that MUST provide comprehensive cover of even the worst potential non-fatal RRBI and be linked with a life cover commensurate with prevailing market value. This insurance must be valid for a duration of at least 24 weeks after the participant has exited the study. Any such insurance cover MUST be from a financial service provider registered with the Financial Services Board of South Africa.

7.8 HREC insurance: WSU will provide insurance cover for the REC pertaining to its associated day-to-day processes, and this will be extended to research-related bodily injury that eventuates in a non-commercially sponsored (student initiated) interventional study.

7.9 Proof of the RRBI insurance must always be provided as part of the attachments accompanying the application for ethics approval.

7.10 Research sponsored by the DOH (state) or a full-time employed DOH employee need not include any insurance cover, unless otherwise advised by the HREC. This is because, were a research-related bodily injury to occur, the necessary consequent medical treatment will be freely provided by the respective health facility.

7.11 Research conducted by and individual or individuals outside as stated above are as per SA GCP (section 4.11) required to take out insurance cover that will pay the medical costs of necessary treatment to restore the participant to his/ her previous position, if possible.

8. COMPENSATION OF RESEARCH PARTICIPANTS

8.1 To ensure that research participants are adequately and appropriately compensated for their time and inconvenience and reimbursed for their research-related expenses, with an amount and method of payment that does not present an undue influence.

8.2 Requirements for appropriate participant compensation:

8.2.1 Neither the amount nor method of compensation for research participants must present the potential for undue influence.

8.2.2 Compensation to participants must be prorated and not wholly contingent on completion of the study by the participant.

8.2.3 Compensation to child participants must be child appropriate. Compensation should also be offered to the child's parent/caregiver for time and expenses incurred for accompanying the child on research visits.

8.2.4 Research participants should be compensated appropriately according to NHREC rates:

8.2.4.1 Time payments should be made at rates commensurate with unskilled labour rates. This acknowledges that research participation (while valuable) does not necessarily require special skills and training but does entail expending effort.

8.2.4.2 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.

8.2.4.3 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.

8.2.4.4 Investigators will be asked to estimate the amount of time participants will spend engaged in research activities for each research visit.

8.2.5 Research participants may be compensated for inconvenience.

8.2.5.1 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.

8.2.5.2 Payment amounts for inconvenient procedures should reasonably reflect the extent of such inconvenience.

8.2.5.3 Slightly higher payments for inconvenience may complement time payments that usually turn out to be very modest.

8.2.6 Research participants should be reimbursed for their expenses:

8.2.6.1 Direct costs incurred by participants for research participation should be reimbursed.

8.2.6.2 Investigators will be asked to estimate costs that participants will incur because of their research participation.

8.2.6.3 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. Investigators are well-placed to consult representatives regarding these expenses.

8.2.6.4 The cost for participants of being away from their individual place of work should not be considered.

9. HANDLING WHISTLE BLOWING, COMPLAINTS, ALLEGED RESEARCH NON- COMPLIANCE, VIOLATION OF GOOD RESEARCH PRACTICE & RESEARCH MISCONDUCT

9.1 Complaints may arise from a study because the HREC has rejected, disapproved or withdrawn ethical clearance, alleged procedural irregularities, breach of researcher confidentiality, unacceptable delays, conflict of interest and participants have complained.

9.2 Investigator/s can come forth to lodge their complaint or dissatisfaction in writing to the HREC Chairperson or any member delegated to receive the complaints.

9.3 These are dealt with by a panel inclusive of the Chairperson, Deputy Chairperson and three other HREC members (a total of five members) who should make every effort to investigate the complaint thoroughly, resolve the issue and communicate the outcome of the investigation to the complainant.

9.4 The HREC Chairperson and panel, if unable to resolve the issue, it will be referred to the full committee for discussion and resolution.

9.5 The committee is the last resort, a solution must be found, if not found the committee may decide to appoint an external independent investigator (appropriate privacy and confidentiality must be maintained at all times).

9.6 When handling whistle blowing, there has to an investigation to confirm wrongdoing. If the allegations are true, the HREC follows the steps for the complaints process highlighted in 9.3.

9.7 All complaints against the HREC for matters described above should be submitted to the REC Chairperson. Only complaints that cannot be resolved effectively by the HREC Chairperson or that are deemed irresolvable by the researcher or Chairperson should be escalated to the appointed adhoc panel and the HREC in totality.

9.8 A report of the findings and recommended action must be compiled and shared with the HREC Chairperson, the PI and other relevant parties.

9.9 The HREC office must acknowledge receipt of the complaint.

9.10 Appropriate privacy and confidentiality must be maintained at all times.

9.11 Complaints of non-compliance must be dealt with within one week.

9.12 For researchers, the turnaround time is 5-7 weeks.

9.13 For study participants it is 7 days.

10. MUTUAL RECIPROCAL REVIEWS

10. 1 Background

10.1.1. The Department of Health guidelines, Ethics in Health Research- Principles, Processes and Structures (2015) section 4.5.1.4. allows reciprocal recognition of review between RECs as mentioned below:

i. RECs may, at their own discretion, recognize prior review and approval of a research proposal by another registered REC to avoid duplication of effort.

ii. Reciprocal recognition means that two or more registered RECs decide to recognize each other's prior review.

iii. RECs that recognize prior review in this manner must determine the nature of the documents to be filed locally, which must, at minimum, include a copy of the approval letter from the other REC.

iv. RECs that recognize prior review in this manner may revise their decision to do so if justifying circumstances arise. The reasoning supporting a reversal of recognition should be documented.

10.1.2. Walter Sisulu University Faculty of Health Sciences Research Ethics & Biosafety Committee has no formal agreements or understanding with other RECs registered with the National Health Research Ethics Committee (NHREC).

10.1.3. Reciprocal recognition does not give researchers liberty to bypass WSU HREC submission of the research proposal. The HREC recognizes and accepts ethical clearance from other RECs for minimal risk studies that are then sent for expedited reviews to determine relevance to local needs of the study. This does not extend to randomized clinical trials (RCT) and studies with medium and maximum risk.

10.2. Purpose

10.2.1. To guide the HREC how to handle proposals applying for reciprocity in reviews that have been granted ethical approval by RECs with whom an understanding or agreement has been entered into.

10.3. Scope

10.3.1. This SOP applies to all proposals of multi-centre studies with minimal risk that have been reviewed and cleared for ethics by other RECs that have an understanding or agreement with the WSU FHS REC. The study sites need to include the area/s where the WSU HREC has jurisdiction.

10.4. Responsibility

10.4.1. The Chairperson determines whether the application qualifies for reciprocal review and whether to acknowledge the ethical clearances by another NHREC registered REC.

10.5. Procedure

10.5.1. The primary REC, where the initial application for ethical clearance was submitted and approved, takes full responsibility of approval and monitoring of the study.

10.5.2. The primary REC must be based in South Africa and registered with and accredited by NHREC.

10.5.3. The primary REC must have proven expertise and experience in reviewing research involving human participants, depending on the nature of the study.

10.5.4. For a multicentre study, the local Principal Investigator (PI) (affiliated to Walter Sisulu University) and the overall or lead PI should be the ones submitting the application, after the study has been granted ethical clearance by the NHREC registered and accredited primary REC.
10.5.5. The application needs to be submitted with the following documents:
10.5.5.1. The local PI's covering letter indicating the request and all arrangements relevant to the local context signed by the lead and local PI.
10.5.5.2. Reciprocal review form (to be developed)
10.5.5.3. Full protocol/ proposal, data collection tools, participant information document, informed consent document/s, all translated where necessary, clearance certificate/ letter from the primary/ host REC and any other documents linked to the study.
10.5.6. On receiving the application, the HREC Chairperson can decide if the application qualifies for an expedited review to fast-track the approval of proposed activities for the local site, while avoiding duplication of review efforts. The Chairperson can also decide to suggest that the application be reviewed by one or two members, send or not to send the application for discussion in the HREC meeting by all committee members.
10.5.7. Generally, a reciprocal review is done by the HREC Chairperson, Deputy Chairperson or another designated HREC member within 14 days after receipt of the application.
10.5.8. In the local site, reporting on adverse events, protocol amendments, progress reports, amendments of informed consent documents or any other documents will be done by the local site.
10.5.9. Communication of the review outcome will be done by the local HREC to the local PI who will share it with the lead PI.
10.5.10. Oversight of the study in the local site will be done by the local REC.
10.5.11. Withdrawal of approval by the local REC in the local site will not influence the decision of the primary REC.

11. PROTECTION OF PERSONAL INFORMATION ACT (POPIA) AND RESEARCH ETHICS

11.1 Background

The SOP is based on the POPI Act No. 4 of 2013 which aims to give effect to the right to privacy and data protection by introducing measures to ensure that personal information of a person is safeguarded when processed by responsible parties. The Act also aims to balance the right to privacy with the right to access to information while protecting important interests that includes free flow of information within and across the borders of South Africa. Within research settings, POPIA regulates the processing of personal information of participants, researchers and sites, data flow within and across South Africa, ensures right to privacy limitations are justified and protection of rights and interests of research participants (Adams, Adeleke, Anderson & others, June 2021). To note is that POPIA does not apply to information available in the public domain.

11.2 Purpose of the SOP

To provide guidance to the HREC when reviewing proposals to identify/ determine processes indicating POPIA compliance by investigators in their proposed research submitted to the HREC.

11.3 Scope

The SOP applies to all research proposals/ protocols submitted for review and approval to the HREC.

11.4 Key concepts

Personal information refers to information relating to an identifiable, living, natural person (data subject) including but not limited to

- Race, gender, sex, marital status, pregnancy, disability, sexual orientation, age, language, culture, belief, mental health, language and ethnicity.

- Information relating to education, medical, financial, criminal or employment history.

- Any identifying symbol, number, email address, physical address, telephone number, location information, online identifier, or any other assignment to the data subject.

- Biometric data of the data subject.

- Personal opinions, views or preferences of the data subject.

- 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. Views or opinions of other/s about the data subject.

- The name of the person if it appears with other personal information relating t the person or if the disclosure of the name itself would reveal information about the data subject.

Data subject: A person whose information is processed i.e., collected, processed and stored in a research trial. In research this is a research participant.

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 a research context the responsible person is the researcher.

Operator: a third party contracted by the responsible party to process persona information on their behalf.

Information officer: designated individual within an institution (WSU in our case) responsible for ensuring compliance to the POPIA.

11.5 Responsibility

The HREC executive committee delegates the responsibility to HREC members to determine compliance to POPIA by all proposed research that they review and grant ethical clearance/ approval.

11.6 Procedure

11.6.1 Lawful processing of personal information: this is guided by 8 principles, namely:

Principle 1: Accountability- the responsible party must ensure that al the conditions for the lawful processing of personal information laid out in POPIA are complied with at the time of the determination of the purpose of processing and during processing.

Principle 2: Processing limitation – the principle deals with the lawfulness of processing, minimality of information collected, consent, justification and objection, and the collection of personal in formation directly from the data subject.

Principle 3: Purpose specification- collection and processing of personal information must be for a defined purpose, records should not be retained longer than is necessary and must be deleted or destroyed after purpose for collection and processing has been fulfilled. The retention of records containing personal information is allowed for research purposes where there is a specifically defined need to retain such information and where further relevant safeguards are in place.

Principle 4: Further processing limitation- this is permitted when such information is used for research and only research purposes.

Principle 5: Information quality- personal information collected and stored must be accurate, up to date, complete and not misleading.

Principle 6: Openness- a record of all processing of personal information must be maintained by responsible parties. The data subject must be made aware that personal information will be collected, the purpose for collection and processing, which personal information, how it will be stored and for how long, rights of the data subject to the information in terms of access and deletion/ correcting data and if the data will be transferred to a third party and/ or internationally during processing.

Principle 7: Security safeguards- responsible parties must ensure that personal information is kept secure to maintain confidentiality and integrity, prevent data breaches according to technical and organisational control measures.

Principle 8: Data subject participation- the data subject must be informed of their right to access, correct, and delete their personal information and the manner in which to do so.

11.6.2 Minimality: personal information to be collected and processed must be minimal and specific for the intended purpose. No unnecessary personal information must be collected.

11.6.3 Lawful sources: personal information must only be accessed from lawful sources. These sources include the data subject, clinical records, identity documents, etc.

11.6.4 Limited sharing of personal information: personal information must be shared with the consent of the data subject and only for the purpose/s that they have consented for.

11.6.5 Data privacy: the responsible party must ensure privacy for all personal information collected and/ or processed with limited access as agreed upon through informed consent with the data subject.

11.6.6 Records management: the data subject must be made aware of the how and where records will be retained, for how long (period), who will have access and how data safety will be ensured.

11.6.7 Incident management and response: responsible parties must report data breaches to the data subject and Health Research Ethics Committee and the Information Officer within 7 days of learning about the breach. Participants must be informed of the breach, which information was unlawfully accessed and what steps have been taken to correct the situation, mitigate the risk and prevent further security breaches.

11.6.8 High-risk information and risk assessment: High-risk personal information include but not limited to right to privacy, individual identification, loss of privacy and unconsented identification, stigmatisation, discrimination, trauma, mental well-being, vulnerable and marginalised groups. Responsible parties must conduct a risk assessment for all personal information to be collected and processed to determine how high the risk can be. Risk assessment should be documented under the data management plan, together with the lawful basis for processing of personal information and details of the accountable party. Further safeguards must be ensured when processing high risk personal information. The responsible parties must also stipulate whether personal information will be transferred outside the borders of South Africa and the extent of data protection regulations in the country where person al data will be received and/ or processed.

12. Appendices

Annual WSU HREC Meeting Dates

Appendix Form Application for ministerial consent non-therapeutic research with minors

Complaints Form

Human Research Ethics Application Form

Protocol Amendment Form

Protocol Deviation Form

HREC Biosketch Template

Risk Assessment Checklist

SAE Reporting Template

Whistleblower Form

WSU HREC Progress Report Template

Consent Document Guide

13. References

Department of Health 2015. Ethics in Health Research (2015, DOH South Africa); Chapter 3, subsection 3.5.3

ICH-GCP Guidelines E6(R2) (09 November 2016); section 4.3

Integrated Addendum to ICH E6(R1) Guideline for Good Clinical Practice E6 (R2) Current Step 4 version dated 9 November 2016

International Conference on Harmonisation (ICH)-GCP guidelines

International reporting of Adverse Drug Reactions. Final report of the CIOMS working group Geneva 1990

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Bill of Rights Chapter of the Constitution of the Republic of South Africa. http://www.justice.gov.za/legislation/constitution/SAConstitution-web-eng-02.pdf
Medicines Control Council Reporting of Post-marketing Adverse Drug Reactions to Human Medicinal Products in South Africa. November 2015.

National Department of Health, 2003. National Health Act 61 of 2003, http://www.hpcsa.co.za/uploads/editor/UserFiles/National%20Health%20Act.pdf
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The Declaration of Helsinki 2013

Stellenbosch University. 2016. Standard procedures and guidelines Vers. 4.3. www.sun.ac.za/healthresearchethics