ANNEXURE 32

NELSON MANDELA UNIVERSITY

Standard Operating Procedures
Research Ethics Committee (Human) (REC-H)

Version 1.3

October 2022

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All Standard Operating Procedures (SOPs) and associated documentation must only be accessed through the Nelson Mandela University Research Ethics (Human) website at https://rd.mandela.ac.za/Research-Ethics/Research-Ethics-Committee-Human-(REC-H)/Human-Ethics-Reference-Documentation to ensure that the correct and most recent version is being used. It is the responsibility of the user of the documentation to ensure that the current version of the SOPs and associated documentation is being used.

Acknowledgement is given to the following institutions for access to documents on their Standard Operating Procedures which supported the development of this document:

- University of Cape Town [1]
- University of Stellenbosch [2]
- University of Free State [3]

1 VERSION HISTORY LOG

Version	Date	Reason for change	Implementation Plan
1.1	February 2022	Updated following National Health Research Ethics Council (NHREC) Quality Assurance Audit Report (July 2018)	Administrative support staff will receive training regarding the new SOPs. All users to be notified of the revised SOPs. Current version of SOPs to be available on REC-H website.

2 SYNOPSIS OF POLICY AND PURPOSE OF GUIDING PRINCIPLES CONTAINED WITHIN THE STANDARD OPERATING PROCEDURE (SOP)

1. Policy: Any activity, defined as research that involves human participants, planned and conducted by staff and/or students of Nelson Mandela University and affiliated institutions or on its premises, is subject to prior approval by REC-H.
2. The purpose of these guidelines is to define
   a. those activities that constitute human research and fall under the jurisdiction of REC-H;
   b. the terminology used in the context of the application, review and approval of research involving human participants; and
   c. the REC-H SOP documents relating to tasks and practices associated with the functions of REC-H, review and approval of research involving human participants, requirements for conducting and managing research involving human participants and continuing review of such research.

3 WRITING, REVISING AND MANAGING STANDARD OPERATING PROCEDURE (SOP)

This SOP will be written, revised, and managed as indicated in the table below.

SOP Title	Standard Operating Procedure Research Ethics Committee Human (REC-H)
Field of application	All staff and students engaged in research activities, Research Associates, External Researchers
Person(s) responsible for implementation	Research project leaders, study leaders, promoters, HODs, Deans, Directors, Research Development, DVC:RII
Person(s) responsible for drafting, review and revision	REC-H Chairperson Director: Research Development REC-H Secretariat
Status	Revised
Approval route	REC-H
Approving authority	Research and Engagement Committee
Relevant related policies	Policy on Research Ethics Code of Conduct for Researchers Whistleblowing Policy and Procedure Supply Chain Management
Stakeholder consultation	Research and Engagement Committees, Research Ethics Committees, Senate
SOP owner	DVC: RII, Director: Research Development, REC-H Chairperson
Approval date	Date Month 2022

4 ETHICAL AND REGULATORY REQUIREMENTS FOR HUMAN RESEARCH

1. Nelson Mandela University sets itself the aim of conducting research with:
   a. scholarly integrity and excellence,
   b. social sensitivity and responsibility,
   c. respect for the dignity and self-esteem of the individual and for basic human rights,
   d. reference to clearly specified standards of conduct and procedures that ensure proper accountability.
2. In the pursuit of this ideal, the University subscribes to the interdependent principles of scholarly responsibility, integrity and honesty, of human dignity and of academic freedom and openness. In the research context, these principles manifest in the relationships between the researcher and the research community and its ethos, research participants, society as a whole, and funders of research.
3. Mandela University therefore affirms the requirement that all research involving human participants be subject to prior ethics review, according to faculty and institutional guidelines, in order to ensure that harm to research participants is prevented or minimized and balanced against the likelihood of benefit. The Nelson Mandela University Research Ethics Committee (Human) (REC-H) is responsible for *inter alia* reviewing, approving and monitoring research involving humans.
4. REC-H does so by following ethical guidelines for research as stated by
   a. The Belmont Report 1979
   b. the World Medical Association Declaration of Helsinki[5]

c. the Department of Health of South Africa[4]
d. as well as other relevant declarations and statements in the area of research ethics, but not limited to the following documents and guidelines, to ensure compliance with national and international practices, including POPIA[6-26], through the Terms of Reference, relevant Standard Operating Procedures (SOPs), the Code of Conduct for Researchers and the Research Ethics Policy functions. The documentation related to ethical and regulatory requirements for human research can be accessed at https://rd.mandela.ac.za/Research-Ethics/Research-Ethics-Committee-Human-(REC-H)/Human-Ethics-Reference-Documentation

5. REC-H is committed to the following ethical requirements.
   a. Social value
   b. Scientific merit
      i. It aims to protect the rights and welfare of research participants and researchers by adhering to the principles of beneficence, justice and respect for people, especially vulnerable populations. In so doing, it assesses the ethical implications of the **study design and research methodology.**
   c. Respect for persons
   d. Respect for vulnerable persons
   e. Privacy and confidentiality
   f. Fair participant and community selection
   g. Favourable balance of benefits and harms
   h. Collaborative partnerships
      i. To ensure that research is relevant and acceptable, researchers should engage key stakeholders such as community representatives and policy makers in designing the protocol, conducting the research and distributing the findings.
      ii. Moreover, community participation could include input into a suitable informed consent process, appropriate risk reduction interventions and decisions regarding treatment and care linked to the research. Collaborative partnerships should allow community members to become genuine, active partners in the research process. This requires sustainable forums for regular communication and problem solving.
      iii. Similarly, in international multi-centre research, collaborative partnerships between researchers and sponsors from developed countries and researchers and communities in the host country are likely to reduce exploitation, facilitate the negotiation of fair benefits and show awareness of and respect for cultural differences.
   i. Ethical review
   j. Professional competence
6. Prior authorisation
   a. Some research activities are so high risk that the Information Regulator must be approached for prior authorisation before the activity commences or continues. This is to allow the Information Regulator to determine whether there are satisfactory safeguards in place to protect the personal information i.e., assessing the security of the information.
   b. Nelson Mandela University REC-H notes that the application for exemption from section 57(1) of POPIA on public interest grounds is in progress on behalf of all universities via the USAF Code of Conduct (CoC) for Universities 2020. As the CoC has not been approved by February 2022, it means that in order to comply, Mandela University REC-H has to -
      i. identify which projects are affected,
      ii. apply for prior authorisation from the Information Regulator, and
      iii. suspend processing until authorization is received or the statutory periods of four weeks and 17 weeks expire.

7. Insurance coverage
    a. The university has insurance coverage for research related injuries for participants and/or researchers. In the event of a research activity having known risk of such incidents, full details are to be provided of such risks prior to approval. In the case of an unexpected adverse event occurring, it is the researchers' responsibility to immediately log a record of such an event with REC-H.

5 ACTIVITIES THAT MAY NOT REQUIRE REC-H APPROVAL

1. The implications of engaging in research activities that require prior REC-H review without obtaining such review and approval are grave. The use and/or publishing of results obtained from unapproved research activities is in violation of national and international norms and standards, University policy and the DoH Ethics in Health Research Guidelines (2015)[7]. Further, such data should not be included in a thesis or dissertation. Researchers are encouraged to consult a journal's publishing policies before initiating unapproved studies since many journal editors require evidence of REC approval as a condition of publication of research involving human participants. Even if the study involving human participants is for audit and/or quality improvement purposes or record reviews, if any publication and/or academic qualification could possibly arise from the findings, prior ethical approval is required. REC-H does NOT give retrospective approval for completed audits and/or record reviews, nor for any research study involving human participants. Prior ethical approval is a requirement.
2. Researchers who regularly collect data and/or biological samples from human participants for non-research purposes are encouraged to register such databases and/or repositories with REC-H which will facilitate the use of these repositories for research purposes at some future date.
3. Scholarship of Teaching of Learning (SoTL) involves staff (sometimes in partnership with their students) undertaking systematic inquiry about student learning. This is informed by prior scholarship on teaching and learning and could involve sharing the results with the public. SoTL studies require approval from REC-H.
4. A list of activities that may not require REC-H approval includes but is not limited to (refer to Does-my-Study-require-Ethical-Approval for further guidance):
    a. Research that makes use exclusively of documents and/or data that is accessible in the public domain i.e., secondary data or accessible through legislation or regulation usually need not undergo formal ethics review.
    b. Research that relies exclusively on secondary use of anonymous information or anonymous human biological materials usually need not undergo formal ethics review, provided that no identifiable information is generated.
    c. Research involving observation of people in public spaces and natural environments usually need not undergo formal ethics review provided that
        - the researcher does not interact directly with individuals or groups
        - the researcher does not stage any intervention
        - the individual or groups do not have a reasonable expectation of privacy
        - dissemination of research findings does not identify individuals or groups
    d. Quality assurance and quality improvement studies (audits), programme evaluation activities and performance reviews usually do not constitute research and thus usually do not undergo formal ethics review. However, if there is any potential for these activities to be published in any form external to the local University context, it is prudent to obtain ethics approval prior to commencing the study. Retrospective approval for studies is not possible.
    e. Certain undergraduate course related activities such as assignments which involves human participants that are not vulnerable groups should be exempt from ethics review, provided that the work will not be published, and that the relevant faculty takes responsibility to issue a letter for that

particular course related activity which covers any institutional risk. However, this course assignment activity must be differentiated from the undergraduate 4th year Research projects.

5. In the case of any doubt, it is advised to err on the side of caution and apply for ethics approval. In such cases it is also advised to liaise directly with the REC-H Chairperson for guidance.

6 DEFINITION OF TERMINOLOGY USED IN THE REVIEW AND APPROVAL OF REC-H APPLICATIONS

1. REC-H uses the following definitions in its processes. The relevant documents can be accessed here.

TERM	***EXPLANATION***	***DOCUMENT REFERENCE***
Adverse event	An undesirable experience on the part of a participant.	Progress Report (RECH-004)
Advisory recommendations	Those recommendations which the PI/PRP are advised to note but which are not subject to approval.	Application Form (RECH-001)
Amendment	A minor change or addition with the aim of improving the data collection procedure.	Progress Report (RECH-004)
Anonymity	A situation where any data collected does not have any identifying information or direct link to any individual participant or group of participants.	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Approved with major modifications	Application in current form requires review in terms of the identified human ethics deficiencies.	Application Review Feedback Form (received by PI/PRP upon review of the application submission)
Approved with minor modifications	Application in current form requires review in terms of the identified deficiencies – generally sufficient consideration has been given to human ethics matters.	Application Review Feedback Form (received by PI/PRP upon review of the application submission)
Approved with no corrections	Application approved and approval letter is issued.	Application Review Feedback Form (received by PI/PRP upon review of the application submission)
Assent	Any record of agreement for a minor/child to participate in the data collection process. Parents/guardians are required to give consent for researchers to approach minors/children to participate in any data collection activities and minors are required to give assent. Consent from a parent/guardian does not automatically imply	Application Form (RECH-001); Application Form Sub-study (RECH-003S)

TERM	***EXPLANATION***	***DOCUMENT REFERENCE***
	that the affected minor(s)/child(ren) are obligated to assent to participate in the data collection procedure.	
Benefit	Any possible direct positive effect of any data collection activity on the welfare of a participant over and above what would be expected from such a participant as a result of routine daily tasks.	Application Form (RECH-001); Application Form Sub-study (RECH-003S); Progress Report (RECH-004)
Child / minor	'Child' is defined the POPIA 2013 as 'a natural person under the age of 18 years who is not legally competent, without the assistance of a competent person, to take action or to make decisions in respect of any matter concerning him- or herself'	
Compliance audit	The audit of the conduct and records of the approved research to verify compliance with REC-H requirements and conditions.	Standard Operating Procedures
Collaborative research	Research involving coordination between the researchers, institutions, organizations, and/or communities.	
Conflict of interest	A compromised situation as regards ethical conduct of research as a result of conflicting duties, responsibilities or interests (personal, professional or otherwise) on the part of the PI and/or PRP and/or participant recruiter and/or gatekeeper and/or sponsor of the study.	Application Form (RECH-001); Application Form Sub-study (RECH-003S); Application Form Umbrella (RECH-003U); Progress Report (RECH-004); Request for Access to Staff and Students (RECH-011)
Consent	Any record of **voluntary, specific and informed** expression of will in terms of which permission is given for the participation in the data collection process, and for the processing of personal information. Consent must be specific to be valid. The consent must always relate to a specific processing purpose. A blanket consent to the processing of personal information will not be valid. If the consent relates to multiple processing purposes, separate consent should be obtained for each processing purpose. In other words, the consent must be granular. Consent must be informed. Prior to consenting in this manner, data subjects must be given information about the consent before they make their decision, e.g. participants must have received information on the study	Application Form (RECH-001); Application Form Sub-study (RECH-003S)

TERM	***EXPLANATION***	***DOCUMENT REFERENCE***
	and what would be required from them as well as been given the opportunity to engage with the researcher regarding the study, giving rise to informed consent, a legal requirement. The consent must be drafted in clear, plain language and for this the institution must take the kind of audience the consent is aimed at into account. Consent must be explicit. The consent must be explicit. This means that consent has to be given through a clear, unambiguous, affirmative act. Silence or inactivity cannot be taken as consent which is why the use of pre-ticked opt-in boxes is not allowed. Data subjects must be free to withdraw consent without undue effort. It is considered best practice for the withdrawal of consent to be possible through the same channel that consent was obtained.	
Data analysis	The process of systematically applying statistical and / or logical techniques to describe and illustrate, condense and recap, and evaluate data. Analysis transforms the data into insights.	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Data collection instruments	Research methods / techniques used for the collection of data from human subjects (e.g. survey, questionnaire, interview schedule, etc.).	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Data collection procedure/process	The systematic process by which observations or measurements are collected, using research methods/techniques, on targeted variables in an established system, which enables one to answer relevant questions and evaluate outcomes.	Application Form (RECH-001) Application Form Sub-study (RECH-003S)
Data processing (referring to personal information)	‘‘**processing’’** means any operation or activity or any set of operations, whether or not by automatic means, concerning personal information, including— (a) the collection, receipt, recording, organisation, collation, storage, updating or modification, retrieval, alteration, consultation or use; (b) dissemination by means of transmission, distribution or making available in any other form; or (c) merging, linking, as well as restriction, degradation, erasure or destruction of information;	POPIA 2013
Data record	**‘‘record’’** means any recorded information— (a) regardless of form or medium, including any of the following: (i) Writing on any material; (ii) information produced, recorded or stored by means of any tape-recorder, computer equipment, whether hardware or software or both, or other device, and any material	POPIA 2013

TERM	***EXPLANATION***	***DOCUMENT REFERENCE***
	subsequently derived from information so produced, recorded or stored; (iii) label, marking or other writing that identifies or describes anything of which it forms part, or to which it is attached by any means; (iv) book, map, plan, graph or drawing; (v) 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; (b) in the possession or under the control of a responsible party; (c) whether or not it was created by a responsible party; and (d) regardless of when it came into existence;	
Data reporting	The process of collecting and submitting data which gives rise to accurate analyses of the facts. Data reporting is the step that translates raw data into information i.e. the step before data analyses.	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Data re-use	The use of data collected and entrusted to researchers in the context of the current study for other research purposes. The publication of research manuscripts as a result of the current study is not classified as re-use of data.	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Data storage	The manner in which data is stored for short and long term, with due consideration given to the protection of privacy and anonymity of the data. Personal data to be stored in line with the POPI Act, whereby personal information may be processed with the consent of the data subject or a competent person where the data subject is a child, if the data subject or a competent person where the data subject is a child, consents to the processing, then the processing of personal information is justified.	Application Form (RECH-001) Universities South Africa. 2020. POPIA Industry Code of Conduct: Public Universities (the code) [25] POPIA 2013
Date of commencement of data collection	The date upon which data collection for the study will commence. This date must occur after the anticipated date of ethics approval and at least 6 weeks after the date of submission of the application for review.	Application Form (RECH-001); Application Form Sub-study (RECH-003S); Application Form Umbrella (RECH-003U)
De-identify / de-identified (referring to personal information)	‘‘**de-identify**’’, in relation to personal information of a data subject, means to delete any information that— (a) identifies the data subject; (b) can be used or manipulated by a reasonably foreseeable method to identify the data subject; or (c) can be linked by a reasonably foreseeable method to other information that identifies the data subject.	POPIA 2013

TERM	***EXPLANATION***	***DOCUMENT REFERENCE***
Deviation	That process that falls outside the approved set of processes.	Progress Report (RECH-004)
Discontinuation	Discontinuation of a study refers to an investigator-initiated voluntary suspension or termination, whereby an investigator may choose to voluntarily suspend or terminate some or all activities of an approved protocol.	
Duration of data collection	The anticipated maximum period (in months) of the PI/PRP/research assistants' direct interaction with human subjects from date of commencement of data collection. This period shall not exceed 12 months. Should the approved data collection procedure require a period exceeding 12 months, the PI/PRP shall apply for an extension of the data collection procedure after 10 months of the approved period of 12 months has passed and submit such extension application together with an annual report of the data collection activities to date for review and approval.	Application Form (RECH-001) Application Form Sub-study (RECH-003S)
Enrolment	The methods/techniques used by researchers to screen, and select participants from those who have volunteered to participate in the study. Evidence must be provided of a fair identification, screening and selection process.	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Exception	That occurrence that is inconsistent with an anticipated outcome.	Progress Report (RECH-004)
Exclusion criteria	That set of characteristics that excludes volunteers (i.e. those individuals who have been recruited and have indicated a willingness to participate) from contributing to the data collection procedure. Unless there are good reasons for deception, exclusion criteria must be made available in writing at the point of recruitment.	Application Form (RECH-001); Application Form Sub-study (RECH-003S); Progress Report (RECH-004)
Extension\renewal	The extension of the period for data collection activities, which is for one year, to a maximum of three years.	Progress Report (RECH-004); Extension (RECH-005)
Feedback	The sharing of findings from the data collection procedure with the original source (i.e. participants) and possibly other sources (e.g. sponsors, gatekeepers, community, etc.). It is preferred that participants, at least, be the recipients of some form of summarised feedback. Should feedback be given to other sources (e.g. sponsors, gatekeepers, community, etc.), the intention to do so should be shared at point of recruitment.	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Gatekeeper	A person(s) who control(s) access to the participant population. A gatekeeper shall not also fulfil the role of participant recruiter.	Application Form (RECH-001); Application Form Sub-study (RECH-003S)

TERM	***EXPLANATION***	***DOCUMENT REFERENCE***
Human participant	An individual about whom an investigator conducting research obtains data through intervention or interaction with individual or identifiable private information.	UCT REC-H SOP
Identifiable	The identity of an individual is or may be readily ascertained or associated with reported information.	Risk Assessment section in Application Form (RECH-001)
Incidental findings	Any unexpected discovery made during the course of data collection/analysis, these findings being outside the scope of the research. Cognisance to be given to relevant mandatory reporting procedures should such be relevant to the context of the study.	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Inclusion criteria	That set of characteristics that all participants must exhibit so as to be included in the data collection procedure. Unless there are good reasons for the deception, inclusion criteria must be made available in writing at the point of recruitment.	Application Form (RECH-001); Application Form Sub-study (RECH-003S); Progress Report (RECH-004)
Insurance	Refers to the insurance or indemnity covering the liability of the investigator in respect of claims made against them by the participants with respect to injury attributable to their participation in a research project.	Application Form (RECH-001); Progress Report (RECH-004)
Institutional environment	Institutions like hospitals, prisons, mental institutions, and so forth.	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Intervention/interaction	Includes physical procedures performed on an individual, manipulation, communication or interpersonal contact with an individual or manipulation of an individual's environment.	Risk Assessment section in Application Form (RECH-001)
Low risk study	A study where the only foreseeable risk is one of discomfort to the participants.	Application Form (RECH-001); Application Form Sub-study (RECH-003S); Application Form Umbrella (RECH-003U)
Minimum number of participants	The minimum number of participants required to make the study viable. It must be noted that it is as unethical to require too many participants than is actually necessary (wasting the time of participants) as it is to require too few participants (also wasting participants' time since the study would then not be viable).	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Negligible risk study	A study where the only foreseeable risk is one of inconvenience to the participants. Inconvenience is of a lower level of risk than discomfort.	Application Form (RECH-001); Application Form Sub-study (RECH-003S);

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		Application Form Umbrella (RECH-003U)
Non-compliance	The result of deviating from approved processes.	Standard Operating Procedures
Not approved application	Application in current form is rejected on human ethics grounds.	Application Review Feedback Form (received by PI/PRP upon review of the application submission)
Obligatory recommendations	Those recommendations that are required to be addressed as part of the response to the initial review.	Application Review Feedback Form (received by PI/PRP upon review of the application submission)
OHRP	US Office for Human Research Protections	US Department of Health and Human Services
Participant	A living individual (or group of living individuals) about whom a researcher conducting research obtains data through an intervention or interaction with the individual or identifiable private information. A participant is an individual who has indicated a willingness to participate and who has subsequently been selected for participation.	Application Form (RECH-001)
PI	Primary investigator. The person undertaking the study.	Application Form (RECH-001); Application Form Umbrella (RECH-003U); Progress Report (RECH-004); Request for Access to Staff and Students (RECH-011)
Personal information	'Personal information' means information relating to an identifiable, living, natural person, and where it is applicable, an identifiable, existing juristic person, including, but not limited to – (a) 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 person; (b) information relating to the education or the medical, financial, criminal or employment history of the	POPIA 2015. Universities South Africa. 2020. POPIA Industry Code of Conduct: Public Universities (the code) [25]

TERM	***EXPLANATION***	***DOCUMENT REFERENCE***
	person; (c) any identifying number, symbol, email address, physical address, telephone number, location information, online identifier or other particular assignment to the person; (d) the biometric information of the person; (e) the personal opinions, views or preferences of the person; (f) correspondence sent by the person that is implicitly or explicitly of a private or confidential nature or further correspondence that would reveal the contents of the original correspondence; (g) the views or opinions of another individual about the person; and (h) 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 person. If the link between the information and the data subject can be severed, a process referred to as de-identification or anonymisation, the POPIA no longer applies, however, ethics approval would still apply.	
Power relationship	A situation where the PI and/or PRP and/or participant recruiter (a co-worker/gatekeeper or similar) might be in a position of authority when recruiting participants, thereby creating an effect of undue influence and compromising the voluntariness of the recruitment and enrolment processes.	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Privacy and confidentiality	A situation where the researchers have the responsibility to protect data collected and entrusted to them for research purposes from unauthorised access, use, disclosure, modification, loss, theft, and so forth. Private information includes information that an individual can reasonably expect will not be made public, and information about behaviour that an individual can reasonably expect will not be observed or recorded.	Application Form (RECH-001); Application Form Sub-study (RECH-003S)
Processing of information	'Processing' means any operation or activity or any set of operations, whether or not by automatic means, concerning personal information, including – (a) the collection, receipt, recording, organisation, collation, storage, updating or modification, retrieval, alteration, consultation or use; (b) dissemination by means of transmission, distribution or making available in any other form; or (c) merging, linking, as well as restriction, degradation, erasure or destruction of information.	POPIA 2015. Universities South Africa. 2020. POPIA Industry Code of Conduct: Public Universities (the code) [25]
PRP	Primary responsible person. This individual must be a fulltime member of permanent staff, or a research associate and professional associate, and usually the	Application Form (RECH-001); Application Form Umbrella (RECH-003U);

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	supervisor of the student in the case of the study being for the purposes of acquiring a qualification.	Progress Report (RECH-004); Request for Access to Staff and Students (RECH-011)
Recruitment	The process used by researchers to identify and approach individuals to volunteer to contribute to the data collection for a study (these individuals being referred to as "**volunteers**"). A reasonable period of time should elapse between recruitment of volunteers and enrolment of "**participants**" (those individuals who have indicated a willingness to participate and who have been subsequently selected for participation).	Application Form (RECH-001); Application Form Sub-study (RECH-003S); Progress Report (RECH-004)
Research	A systematic investigation, including research development, and testing and evaluation, designed to develop or contribute to generalizable knowledge.	
Researcher	Researchers may include academic staff, non-academic staff, post-doctoral fellows, graduate and undergraduate students and visiting scholars.	
Research Participant	A living individual (or group of living individuals) about whom a researcher conducting research obtains data through an intervention or interaction with the individual or identifiable private information. A participant is an individual who has indicated a willingness to participate and who has subsequently been selected for participation.	Application Form (RECH-001)
Research repository	Collection of information and/or human biological materials for research purposes which includes but is not limited to data from multiple sources, modified over time with access controlled via a gatekeeper. Data may or may not be anonymised.	Standard Operating Procedures
Researcher competence and expertise	All listed collaborators and personnel assisting with the research are expected to be appropriately qualified and competent to conduct the research component in which they are involved.	Application Form (RECH-001)
Resolution on formal review feedback form	**NOT APPROVED**: application in current form is rejected on human ethics grounds. **RESUBMISSION**: application in current form is rejected on human ethics grounds, but the researchers are invited to review extensively and resubmit for review. **APPROVED WITH MAJOR MODIFICATIONS**: application in current form requires review in terms of the identified human ethics deficiencies. **APPROVED WITH MINOR MODIFICATIONS**: application in current form requires review in terms of the identified	Application Review Feedback Form (received by PI/PRP upon review of the application submission)

TERM	***EXPLANATION***	***DOCUMENT REFERENCE***
	deficiencies – generally sufficient consideration has been given to human ethics matters. **APPROVED WITH NO CORRECTIONS**: application approved unconditionally.	
Resubmission of application invited	Application in current form is rejected on human ethics grounds, but the researchers are invited to review extensively and resubmit for review.	Application Review Feedback Form (received by PI/PRP upon review of the application submission)
Risk	Any possible negative effect of any data collection activity on the welfare of a participant over and above what would be expected from such a participant because of routine daily tasks.	Application Form (RECH-001); Application Form Sub-study (RECH-003S); Progress Report (RECH-004)
Safety of researchers	Any possible risk to the safety of the researchers during the data collection activity.	Application Form (RECH-001); Progress Report (RECH-004)
Secondary data	Documents and/or data that is accessible in the public domain.	
Societal and/or ethical value	Any possible benefit as a result of the study/data collection procedure that would be either temporarily or permanently transferred to the community from which participants are drawn.	Application Form (RECH-001); Application Form Sub-study (RECH-003S); Progress Report (RECH-004)
Study	The research project being conducted.	Application Form (RECH-001); Application Form Sub-study (RECH-003S); Application Form Umbrella (RECH-003U); Request for Access to Staff and Students (RECH-011)
Study closure	A suspension due to lapse of Committee approval will be referred to as an 'administrative closure' which will automatically occur when the Committee approval period expires.	
Sub-study	Any research projects being conducted as sub-projects of this study.	Progress Report (RECH-004)
Suspension	A suspension occurs when the REC-H Committee or Chair places a temporary hold on research that has been previously approved so that no new participants may be	

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	accrued, no research interventions may occur unless necessary for currently enrolled participants' safety and welfare, and no follow-up may be conducted unless it is in the best interest of participants and approved by the Committee. Suspension describes suspensions as a result of the REC-H decision but can also describe suspensions that occur automatically due to a lapse of Committee approval. A suspension due to lapse of Committee approval will be referred to as an 'administrative closure' which will automatically occur when the Committee approval period expires. An investigator may choose to voluntarily suspend some or all activities of an approved protocol.	
Termination	Termination of a previously approved protocol occurs when the REC-H withdraws approval and stops all research activity permanently. No new participants may be enrolled, and no further research interventions can occur. Where indicated, follow-up visits may be conducted with Committee approval to monitor participants' safety and welfare. An investigator may choose to voluntarily terminate some or all activities of an approved protocol.	
Umbrella research project	A broad research project under which a number of smaller research projects fall. Typically, an umbrella research project is one in which a number of individual masters and doctoral students collaborate, with each individual masters and doctoral student conducting research to realise at least one objective of the umbrella research project. It is required that the individual masters and doctoral students submit independent ethics applications for their parts of the umbrella project. An umbrella research project is advised for groups of undergraduate and/or honours students undertaking small research projects. In this case, individual students are not required to submit independent ethics applications for as long as the data collection procedures and instruments are significantly similar.	Application Form (RECH-001) Application Form Sub-study (RECH-003S)
Violation	That occurrence/process that fails to comply with the data collection procedures for which approval was granted.	Progress Report (RECH-004)
Volunteers	Individuals approached during the recruitment process to volunteer to contribute to the data collection for a study.	Application Form (RECH-001)

TERM	***EXPLANATION***	***DOCUMENT REFERENCE***
Vulnerable group	The term is usually synonymous with "groups at risk". A group is generally considered vulnerable because there is good reason to suspect that the individuals in the group may have special difficulty giving free and informed consent to being the subjects of research. The vulnerability may be due to an inability to understand and give informed consent or to unequal power relationships that hinder basic rights. Although vulnerability is not an absolute condition certain groups of participants require careful consideration to ensure that, where appropriate, additional precautions are put into place. Vulnerable groups include minors (under 18 years of age), women, adults with factual incapacity to provide informed consent (e.g. mental impairment), persons in dependent relationships or comparable situations, persons highly dependent on medical care, persons with physical disabilities, prisoners, collectivities (persons participating in research as groups).	Department of Health. 2015. Ethics in Health Research.[7] Department of Health. 2020. SA Good Clinical Practice: Clinical Trial Guidelines.[8]

7 RESEARCH AMONG NELSON MANDELA UNIVERSITY STAFF AND/OR STUDENTS

7.1 GATEKEEPERS PERMISSION

1. Relevant gatekeepers are required to be approached in order to gain access to participants ***after*** REC-H approval of the study and ***prior*** to recruitment.
2. All communications granting permission to access staff and/or students must be retained by researchers for possible active monitoring or auditing of the study.

7.2 UNIVERSITY STAFF AS PARTICIPANTS

1. Subsequent to REC-H review and approval of the study, researchers must request and obtain permission from the DVC Research, Innovation and Internationalisation (DVC: RII) (refer to https://rd.mandela.ac.za/Research-Ethics/Research-Ethics-Committee-Human-(REC-H)/External-Parties-wishing-to-conduct-Research-using) in order to access University staff for research purposes.
2. All requests must have prior research ethics approval for the planned study from REC-H.

7.3 UNIVERSITY STUDENTS AS PARTICIPANTS

1. Subsequent to REC-H review and approval of the study, researchers must request and obtain permission from one/more of the following relevant levels of authority in order to access University students for research purposes. All requests must have prior research ethics approval for the planned study from REC-H.
   a. For student participants across more than a single Faculty, the DVC Research, Innovation and Internationalisation (DVC: RII);

b. For student participants across multiple Departments in a single Faculty, the Executive Dean of the relevant Faculty;
c. For student participants across a single Department, the Head of Department of the relevant Department.

2. As a matter of courtesy, it is advised that lower levels of authority (secondary gatekeepers such as the HOD and Dean in the case of the DVC: RII, and the HOD in the case of the Faculty Dean) to that of the primary gatekeeper also be informed of the conducting of the study with the relevant student group(s).

8 RESEARCH CONDUCTED OFF-CAMPUS OR INVOLVING OTHER SITES OR SECTORS

8.1 GATEKEEPER PERMISSION

1. Research conducted by university researchers (staff and/or students) under the auspices of Nelson Mandela University at sites other than the university premises requires relevant gatekeeper permission.
2. Relevant gatekeepers are required to be approached in order to gain access to participants *after* REC-H approval of the study and *prior* to recruitment.
3. Researchers, when planning their study, must allow for the extra time incurred in obtaining these permissions.
4. All communications granting permission to access staff and/or students must be retained by researchers for possible active monitoring or auditing of the study.

8.2 PUBLIC SECTOR HEALTH FACILITIES

1. To co-ordinate health research, facilitate efficient use of limited health research resources and minimise the impact of research on staff and patients in the public health sector, the relevant Health Research Committee may require an independent review of the study to be conducted.
2. In addition, researchers must obtain administrative permission from medical superintendents or health facility managers to conduct research in their facilities.
3. Failure to obtain permission may result in the institutional suspension of the study.
4. Copies of permission letters signed by the relevant Health Research Committee, and relevant medical superintendents/facility managers must be forwarded to REC-H for filing with the researchers' protocols within 14 days of receiving such permission letters.

8.3 EDUCATIONAL FACILITIES

1. The Department of Education (DoE) has confirmed that it is a requirement that **ALL** research done at schools needs ethics approval from the DoE. In addition, the DoE need an undertaking that they will receive a full research report (bound copy).
2. Internal ethics processes need to be completed (FRTI & REC-H, where applicable) before seeking approval from the DoE as they require a complete copy of the NMMU-approved protocol.
3. To co-ordinate research in educational facilities, facilitate efficient use of limited educational research resources and minimise the impact of research on staff and learners in the educational sector, the relevant provincial Education Department does require an independent review of the study to be conducted.
4. Researchers must obtain administrative permission from school principals to conduct research in their facilities.
5. Further, written parental/legal guardian consent and written learner assent, where relevant, is required.
6. Failure to obtain permission/consent/assent from all stakeholders in the study may result in the institutional suspension of the study.

7. Copies of permission letters signed by the relevant Education Department and school principals must be forwarded to REC-H for filing with researchers' protocols within 14 days of receiving such permission letters.
8. All signed consent and assent forms (whichever is relevant) must be retained by the researchers in the case of an audit or active monitoring being required.

8.4 Other Facilities

1. Researchers must obtain permission from relevant authorities to undertake research in institutions, including but not limited to, homes for the aged, homes for children in need of care or homes for the disabled.
2. Copies of permission letters signed by the relevant facility manager must be forwarded to REC-H for filing with the researchers' protocols within 14 days of receiving such permission letters.

8.5 Private Property

1. Researchers must obtain administrative permission owners of private property to conduct research in their facilities.
2. Copies of permission letters signed by the relevant private property owners must be forwarded to REC-H for filing with the researchers' protocols within 14 days of receiving such permission letters.

9 Institutional Lines of Authority and Responsibilities

9.1 Institutional Lines of Authority

1. REC-H reports directly to the Research Committee (REC) under chair of the DVC Research, Innovation and Internationalisation (DVC: RII).

9.2 REC-H Responsibilities

1. REC-H is responsible for developing and implementing processes and procedures to ensure that research involving human participants meets the highest standards and norms in terms of protecting, in particular, the welfare and rights of human participants in research.
2. All research involving human participants conducted on the premises of Nelson Mandela University or on other premises under the auspices of the university must be reviewed and approved by REC-H prior to commencement of the study.
3. REC-H is authorised to perform the functions outlined below.
    a. Approve, require revisions, or disapprove all research submitted for review. The criteria used in the review of applications is based on ethical principles, regulatory guidance, applicable law, scientific merit of the methodology, sensitivity to community standards and attitudes and, where applicable, professional standards of practice and conduct. To approve research with human participants, REC-H must review the full research proposal, consent forms as well as all supplementary material, including, but not limited to, recruiting materials and data collection instruments. A description of the review and approval process is summarized in Figure 1.
    b. For negligible/minimal/low risk studies, an expedited approval process is conducted. To this end at least two (2) co-opted trained reviewers with the required disciplinary expertise from the Faculty from where the study originates review and provide relevant feedback to the applicant/researcher.

All Faculty approved studies are ratified at the next REC-H meeting. As a quality control measure, REC-H inspects samples of these protocols that have been approved in an expedited manner.

c. For ethics approval of research stemming from a support division (including those not for degree purposes) the application goes to the related faculty, and then to REC-H where relevant as per normal protocols.
d. For medium/high risk studies, the protocol serves at the relevant Faculty Postgraduate Studies Committee (FPGSC), or equivalent where it is reviewed for scientific rigor of the methodology. Only once the proposal has been approved at Faculty level does the protocol escalate to REC-H for human ethics review.
e. Any collaborative research is required to have the PRP affiliated with Nelson Mandela University. This includes protocols stemming from a PI registered at another university.
f. For any study serving at REC-H, at least 2 REC-H members will review the submission in depth and lead relevant discussions at a meeting. Formal feedback to the applicant/researchers is in the form of a resolution (i.e., NOT APPROVED; RESUBMISSION; APPROVED WITH MAJOR MODIFICATIONS; APPROVED WITH MINOR MODIFICATIONS; or APPROVED WITH NO CORRECTIONS) supported by detailed anonymised mandatory and advisory feedback (form RECH-REV-01 Review Criteria and Feedback). In the case of provisional approval of an application, a REC-H member is nominated as the liaison between the committee and the applicant to ensure that the applicant comprehends and implements the feedback of the committee in a satisfactory manner so that the study is granted final approval. To be approved, all mandatory feedback is required to be addressed within a maximum period of 3 months from date of the original application serving at a REC-H meeting. Neglecting to finalise the approval of a study timeously results in the protocol being recorded as withdrawn and the process has to commence all over again. Advisory feedback is intended to be considered at the discretion of the Faculty, PRP and PI.
g. All of the above also applies to the review of doctoral studies.
h. Conduct ongoing review of approved research at least once a year. This process is the responsibility of the PRP and PI who initiate the process with the completion and submission of a progress report (form RECH-004 Progress Report), usually submitted no later than 15 November annually. Neglecting to submit the progress report timeously might result in the suspension of the study.
i. Suspend or terminate approval of research not conducted according to sound ethical and scientific principles or regulatory requirements, or that is associated with unexpected risk or harm to participants.
j. Audit, or have a third-party audit, the conduct of the research to verify compliance with REC-H requirements and conditions, if applicable.
k. Observe, or have a third party observe, the recruitment, enrolment and consent process(es).
l. Respond to complaints about the unethical conduct of a study. REC-H must protect whistle-blowers who, in good faith, disclose unethical conduct. Refer to Section 14: Complaints Process

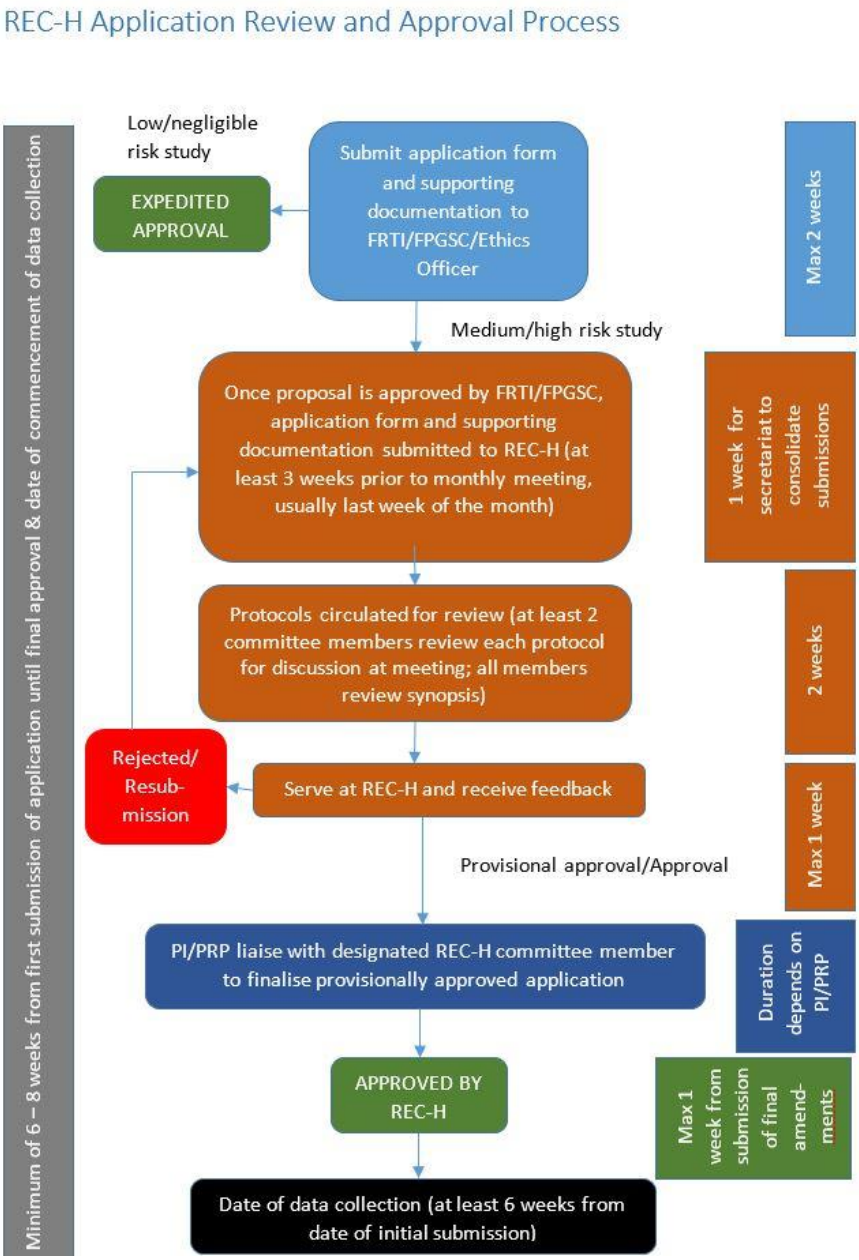

Figure 1: REC-H Application Review and Approval Process

9.3 PRP AND PI RESPONSIBILITIES

1. The Primary Responsible Person (PRP) is a full-time staff member, research associate or professional associate for an internal study, and usually the supervisor of the student in the case of the study being for the purposes of acquiring a qualification.
2. In the case of a reciprocal study with a university registered with the NHREC, the PRP should be the main researcher who obtained ethics approval from the institution he/she is affiliated to.
3. In the case of a study where:
   a. the main PRP is from another university,
   b. and the PI is a staff member engaging in the study for degree purposes at that other university

c. and the study involves the collection of data from Nelson Mandela university students or staff,
d. an application for ethics approval must be submitted through the most related Nelson Mandela faculty,
e. with the support of a willing PRP from the related Nelson Mandela faculty,
f. and follow the usual ethics approval protocol.

4. Prior to completing and submitting an application form for review, the primary responsible person (PRP) and primary investigator (PI) are expected to familiarise themselves with the contents of at least the following documentation (links available at https://rd.mandela.ac.za/Research-Ethics/Research-Ethics-Committee-Human-(REC-H)/Human-Ethics-Reference-Documentation)
   a. Department of Health Ethics in Health Research Guidelines (2015)[7]
   b. Department of Health Guideline 3.4.1 Major incidents and research, including public health emergencies [26]
   c. Protection of Personal Information Act (POPIA) Summary
   d. USAf adopted Code. 2020. POPIA Industry Code of Conduct: Public Universities[24]
   e. ASSAfs Code of Conduct for Research (2022 update for POPIA)[25]
   f. Nelson Mandela University Code of Conduct for Researchers
   g. Nelson Mandela University Research Ethics Policy
   h. Risk Assessment for the study (available as pp 6 – 10 of the RECH-001 application form template)
5. The PRP and PI (collectively referred to as the researchers) have the ultimate responsibility for the ethical, scientific, financial and administrative conduct of the study. All official REC-H correspondence is addressed to both the PRP and PI with a copy to the relevant faculty administrator. Any correspondence from stakeholders in the study to REC-H must be directed to REC-H via the researchers. Only in exceptional circumstances, for example in the case of suspected irregularities in a study, will REC-H accept direct correspondence from such stakeholders.
6. The researchers must:
   a. Observe and apply the ethical and regulatory principles detailed in the REC-H Standard Operating Procedures.
   b. Have thoroughly read, understood, critically analysed and be in agreement with the study protocol and all accompanying documentation including recruitment material, consent forms and survey materials (where applicable).
   c. In the recruitment information to be shared with potential participants and the consent forms, have ensured that:
      i. the application for ethics approval includes a copy of the NHREC newsletter (https://rd.mandela.ac.za/Research-Ethics/Research-Ethics-Committee-Human-(REC-H)/NHREC-Newsletter-May-202227)
      ii. participants are informed that complaints or concerns can be expressed to the researcher, REC-H, then to NHREC, and then to SAHPRA,
      iii. the REC-H ethics approval number is included in the consent form, and
      iv. the contact details of the researcher(s), the REC-H (rd@mandela.ac.za), and the relevant regulatory authority is included in the consent form.
   d. Submit prospective research for faculty peer review via the FPGSC (or equivalent) to determine its scientific merit prior to submission for ethics review. Submissions are thus conducted via the relevant FPGSC upon conclusion of a successful departmental peer review process.
   e. Be in receipt of an official approval letter from REC-H and have submitted acknowledgement and acceptance of the approval conditions to REC-H prior to the commencement of any data collection involving human participants. The approval conditions include, but are not limited to, a declaration by the researchers that they will -
      i. undertake only scientifically sound peer-reviewed research designed to produce valid results,
      ii. conduct the study according to the REC-H approved protocol,

iii. have a working knowledge of ethical and regulatory requirements applicable to the study,
iv. possess the necessary expertise and/or qualifications to conduct the study, and conduct research within the scope of their practice or involve a co-researcher relevant for the specific discipline of the study as per the Health Professions Act and the Regulations Defining The Scope Of The Profession
v. ensure that all research personnel are adequately trained and supervised,
vi. protect the rights and welfare of participants, including their privacy and confidentiality,
vii. disclose any potential conflict of interest,
viii. follow relevant professional standards and norms,
ix. report promptly on any new information, changes or unanticipated events/problems,
x. implement changes to a study only after REC-H approval,
xi. submit progress reports, at least annually,
xii. accommodate active monitoring of the study at the request of REC-H, and
xiii. obtain annual re-approval as required.

f. Provide REC-H with comprehensive information and supporting materials about the research so that REC-H is empowered to fulfil its responsibilities to protect participants' safety and wellbeing in terms of national and international ethical and regulatory guidelines.
g. Be forthcoming and declare any conflict of interest.
h. Ensure that all research collaborators and personnel assisting with the research are listed as such.
i. Ensure that adequate resources and facilities are available to conduct and complete the study.
j. Ensure that all listed collaborators and personnel assisting with the research are appropriately qualified and competent to conduct the research component in which they are involved.
k. Ensure that, where data collection is planned to exceed one year, to apply for (for example) Phase 1 approval, then at the end of that year, an application for an extension is submitted, along with an amendment form to notify the REC-H of Phase 2 changes in methodology.
l. Ensure that all listed collaborators and personnel assisting with the research are fully informed of current and amended study procedures and requirements for recruitment, enrolment and acquiring consent form participants.
m. Address any concerns and questions raised by any member of the research team. This includes (but is not limited to) -
    i. meeting regularly with team members to review progress of the study and reflect on any arising concerns about the study in general, or any participant in particular,
    ii. reassuring team members that concerns may be raised without any fear of repercussions,
    iii. investigating concerns and responding appropriately to individuals who raised such concerns,
    iv. reporting to REC-H on any matters that raise concerns about participants' safety, compliance with the approved research protocol, informed consent violations or the integrity of the research data, and
    v. reporting to REC-H on any matters that raise concerns about research team members' safety or compliance with the approved research protocol.
n. Protect participants' privacy and the confidentiality of their data (by removing personal identifying information from data collection materials and computer files, storing codes linking individuals to data in a secure storage away from the actual data collected, and allowing access to identifying data only to authorised persons via password-protected control mechanisms) by -
    i. complying with the Mandela University research data management policy and procedure, which includes the requirements for a research data management plan and valid research consents,
    ii. completing the Mandela University privacy impact assessment to identify research projects which have critical privacy implications for research participants,
    iii. completing certified training for all PIs in research data management and privacy, and

iv. all other researchers to complete awareness training in research data management and privacy.

o. Use data and/or biological samples only for purposes approved by REC-H.

p. For research which prospectively assigns human subjects to one or more health-related interventions to evaluate the effects on health outcomes are encouraged to register such research with the South African National Clinical Trial Registry after REC-H approval has been granted. This will allow research by NMU researchers of health-related topics to be widely publicized and to maintain some exclusivity whilst the research is being conducted.

q. Ensure the ongoing ethical conduct of research approved by REC-H by -
   i. obtaining informed consent from participants or their legally authorised representatives prior to participants taking part in the study,
   ii. offering a copy of the informed consent documentation to each participant (or the participant's legally authorised representative) and keeping the record of consent for the researcher records. Researchers may delegate to suitably qualified and trained collaborators and personnel assisting with the research the authority to obtain consent; however, the researchers are ultimately responsible,
   iii. keeping participants fully informed of any new information that may affect their willingness to continue taking part in the study,
   iv. obtaining REC-H approval for any modifications to previously approved research, including extension of data collection period, changes to the informed consent process and document, except for those modifications necessary to prevent immediate hazards to participants. In the case of modifications made to the study without REC-H approval to prevent immediate hazards to participants, the researchers shall report such changes to REC-H promptly, and
   v. promptly reporting to REC-H acts of serious and/or continuing non-compliance with the current approved research protocol.

r. The signatures of the researchers (both PRP and PI) on the relevant REC-H application forms testify that the researchers are ultimately responsible for all actions, procedures and interventions performed in the study, and that these actions, procedures and interventions performed in the study will be conducted according to applicable university, national and international ethical and regulatory policies governing research with human participants. Further, the signatures of the researchers (both PRP and PI) testify that any modifications to the protocol as originally approved or extension of data collection after the approval period has lapsed, will be submitted to REC-H for approval prior to implementation.

s. Submit progress reports in time for REC-H to carry out continuing review before the lapsing of the current approval period, in order to have the study extension approved.

t. Promptly submit to REC-H and, if applicable, sponsors and regulatory authorities any unanticipated problems or serious adverse events involving risks to participants.

u. Submit all external reports, if applicable, to REC-H.

v. Ensure that, in the situation of both expected and unexpected adverse events, every reasonable effort is made to provide the participants involved with adequate and suitable care to correct and/or alleviate the consequences of the adverse event.

w. Report any adverse event immediately to the relevant FPGSC and REC-H.

x. Maintain current and accurate records of research data, consent forms, correspondence with REC-H and sponsors, amendments and progress reports and adverse events.

y. Inform REC-H promptly, giving reasons, if the study is voluntarily terminated or suspended before the anticipated completion date.

z. Submit a closure or completion report to REC-H at the end of a research study (i.e., upon completion or suspension). In addition:

i. Honour any other commitments made at the outset of the study, including, but not limited to, the provision of feedback on the study to participants in an approved format.
ii. In collaborative research with pharmaceutical or other companies, make sure there is no interference with the right to publish.
iii. Where applicable, submit a summary of trial results to the South African Clinical Trial Register within a year of trial completion.

aa. Address concerns raised by participants before, during and after the conducting of the study.
bb. Maintain research records for a period of at least 5 years on completion of the study (15 years in the case of clinical trials).

7. A comprehensive account of the responsibilities of the principal and other investigators in clinical trials is provided in Section 3 of Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa. Second Edition, 2006.

9.4 Non-Compliance and the Principal Investigator

1. Every researcher must be familiar with the policies and regulations governing research in health.
2. Non-compliance with these policies and regulations include, but is not limited to, the following:
   a. Failure to disclose a conflict of interest.
   b. Conducting research with human participants without a protocol and / or without Human Research Ethics Committee approval.
   c. Allowing Human Research Ethics approval to expire without renewal.
   d. Not complying with the requirements of continuing review, including annual progress reports, amendments, serious adverse events and unanticipated problems.
   e. Conducting research not covered by the approved protocol or contradictory to the protocol (defined as a protocol violation).
   f. The Human Research Ethics Committee takes non-compliance seriously, and, depending on the degree of non-compliance, may open an investigation of research misconduct. See sections on protocol deviations, non-compliance, suspension and termination and compliance.

9.5 Heads of Departments and Chairs of Faculty Research Committees' Responsibilities

1. Departmental and relevant Faculty Heads and Chairpersons must ensure that -
   a. only well-designed and scientifically sound peer-reviewed research studies are submitted to REC-H for ethics review,
   b. researchers are sufficiently competent to undertake the study,
   c. postgraduate-level research meets the stringent university-wide scientific requirements for postgraduate degrees. REC-H cannot make this assessment although it will indicate when a protocol so lacks scientific merit and is deemed unethical, and
   d. all departments should be represented in their faculty ethics committee (one primary and one secundus per department) on a rotational basis.
2. The signature of the Departmental Head assures that the researchers have appropriate qualifications/training/expertise/resources to conduct the study. The signature of the relevant Faculty Postgraduate Studies Chairperson testifies that the protocol is of sound scientific design which is adequate and appropriate to answer the posed research question(s), minimises risks to human participants and has been subjected to a rigorous peer-review process within the Faculty structures.

9.6 ETHICS ADMINISTRATIVE SUPPORT RESPONSIBILITIES

1. The Research Development (RD) division provides administrative support to REC-H. Secretariat support is provided by the Record and Information Administration (RIAS) division. None of these staff is solely dedicated to the administration of REC-H.
2. Specific responsibilities include -
    a. keeping copies of the REC-H written policies and procedures,
    b. preparing and posting on the website an annual schedule of dates and deadlines for REC-H meetings and protocol submissions (REC-H meet 10 times a year, usually on the last Wednesday of each of the months February – November),
    c. providing logistical support for monthly REC-H meetings: a meeting venue, refreshments, and, if required, assisting lay members with travel arrangements,
    d. serving as a resource for researchers on general administrative information and assisting with forms and applications for REC-H review,
    e. preparing (with assistance from the REC-H Chair) and circulating the agenda prior to full committee meetings,
    f. timely distribution of meeting materials to committee members: main reviewers receive a full package of materials electronically and/or in print. All members receive synopses, consent documents, data collection instruments and recruitment aids electronically and/or in print. In addition, any member may request the full documentation of specific studies prior to a meeting.
    g. assigning studies to reviewers with assistance from the Chair, or in the absence of the Chair, with assistance from the Deputy-chair,
    h. following-up with reviewers to ensure feedback is received in time for monthly meetings,
    i. determining attendance for upcoming committee meetings,
    j. taking minutes during meetings in sufficient detail to show attendance, actions taken by the Committee and the basis for requiring changes in or disapproving studies, and a summary of controversial matters and their resolution,
    k. distributing minutes to members prior to the next meeting, and filing minutes once approved,
    l. in the week following the meeting, sending detailed feedback to researchers specifying REC-H's decision on the study and guiding on required changes, if applicable,
    m. processing and responding to all correspondence between researchers, sponsors, and REC-H,
    n. maintaining a secure database and tracking system of all studies submitted to REC-H for review,
    o. maintaining a current REC-H membership schedule (including Faculty secondi and co-opted members),
    p. referring researchers' requests for amendments and continuing reviews, adverse events information and any other related matters to the Chair, or in the absence of the Chair, to the Deputy-chair, for further action,
    q. keeping accurate records of all correspondence to and from REC-H that is not related to a research protocol, and
    r. maintaining intra-institutional relationships with relevant divisions in the University.
3. Because of the volume of active studies at any one time, the administrative support staff are unable to guarantee the timely notification of studies requiring annual renewal. Annual renewal is therefore not an automatic function. It remains the responsibility of the researchers themselves to submit a timely application to REC-H for an extension of a study.

9.7 RECIPROCAL REVIEWS

1. The Department of Health (DoH) guidelines (2015) allow for reciprocity of reviews (section 4.5.1.4) as follows:

    "4.5.1.4 Reciprocal recognition of review decisions:

i. RECs may, at their own discretion, recognise 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 recognise 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".

2. REC-H currently follows a reciprocal review system whereby the REC-H administrator and Chairperson acknowledges ethics clearance by other South African RECs registered with and accredited by the National Health Research Ethics Council (NHREC). Applications submitted by external researchers for reciprocal approval are assigned by the REC-H Chairperson to the Director of Research Development for review and also under extenuating circumstances, to other REC-H members.
3. Researchers external to Nelson Mandela University who have obtained ethics approval from an accredited research ethics committee, and who are requesting access to University staff and/or students for the purpose of research are required to complete and submit a request for such access a reasonable time period prior to initiating any contact with University staff and/or students. Retrospective approval of such requests is not permitted.
4. The process for external researchers to follow for requesting access to University staff and/or students for a study can be obtained on https://rd.mandela.ac.za/Research-Ethics/Research-Ethics-Committee-Human-(REC-H)/External-Parties-wishing-to-conduct-Research-using

10 REC-H: Composition and Documentation of Activities

10.1 Introduction

1. REC-H is established to oversee the safety, rights and welfare of human participants in research.
2. The composition and functions of REC-H strives to meet the minimum standards and requirements, as set out in the Department of Health (2015) *Ethics in health research: Principles, structures and processes*.
3. Details of current office bearers are available from https://rd.mandela.ac.za/Research-Ethics/Research-Ethics-Committee-Human-(REC-H)/Office-Bearers-and-Committee-Members

10.2 Chairperson: Appointment and Responsibilities

1. The Chairperson is elected by REC-H members for a term of three years which is renewable for a maximum of 2 cycles.
2. The Chairperson's responsibilities are to:
   a. Lead monthly REC-H meetings.
   b. Conduct expedited reviews or delegate this task to suitably qualified individuals who may or may not be REC-H members.
   c. Identify suitable reviewers to perform initial and ongoing protocol reviews.
   d. Engage with researchers on research ethics-related issues.
   e. Compile an annual report on the activities of REC-H for submission to the Research Innovation and Internationalisation Committee, Senate and to the National Health Research Ethics Council (NHREC). The latter report is for the purpose of maintaining accreditation and registration as a compliant health research ethics committee.
   f. Participate in non-compliance investigations.
   g. Contribute to the development of REC-H policies and procedures.
   h. Liaise with the Deputy Vice-Chancellor via the Department of Research Development regarding

appropriate and sufficient administrative support and resources to function optimally.

i. Liaise with and assist REC-H administration to prepare the agenda before meetings, and to review minutes after meetings.
j. Review and sign letters to researchers conveying REC-H's decisions relating to their submitted research protocols.
k. Consult with chairpersons of FPGSCs (or equivalent) and where appropriate advise on best practice regarding research protocol ethics reviewing.
l. Consult with Chairpersons from other human research ethics committees throughout the country in order to develop and promote best practices in research ethics oversight.

10.3 Deputy Chairperson: Appointment and Responsibilities

1. The Deputy Chairperson is elected by REC-H members for a term of three years which is renewable for a maximum of 2 cycles.
2. The Deputy Chairperson's responsibilities are to:
   a. Perform functions delegated by the chairperson, including conducting expedited reviews.
   b. Perform the functions of the Chairperson in his/her absence.

10.4 REC-H Committee members: Composition, Appointment and Responsibilities

1. The primary mandate of REC-H is to protect the rights and welfare of human participants in research. The Committee therefore requires diverse membership to provide expertise in and sensitivity to a broad range of scientific and ethical considerations.
2. Furthermore, the composition and functions of the REC-H must meet the minimum standards and requirements, as set out in:
   a. Department of Health. 2015. *Ethics in Health Research: Principles, Processes and Structures.* Department of Health: Pretoria, South Africa.
   b. 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.
3. According to the Department of Health requirements as stipulated in Ethics in Health Research: Principles, Processes and Structures 2nd Edition (2015) REC-H membership must meet the following requirements -
   a. at least nine members with a quorum being a simple majority,
   b. where the number of members is more than 15, the quorum may be 33%,
   c. at least one layperson,
   d. 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 e.g., a medical practitioner, psychologist, social worker or nurse,
   e. at least one member with professional training and experience in qualitative research methodologies,
   f. members with professional training and experience in quantitative research methodologies,
   g. a member with expertise in bio-statistics,
   h. a member with expertise in research ethics, and
   i. at least one member who is legally qualified.
4. RECH members and their respective secondi are nominated for appointment by:
   a. The respective FPGSC (or equivalent) according to the number of members per faculty allocated by the REC-H:
      i. Arts (at least 1 member)
      ii. Business and Economic Sciences (at least 1 member)

iii. Education (at least 1 member)
iv. Engineering, the Built Environment and Information Technology (at least 1 member)
v. Health Sciences (at least 2 members)
vi. Law (at least 1 member)
vii. Science (at least 2 members)
viii. LT Collab (at least 1 member)

b. REC-H, in the case where a shortfall of expertise and or knowledge in a particular area is identified.

5. Nominated candidates are appointed as REC-H members for a three-year renewable term if they meet at least the following criteria:
   a. Provide evidence of having successfully completed at least the following training
      i. TRREE Module 1: Introduction to Research Ethics
      ii. TRREE Module 2.1: Research Ethics Evaluation
      iii. TRREE Module 3.1: Informed Consent
   b. If the above has not been completed in the 3 years prior to appointment, provide evidence of any additional ethics training acquired in the 3 years prior to appointment.
   c. Have a working knowledge of the Department of Health Research Ethics Guidelines (2015) and POPI Act.
6. New appointments are staggered to ensure appropriate balance and maintain continuity. Members are informed in writing that they have been appointed on the REC-H. On appointment, RECH members are required to sign a statement undertaking that:
   a. All matters of which he/she becomes aware during the course of his/her work on the REC-H will be kept confidential.
   b. Any conflicts of interest, which exist or may arise during his/her tenure on the REC-H will be declared.
7. Members are not offered remuneration, except in exceptional cases lay members who may be reimbursed for traveling expenses to attend meetings.
8. The membership and composition of the REC-H will be continuously monitored to ensure appropriate representation. The Chairperson and Deputy Chairperson will perform an annual review of the composition, expertise and contribution of members. When a member resigns from the REC-H, the choice of a replacement takes into account the Faculty from which the member was nominated, the overall balance of the REC-H and specific expertise that is needed.
9. The university will provide protection in respect of liabilities that may arise when members are acting in good faith whilst performing their REC-H responsibilities.
10. REC-H members' responsibility include -
    a. proof of research ethics training, refreshed at least once within the period of appointment,
    b. GCP training, evident by certificate issued not more than 2 years previously, for members who review clinical trials proposals,
    c. attending meetings on a regular basis and not leaving until meetings are adjourned,
    d. attending a minimum of seven meetings per year (excluding sabbatical or other leave periods),
    e. maintaining strict confidentiality regarding information, reviews and decisions and all matters discussed at committee meetings,
    f. disclosing conflict of interest and where conflict does exist with respect to a study, not reviewing the protocol or leaving the room during discussion of and voting on the protocol,
    g. indicating with a signature on the attendance register that they will maintain confidentiality of all proceedings and declare any conflict of interest.
    h. respecting each other's views and the deliberative process,
    i. deciding independently if the design and conduct of proposed studies will protect participants' safety, rights and welfare,
    j. remaining impartial and objective when reviewing protocols,

k. serving as main reviewer at the request of the Chairperson, preferably but not necessarily, in their areas of expertise,
l. serving as general reviewer of all research discussed at committee meetings,
m. deciding by vote or consensus, whether to approve, require revisions, not approve or defer studies following deliberation at committee meetings,
n. performing expedited reviews **of minimal risk studies**,
o. keeping up to date with national and international research ethics and regulatory guidance, and
p. taking part in research ethics-related continuing education.

10.5 Ad Hoc/Co-opted Reviewers: Appointment and Responsibilities

1. REC-H may make use of *ad hoc* reviewer(s) to evaluate specific protocols. Such reviewers may be asked to review a specific protocol or attend a meeting to provide expert opinion on any relevant issue under consideration by REC-H. Such reviewers -
   a. must have access to the relevant study documentation, submitted to REC-H,
   b. may attend the relevant REC-H meeting, contribute to the discussions, make recommendations, but may not vote,
   c. must declare no conflict of interest in respect of the relevant study under review,
   d. must pledge confidentiality regarding the specific protocol and the meeting proceedings by signing a confidentiality and non- disclosure agreement, and
   e. may provide information about a specific study by written report, attending the meeting or both.
2. Where expedited approval of minimal risk studies is required, REC-H may make use of appropriately trained reviewers as co-opted reviewers from the faculty from which the studies originate to evaluate specific protocols. Such reviewers may be asked to review a specific protocol or attend a meeting to provide an opinion on any relevant issue under consideration by REC-H. Such reviewers -
   a. must have access to the relevant study documentation, submitted to the Faculty and REC-H,
   b. may attend the relevant REC-H meeting, contribute to the discussions, make recommendations, but may not vote,
   c. must declare no conflict of interest in respect of the relevant study under review,
   d. must pledge confidentiality regarding the specific protocol and the meeting proceedings by signing a confidentiality and non- disclosure agreement, and
   e. may provide information about a specific study by written report, attending the meeting or both.
3. At the very least, co-opted reviewers must have:
   a. Successfully completed at least the following <u>training modules -</u>
      i. TRREE Module 1: Introduction to Research Ethics
      ii. TRREE Module 2.1: Research Ethics Evaluation
      iii. TRREE Module 3.1: Informed Consent
   b. If the above has not been completed in the 3 years prior to being requested to conduct the review, provide evidence of any additional ethics training acquired in the 3 years prior to appointment.
   c. Have a working knowledge of the Department of Health Research Ethics Guidelines (2015) and POPI Act.
4. Co-opted reviewers are, for each study reviewed, required to submit a written review on the study for safe keeping by REC-H. The FPGSC (or equivalent) records and summarises the contributions of all co-opted reviewers for tabling at a REC-H meeting.

10.6 Observers and Guests

1. Observers and guests may attend a REC-H meeting at the Chairperson's discretion or invitation. Such observers and guests -
   a. do not contribute to the quorum, and

b. must pledge confidentiality with respect to the protocols and proceedings by signing a confidentiality and non-disclosure agreement.

10.7 Ex-officio Members

1. Ex-officio member means an individual is an automatic committee member by virtue of the individual's status. Ex-officio representatives on the committee are:
   a. Deputy Vice-Chancellor Research Innovation and Internationalisation (DVC: RII).
   b. Director of Research Development (RD).
   c. REC-H Administrative support staff.
2. Ex officio members -
   a. may participate in REC-H's deliberations to provide information and expertise,
   b. may not vote on any REC-H decision, and
   c. must comply with REC-H's conflict of interest requirements.

10.8 Quorum

1. Except when an expedited procedure is used, the REC-H must review initial and continuing studies at committee meetings at which a quorum is present. A quorum is considered to be upheld if 50% + 1 of appointed REC-H members, including the Chair- and Deputy Chairperson, are in attendance. A quorum must be maintained for each vote. If a quorum fails at any point during a meeting, further studies cannot be approved and must be held over until the next convened meeting.
2. Any member with a conflict of interest with respect to a specific study must leave the room during deliberations and decision-making relating to the study. This member may not vote on the study. Voting by proxy is not allowed. Ad hoc/co-opted reviewers and ex officio members may not vote.
3. Generally, decision-making at REC-H meetings is by consensus. At the Chairperson's discretion, voting may be decided by a show of hands.

10.9 Permissible Actions of REC-H on Review

1. On review the full committee may:
   a. Approve the protocol with no corrections, implying that no change to any aspect of the protocol or consent forms are required.
   b. Approve the protocol with minor modifications, implying that a simple agreement is required from the researcher and that the Chairperson, or a designee could approve the researcher's compliance via an expedited procedure.
   c. Approve the protocol with major modifications based on the magnitude and/or number of concerns identified. The Committee will decide whether the revisions must be submitted to a convened meeting, the main reviewer(s), the Chairperson, or a designee for a decision to approve or require further changes.
   d. Reject/not approve the protocol.
   e. Not approve the protocol in its present form and call for a re-submission of the protocol.
   f. Defer a decision until the following meeting. A protocol may be held over to the next convened meeting for one or more of the following reasons:
      i. Lack of appropriate expertise at the meeting.
      ii. Insufficient information to conduct an adequate review.
      iii. Loss of a quorum.
      iv. Lack of time.
   g. Condone the approval given by co-opted reviewers from relevant FPGSC (or equivalent) to minimal risk protocols.

10.10 CONFLICT OF INTEREST

1. Conflict of interest of a REC-H member generally includes the following:
    a. Relationship to the research study: The REC-H member (his/her spouse or immediate family member) is listed as -
        i. one of the research team members of the study,
        ii. one of the supervisory team of a postgraduate student's study,
    b. Personal relationship: The REC-H member has an immediate family relationship or other close relationship with one of the researchers (immediate family' means the REC-H member's spouse or domestic partner and dependent children).
    c. A financial interest: The REC-H member holds significant equity or stock options, receives or expects to receive compensation with a value that may be affected by the outcome of the study, has an ownership interest (including patent, trademark or copyright interest) in the drug, product or technology that is the subject of the research, or receives a significant amount annually as a salary, consulting income or other compensation from the sponsor.
    d. A fiduciary relationship to the sponsor: The REC-H member serves as an executive to a company sponsoring the research or serves on the company's board of directors.
    e. Other examples of conflicting interests include but are not limited to the following:
        i. Committee member has an interest that he/she believes conflicts with the member's ability to review a protocol objectively.
        ii. Committee member is in direct competition with the investigators for limited resources, funding, sponsorship or research participants, or the Committee member is considered a personal or professional adversary of the investigator. Since such situations may depend on the circumstances, the Committee member should raise such a situation as soon as possible with the Chairperson. The standard used by the Chairperson is whether an independent observer could reasonably question whether the individual's actions or decisions would be based on factors other than the rights, welfare and safety of participant.
        iii. Any other reason for which the Committee member believes he/she has a conflicting interest with the research.
2. The procedure to follow when a conflict of interest is identified:
    a. The REC-H member discloses those interests that pertain to the subject of the research proposal and that might otherwise reasonably be perceived to affect their independent unbiased judgment with respect to the review of the protocol or related matters.
    b. The REC-H member should not accept the relevant protocol for review and should return it for assignment to another reviewer.
    c. The Chairperson must ensure that the relevant REC-H member does not participate in the discussions or vote on the protocol and leaves the room.
    d. Should the Committee need information on the study from the member with a conflicting interest, the member may remain in the meeting room during the presentation of the study. The member must then leave the meeting room during the deliberative discussion and voting on the protocol.
    e. The REC-H member with a conflict of interest will not be counted as part of the quorum for the review of the study. If the quorum fails, the Committee cannot take further action or vote on the study.
    f. The name of the person leaving the room due to a conflict of interest will be recorded in the Minutes as recused.
    g. In the event that the conflict of interest involves the Chairperson, he/she will appoint the Deputy Chairperson, or another member as acting chairperson (with approval of the REC-H). The acting chairperson will conduct the meeting, for the remainder of the discussion of the item in question.

10.11 MINUTES AND RECORD KEEPING OF REC-H ACTIVITIES

1. REC-H will have 10 meetings per year.
2. Prior to a scheduled meeting, the agenda and supporting documents are prepared by the Administrator.
3. After being approved by the Chairperson they are electronically circulated to REC-H members.
4. Documenting the activities of REC-H is via minutes of Committee meetings and comprehensive record keeping of protocols reviewed by the Committee. Minutes should be:
    a. A reflection of the agenda of the meeting and must record the discussion and action taken on each agenda item.
    b. An accurate reflection of the matters considered and the justification for the subsequent decisions taken.
    c. Detailed enough to reconstruct its decisions at a later date if necessary to protect itself and the institution.
    d. Such that it shows concern for participant's rights, safety and well-being.
5. Draft minutes are reviewed by the Chairperson prior to distribution.
6. Corrections or comments on the minutes are made at the following convened meeting. If none is made, a motion to approve the minutes is made and voted on. After approval, the REC-H administrative staff member files a copy of the minutes in the REC-H record depository. The REC-H Secretariat also keeps copies of all documentation (agenda, minutes, protocols and approval letters) on the secure University Scorpio Drive.
7. Approved minutes are distributed to REC-H members, Research Ethics Committee (REC) for their records. Action memos are distributed to PI, PRP and relevant REC-H liaison person.
8. Minutes must include at least the following:
    a. Starting time, end time, date and location.
    b. Approved changes to and final approval of minutes of previous meeting.
    c. Attendees and their relevant designations (or reasons for attending if not an official REC-H member).
    d. Which and when a member was recused from discussions and voting due to a conflict of interest. The minutes will also indicate whether prior to recusing him/herself the member remained in the room to provide information at the committee's request.
    e. For all protocols under review at the meeting, the minutes must reflect:
        i. The REC-H reference number, names of PRP and PI, and study title.
        ii. Deliberations, actions and votes (if applicable) on each study undergoing initial or continuing review, and each amendment or revision requiring full-committee review.
        iii. Actions taken: voting is recorded as follows:
            - Not approved
            - Resubmission
            - Approved with minor modifications
            - Approved with major modifications
            - Approved with no corrections
            - Deferred
        iv. If a protocol is approved conditionally (i.e. revisions are required before approval), the minutes must state whether subsequent revisions and/or recommendations are required to be reviewed by the Chairperson, a designee or by the full committee.
        v. Reasons for specific decisions.
        vi. Duration of approval, usually 1 year.
        vii. The minutes will include a summary of the discussion of controversial issues and resolutions. Opinions expressed by members will be reported impartially and shall not be attributed to them by name.
        viii. Minutes will not be made available to others outside the university administration unless otherwise required by law or external regulations.

ix. Expedited/electronic approvals and any other relevant matters discussed will be captured in the minutes.

9. Meeting resolutions and relevant feedback on the studies are communicated to the PI (with a copy to the PRP as well as the relevant REC-H designee) within three to six days working days of the REC-H meeting. The following information is included in the feedback to researchers upon the study serving at a meeting:
   a. Protocol reference number.
   b. Title of the study.
   c. The Committee's decision: approved, revision required (minor or major), not approved, deferred, resubmission.
   d. Date of meeting.
   e. If revisions are required, a list of conditions with reasons, and a statement that the study may not begin until the researcher receives formal notification of REC-H approval after review of the response to the revisions.
   f. If disapproved, the reason for the decision.
   g. If deferred, the reasons why the study had to be held over until the next meeting.
10. Upon approval of a study, a letter of approval, including any standard regulatory requirements and/or conditions that must be agreed to before approval, is clearly outlined in a letter drafted by the REC-H Secretariat. Usually, a standard set of conditions is applicable, but in exceptional circumstances the Chairperson or in his/her absence the Deputy Chairperson reviews and signs the approval letter which is then forwarded to the PI (with a copy to the PRP as well as the relevant FPGSC, or equivalent). The following information is included in each letter of approval:
    a. Protocol reference number.
    b. Title of the study.
    c. If approved, the duration of approval and date of approval.
11. The final approval letter reminds the researchers of ethical and regulatory requirements governing their research and these may include:
    a. The study must be conducted in strict accordance with the protocol approved by REC-H.
    b. Any changes to the protocol or relevant consent documents must be approved by REC-H before implementation.
    c. Adverse events or unanticipated problems must be reported promptly to REC-H.
    d. Participants must receive a copy of the consent form, where requested.
    e. The PRP and PI take responsibility for the study conduct.
    f. Future correspondence must include the protocol reference number, study title and its current status.

11 Research In The Context Of A Major Incident

11.1 Broadening The Theoretical Framework For RECs During A Major Incident

1. Research in a major incident e.g., natural, or man-made disasters such as floods, earthquakes, outbreaks of deadly disease or political violence and armed conflict, is important for advancing emergency health care interventions and treatments and refining resource allocation, policymaking and implementation. This led to additional guidelines being published in 3.4.1 of the Department of Health Guidelines 2015 [26]
2. Major incidents such as a COVID-19 pandemic can result in challenges (for example, forced isolation) which have significant effects on clinical trials and community-based research.

3. *Public health emergencies require a public health ethics approach. This will necessitate a broadening of the theoretical framework used by RECs to consider public health principles, focusing on solidarity, mutuality, and reciprocity, among others.* [26]
4. For specific guidance on conducting clinical trials during a pandemic, refer to section 10.11 of SA Good Clinical Practice: Clinical Trial Guidelines 2020.[8]
5. The research must still be conducted in a manner that complies with acceptable principles that underpin the scientific and ethical integrity of research with human participants. Thus, careful ethical review is essential, albeit the urgency.
6. Expedited ethics review procedures will apply to low-risk research, however expedited processing does not equate to curtailing deliberation time. The expedited processes therefore are specific to the administrative processing of the ethics application.
7. In the context of a major incident a rapid ethics review may be conducted. In this case fewer REC members may be required to review the proposal. The time for deliberation by the REC will be reduced to five days. Rapid review is important, but not relevant for all research in such circumstances, as not all research is urgent.

12 PROTOCOL REVIEW PROCESS

12.1 POLICY

1. All protocols must undergo scientific review by a departmental research committee or other equivalent body prior to submission to the Human Research Ethics Committee. In turn, protocols must undergo ethical review by the Human Research Ethics Committee prior to commencement of a study.

12.2 PURPOSE

1. The purpose of this policy is to outline requirements or criteria for scientific and ethical review and describe the process of full-committee and expedited ethical review.

12.3 DEPARTMENTAL SCIENTIFIC REVIEW

1. Departments, Divisions or Institutes are responsible for establishing an explicit and formal scientific review process that evaluates the scientific merit and potential risks of each protocol before that protocol is submitted to the Human Research Ethics Committee. The Committee retains the authority to examine a study's scientific design to determine its impact on the safety and well-being of potential participants.
2. Scientific quality is improved when study objectives and methods are clearly thought through and described. A well-written protocol facilitates high quality science and is an invaluable tool as investigators develop and conduct their studies. A protocol is the formal design or detailed action plan of a study. The protocol explains what will be done, when, how, where, and why.
3. The research question and methodology must be presented in enough detail to permit evaluation of the scientific merit of the study. At a minimum any protocol, including retrospective chart or database reviews, requiring departmental scientific review must include the following elements:
    a. Study purpose and rationale
    b. Description of study population, inclusion, and exclusion criteria
    c. Statement of recruitment practices
    d. Sample size and how sample size was determined
    e. Design and detailed description of methodology
    f. Definition of end points

g. Measurement instruments, data collection forms
h. Data analysis plan
i. Ethical considerations
j. References

4. The following criteria, where applicable, should be considered during the scientific review of quantitative or clinical research:
   a. Are the specific aims, research questions and corresponding hypotheses clearly stated?
   b. Are the primary and secondary outcomes (endpoints) stated and defined?
   c. Is the literature review adequate, current, and relevant (wherever possible, the literature review must include pertinent references to local research in the proposed field of study)?
   d. In the context of previous studies, what is the contribution of the present research?
   e. Will the question or hypothesis being tested add important knowledge to the field?
   f. Are there adequate preliminary data in the literature (or pilot studies) to justify the research?
   g. Will the study design (e.g., cross-sectional survey, medical record review, clinical trial) address the study's aims and objectives?
   h. Is it feasible or reasonable to achieve the results in the proposed time frame, including the time to recruit, retain, or follow participants?
   i. Are the proposed tests or measurements appropriate, valid, and reliable to answer the scientific question in the local context?
   j. Are ALL the proposed tests or measurements needed to answer the scientific question?
   k. Is the use of socially constructed categories, such as race, ethnicity, gender, adequately justified, for instance is the use of racial classification required by the funding agency? Have these categories been explicitly defined?
   l. Are the individuals conducting the research properly qualified and trained to perform the study interventions or measurements?
   m. Does the research present risk to participants and, if so, is it acceptable?
   n. Does the research design minimise risk to participants?
   o. How do the risks of the new treatment or therapy compare to standard treatment or therapy?
   p. Is any standard of care denied as part of this study?
   q. If the study includes a placebo or a requirement to withhold treatment that might present a risk (no matter how small) to participants, are these interventions essential for the conduct of the study? Have or should other designs be considered?
   r. Is the location of the study adequate to assure participants' safety and comfort (e.g. appropriate equipment for monitoring and emergencies, a child-friendly setting for paediatric research)?
   s. Is there an appropriate plan for safety monitoring? Is there a need or plan for performing an interim data analysis? Is there a need for an independent data and safety monitoring board? Are there explicit, operationally defined stopping rules?
   t. Is the study adequately powered and statistically sound?
   u. Are potential limitations or criticisms of the study discussed?
   v. Is there a plan for disseminating the findings?
   w. Is the bibliography complete? Is the style of referencing consistent?
   x. Are the ethical issues described and justified? Although assessment of ethical issues is not a requirement of scientific review, it makes sense to highlight ethical omissions or to seek research ethics advice prior to submission for Human Research Ethics Committee review.
5. The following criteria should be considered during the scientific review of qualitative research:
   a. Is the phenomenon of the study clearly stated?
   b. Is the aim of the study clearly stated and related to the strengths of a qualitative design?
   c. Is the significance of the study adequately explained?
   d. Are the variables operationally defined?

e. Is the literature review clear? Does it identify gaps in the literature, is it appropriately detailed depending on the qualitative method chosen, and does it discuss the major concepts being studied?
f. Is the theoretical premise of the method clearly described?
g. Is the design clearly described and appropriate?
h. Are the population and sample clearly described?
i. Is the method of sample selection appropriate and clear as to how the researcher will determine when adequate sampling has occurred?
j. If the sample size cannot be delineated before the study begins, are a rationale and plan provided?
k. Is the procedure for data collection explicit and appropriate for the specifically chosen qualitative design?
l. Are data analysis plans explicit, appropriate to the question and design, and complete with plans to address the rigor of data collection and analysis?
m. Are the limitations stated, complete and appropriate to the specifically chosen qualitative design?
n. Does the researcher demonstrate an understanding of the qualitative paradigm and method chosen?
o. Does the researcher have experience in conducting qualitative research?
p. Is the scope of the study feasible within the available time and resources?

12.4 Human Research Ethics Committee Review

1. The primary responsibility of the Human Research Ethics Committee is to safeguard the rights and welfare of human participants. Therefore, a principal investigator must provide enough information for the Committee to determine that human participants will be adequately protected and that the research will comply with ethical and regulatory requirements.

12.5 Requirements for Human Research Ethics Committee Review

1. The following criteria should be considered when an investigator is preparing a protocol for submission for Human Research Ethics Committee review:
    a. Specific Aims, Background and Significance
        i. Are the study aims and objectives clearly specified?
        ii. Are there adequate preliminary data to justify the research?
        iii. Are adequate references provided?
        iv. Why is this research important to conduct?
        v. Why is it worth doing in this particular setting?
    b. Scientific Design
        i. Is the scientific design adequate to answer the study's questions?
        ii. Is the scientific design adequately described and justified?
        iii. Does the study involve a placebo?
        iv. If so, why is a placebo needed?
        v. Could the study be done without a placebo?
        vi. Are study aims and objectives achievable in the given time frame?
        vii. Does the protocol have scientific merit?
        viii. Do the principal and co-investigators have adequate experience to conduct the study?
    c. Inclusion and Exclusion Criteria
        i. Are inclusion and exclusion criteria clearly stated and reasonable?
        ii. Are any individuals inappropriately included as participants?
        iii. Are any individuals inappropriately excluded as participants?
        iv. Does the study include vulnerable groups such as children, prisoners, psychiatric patients, individuals with impaired decision-making capacity? If yes, are adequate safeguards

included to protect their rights and welfare?

v. Is the inclusion of vulnerable populations justified?
vi. Can the study be done without involving vulnerable populations?
vii. Will the study target or exclude a particular ethnic or language group?
viii. Who, in the research team, will decide if an individual participant is eligible?
ix. Is the selection of participants appropriate for the question being asked?
x. Are laboratory parameters appropriate?

d. Recruitment and Enrolment
   i. Are recruitment methods well-defined?
   ii. How and by whom will individuals be identified for recruitment into the study?
   iii. Is the individual responsible for recruitment suitable for the task?
   iv. Is the location, setting, and timing of recruitment acceptable?
   v. Are all recruitment materials submitted and acceptable, e.g. flyers, posters, advertisements, radio announcements?
   vi. Are procedures for screening participants prior to recruitment acceptable?
   vii. If recruitment will occur during a critical or stressful period, what precautions are in place to assist voluntary decision-making?

e. Research Procedures
   i. Are the rationale and details of research procedures adequately described and acceptable?
   ii. Is there a clear differentiation between research procedures and standard of care?
   iii. Are there adequate plans to inform participants about specific research results, e.g. incidental findings, clinically relevant findings?
   iv. Are there adequate plans to inform participants about specific research results that might affect their decision to continue participation?
   v. Are individuals who are performing procedures adequately trained?
   vi. Is the location for performing procedures acceptable?

f. Drug, Device and Biologics Considerations
   i. Is the status of the drug or device adequately described?
   ii. If necessary, is the supporting documentation from the sponsor included with the submission; for example, investigator's brochure, package inserts/ labelling, South African Health Products Regulatory Authority (SAHPRA) approval?
   iii. What has the preclinical or initial clinical research shown?
      - Does any evidence suggest the possibility of clinically significant toxicities, such as carcinogenesis or teratogenesis?
      - Is there any evidence of immunogenicity?
      - Is there any evidence to suggest either that it may be unsafe to undertake the study or to justify special safety monitoring?
   iv. Are the drug dose and route of administration appropriate?
   v. Are the drug or device safety data sufficient to warrant the proposed phase of testing?
   vi. If the study involves a marketed drug or device for an unapproved or off-label indication is South African Health Products Regulatory Authority (SAHPRA) approval necessary?
   vii. Does the protocol describe acceptable measures for storage, access and control of the drugs, devices or biologics?

g. Risks and Benefits
   i. Are risks and benefits adequately identified, evaluated and described, including physical, psychological, social, and economic?
   ii. Are there risks to the community or a particular group of individuals, e.g. stigmatisation?
   iii. Do risks stated in the protocol match the risks described in the informed consent form?
   iv. Are risks reasonable in relation to anticipated benefits?

v. Are risks reasonable in relation importance of knowledge to be gained?
vi. Are risks minimised to extent possible?
- Study uses procedures which are consistent with sound research design.
- Study uses procedures which do not unnecessarily expose participants to risk.
- Where possible, study procedures are already being performed on participants for diagnostic or treatment purposes

h. Process of Obtaining Informed Consent and Assent
i. Is the process well-defined?
ii. Does the process minimise the possibility of undue influence?
iii. Does the process provide sufficient time, privacy, and an adequate setting for participants to decide?
iv. Who will obtain consent or assent? Is the individual obtaining consent or assent adequately trained?
v. Is the setting where individuals are being recruited or would report for research-related activities the same as where they are seen for clinical care? If so, this may cause confusion about what is research activity and what is standard care.
vi. Are issues relating to participants' comprehension considered?
vii. How will a researcher decide if a participant has decision-making capacity to choose to enrol in a study?
viii. Is the language used in the consent form appropriate for participants' level of understanding?
ix. Are terms such as 'randomisation' clearly defined and illustrated (e.g., like flipping a coin)?
x. Will an interpreter be necessary to obtain consent?
xi. Will consent forms need translation? Participants are entitled to information in the language of their choice.
xii. Do consent forms include all the elements needed to comply with regulatory and ethical standards

i. Privacy and Confidentiality
i. Privacy refers to persons and to their interest in controlling access of others to themselves. Confidentiality refers to data. (See related policies: Collection of Data or Biological Specimens for Research and Databases, Registries and Repositories)
ii. Are provisions to protect participants' privacy adequate? If participants will be contacted in person, it should be by someone who has reason to know confidential information.
iii. Are provisions to protect confidentiality of data during and after research adequate?
iv. Are provisions for storage, coding and use of identifiers adequate?
v. If the data are not going to be destroyed, who will be responsible for maintaining anonymity, confidentiality and security over time?
vi. In the case of focus groups, are participants told that confidentiality cannot be guaranteed as group members may disclose what was discussed when they leave the research setting?
vii. If audio or videotaping is used, how will tapes be stored and for how long?

j. Storage of Human Biological Specimens
i. Will the study generate new samples, use existing samples or both?
ii. If the study uses existing samples, how were they obtained and were donors informed of their intended use?
iii. If samples are identifiable, how will donors' privacy and confidentiality be protected?
iv. Will biological specimens be stored for future use?
v. In the case of uniquely identified specimens, especially those containing genetic material, do the participant and his family understand where and how their genetic material will be stored and protected and who will have access to it and why?
vi. How will this understanding be verified, and what will be done if a participant withholds or

withdraws consent for such a donation?

vii. Does the PI anticipate potential future use of samples, given technological progress? If so, is this addressed in the informed consent form?

viii. Does the PI anticipate sharing the samples with other investigators? Is this addressed in the informed consent form

k. Data Analysis and Monitoring

i. Does the protocol include a well-formulated plan for interpretation of data and statistical analysis?

ii. Is the rationale for the proposed number of participants reasonable?

iii. Are the plans for data and statistical analysis defined and justified, e.g., stopping rules, end points?

iv. Are there adequate plans for monitoring data?

v. Is a data safety monitoring board part of the study? If so, where is the board located, who are its members, and how will the principal investigator communicate with the board? Is it independent?

vi. In the case of non-interventional or qualitative research is there a mechanism, such as a reference or event monitoring group, to provide ongoing oversight and impartial analysis of unanticipated incidents?

l. Resources

i. Are the resources to conduct the study appropriate and sufficient (equipment, staff, space, funding)?

ii. Will counselling or support services be available, if required?

m. Reimbursement

i. **Note**: Financial or other forms of compensation are not considered to be a benefit but rather recompense for research-related inconvenience.

ii. Is the compensation to participants reasonable?

iii. If the participant does not complete the study, will compensation be pro-rated?

iv. Are there adequate plans to avoid out-of-pocket expenses and costs incurred by participants (e.g., travel expenses, parking costs, and lost wages)?

v. If children or adolescents are involved, who receives the compensation?

vi. Does compensation cover extra costs when parents or caretakers are expected to accompany participants on research visits?

n. Insurance

i. Is there provision for insurance for research-related injuries, if applicable?

ii. In the case of investigator-initiated research, is there cover in terms of NMU's insurance policy?

iii. For clinical trials involving human participants, does it comply with the SAHPRA guidelines[30] for liability insurance for clinical trials?

iv. For clinical trials involving human participants, does it comply with ABPI Guidelines[31] on Insurance and compensation in the event of an injury in for commercially sponsored research?

o. What Happens at the End of the Study?

i. In the case of Phase III safety and efficacy trials, will the investigational intervention, if proven safe and efficacious, be offered to participants at the end of the study and under what conditions; for example, until the drug is licensed in South Africa or for a specified period? If a sponsor does not intend to provide post-trial access, the informed consent document must spell out in bold lettering:

- That even if a participant's condition improves on the study drug it will no longer be provided by the sponsor at the end of the study.

- How participants/patients will be managed at the end of a clinical trial, for example will they resume their previous treatment regimen?

ii. Will the study offer long-term benefits to the community in the form of capacity building and/or medical or research infrastructure?
iii. If proven safe and efficacious, is it likely that the investigational drug will be available in an open- label extension study?
iv. How will participants be informed of important findings?
v. How will findings be disseminated to the wider population and research community?

p. Stakeholder Participation
i. Who are the major stakeholders in the research? Describe how those affected by the study can express their views, clarify their needs, and contribute to the research.

q. Conflicts of Interest
i. Will any research staff receive incentives for recruiting participants or for any other purpose directly related to the study?
ii. Do any personnel involved in the design, conduct or analysis of the research have any proprietary interests (e.g., royalties, patents, trademarks, copyrights, or licensing agreements) involving any agent, device or software being evaluated in the study?

r. General
i. Does the study comply with the latest version of the Helsinki Declaration?
ii. Is there a table of contents for long protocols so that submissions are easier to read and review?
iii. Are pages numbered consecutively?
iv. Has the principal investigator or a colleague proofread the proposal and performed a spell-check?

12.6 Primary Reviewer System

1. The Human Research Ethics Committee uses a system of primary or main reviewers for initial reviews, continuing reviews, and reviews of amendments and adverse or unanticipated events.
2. The Chair and/or Deputy Chair selects two or three primary reviewers for reviews requiring full committee review based on members' knowledge, experience, or expertise.
3. If a Committee member or consultant believes that he or she cannot be a reviewer for any reason, including lack of expertise or a conflict ofinterest, the Chair or administrative staff should be notified immediately.
4. If no Committee members have the required expertise, a consultant will be invited to perform the review.
5. The Chair, Deputy Chair or designee serves as primary reviewer for research meeting the criteria for expedited review.
6. Each Committee member must receive sufficient information to be able to take part actively and constructively in the discussion of the protocol.

12.7 Responsibilities of Primary Reviewers

1. Primary reviewers must:
   a. Conduct an in-depth review of the research materials using review criteria outlined under 'General Requirements for Human Research Ethics Committee Review'.
   b. At reviewers' discretion, contact investigators directly or via the administrative staff to clarify issues identified during the review.
   c. Lead the discussion on the initial or ongoing reviews at full committee meetings.
   d. Submit a written report for presentation if unable to be present at the convened meeting.
   e. At reviewers' discretion, make 'editing' recommendations directly onto consent forms in legible

handwriting. Documents with suggested changes can be returned to investigators.

f. Make a decision for expedited reviews (approve, require revisions, send for full committee review).

12.8 CATEGORIES OF REVIEW

1. Expedited Review

a. The type of review depends on the level and type of risk involved. Expedited review is a valuable mechanism that allows the Human Research Ethics Committee to triage studies to an appropriate level of review. This means that the time and resources of full committee meetings can be concentrated on protecting participants facing the greatest levels of risk or discomfort. 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 a convened meeting.

b. The Chair or Deputy Chair has the final responsibility for determining which new protocols, continuing reviews and amendments are eligible for expedited review and has the authority to designate one ormore experienced Committee members to perform an expedited review. No member with a conflict of interest may serve as a reviewer for any expedited item. A monthly report of all research approvedthrough an expedited procedure is distributed to members before the full committee meeting.

2. Eligibility for Expedited Review

a. Types of research that may undergo expedited include:

i. Research classified as no greater than minimal risk, depending on the details of the study. Minimalrisk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations.

ii. 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.

iii. Amendments to previously approved research where changes to the study protocol or consent documents do not result in significantly increased risk to participants.

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

v. Additional categories of minimal risk research as defined by a convened Committee meeting.

3. Applicability Criteria

a. Research activities that:

i. Present no more than minimal risk to human participants, and

ii. Involve only procedures listed in one or more of the following categories.

b. The categories in the list below apply regardless of participants' age, except as noted.

c. The expedited process may not be used where identification of participants and/or their responses would reasonably place them at risk of criminal or civil liability; be damaging to their financial standing, employability, insurability, or reputation; or be stigmatising, unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

d. The expedited process may not be used for classified research involving human participants.

e. Categories one to seven pertain to both initial and continuing review.

4. Research categories

a. Category 1: Clinical studies of drugs and medical devices only under the following conditions:

i. Research on drugs for which an investigational new drug application is not required,but only if the research does not significantly increase the risks, or decrease the acceptability of the risks, associated with the use of the product.

ii. Research on medical devices for which (i) an investigational device exemption application is not required, or (ii) the medical device is cleared or approved for marketing and the medical device will be used according to its cleared or approved labelling.

b. Category 2: Collection of blood samples by finger prick, heel stick, ear stick or venipuncture as follows:
   i. From healthy, non-pregnant adults who weigh at least 50 kg. Amounts drawn may not exceed 550 ml in an eight-week period and collection may not occur more frequently than two times per week; or
   ii. From other adults and children, considering age, weight and health, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. The amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an eight-week period and may not occur more than two times per week.

c. Category 3: Prospective collection of biological specimens for research purposes by non-invasive means. Examples:
   i. Hair and nail clippings in a non-disfiguring manner.
   ii. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction.
   iii. Excreta and external secretions, including sweat.
   iv. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or applying a dilute citric solution to the tongue.
   v. Placenta removed at delivery.
   vi. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labour.
   vii. Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished according to accepted prophylactic techniques.
   viii. Mucosal or skin cells collected by buccal scraping or swab, skin swab, or mouth washings.
   ix. Sputum collected after saline mist nebulisation.

d. Category 4: Collection of data through non-invasive procedures (that do not involve general anaesthesia or sedation) routinely employed in clinical practice, excluding procedures that involve X-rays or microwaves. Where medical devices are employed, they must be cleared or approved for marketing. Examples:
   i. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the participant or an invasion of the participant's privacy.
   ii. Weighing or testing sensory acuity.
   iii. Magnetic resonance imaging.
   iv. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography.
   v. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given age, weight and health of the individual

e. Category 5: Research involving materials (data, documents, records or specimens) that have been collected or will be collected solely for non-research purposes such medical treatment or diagnosis.

f. Category 6: Collection of data from voice, video, digital, or image recordings made for research purposes.

g. Category 7: Research on individual or group characteristics or behaviour (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behaviour) or research that employs survey, interview, oral history, focus group, programme evaluation, human factors evaluation, or quality assurance methodologies.

h. Category 8: Continuing review of research previously approved by the convened IRB as follows:

i. The research is (i) permanently closed to the enrolment of new participants, and (ii) all participants have completed all research-related interventions, and (iii) the research remains active only for long-term follow-up of participants; or
ii. No participants have been enrolled and no additional risks have been identified; or
iii. The remaining research activities are limited to data analysis.

i. Category 9: Continuing review of research, not conducted under an investigational new drug application or investigational device exemption, where categories two (2) through eight (8) do not apply, but the REC-H has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

12.9 Full Committee Review

1. All research involving greater than minimal risk is reviewed at a full committee meeting where at least 30% of voting members are present and including at least one member whose primary concerns are non-scientific.

12.10 Initial Reviews

1. For initial reviews requiring full committee approval, the following materials are sent to the primary reviewers about three weeks before a scheduled meeting:
   a. Human Research Ethics Committee application.
   b. Full research protocol, including sponsor-generated protocol for commercial trials.
   c. Investigator's brochure, if applicable.
   d. Informed consent and assent documents in English (translation is required only once the English version is approved).
   e. Recruitment materials such as advertisements, flyers, posters.
   f. Questionnaires, surveys, interview or focus group scripts and assessment tools or scales.
   g. Genetic addendum, if applicable.
   h. Letters of support or approval from off-site health or educational facilities.
   i. South African Health Products Regulatory Authority (SAHPRA) approval or application, if applicable.
   j. Principal investigator's CV, if applicable.
   k. Budget summary

12.11 Duration of Approval

1. The Human Research Ethics Committee must conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once a year. (See related policy: Continuing Review).

12.12 DECISION- MAKING PROCESS

1. The criteria used in the review of applications is based on ethical principles, regulatory guidance, applicable law, scientific merit of the methodology, sensitivity to community standards and attitudes and, where applicable, professional standards of practice and conduct. To approve research with human participants, REC-H must review the full research proposal, consent forms as well as all supplementary material, including, but not limited to, recruiting materials and data collection instruments. A description of the review and approval process is summarised in Figure 1.
2. All applications are required to be submitted via their relevant Faculty administrative contact person(s) (refer here at https://rd.mandela.ac.za/research-ethics/research-ethics-committee-human-(rec-h)/faculty-contacts) within a reasonable timeframe to ensure that they will serve at an appropriate REC-

H meeting (see here https://rd.mandela.ac.za/research-ethics/research-ethics-committee-human-(rec-h)/rec-h-meeting-dates). Faculties observe internal protocols for adhering to these guidelines. It is the researchers'' responsibility to determine timeously the extent of these Faculty internal protocols. Failure to do so might delay the review and approval of the submission. For a study coming from a staff member linked to a support division (i.e., the research is not for degree purposes) the application is submitted to the related faculty, and then to REC-H, where relevant.

3. For negligible/low risk studies, an expedited approval process is conducted. This process may only occur once the proposal has been approved at Faculty level. To this end at least two (2) co-opted trained reviewers with the required disciplinary expertise from the Faculty from where the study originates review and provide relevant feedback to researchers. Approved studies are ratified at the next REC-H meeting. As a quality control measure, REC-H inspects samples of these protocols that have been approved in an expedited manner.
4. For medium/high risk studies, the protocol serves at the relevant Faculty Postgraduate Subcommittee (FPGSC), or equivalent where it is reviewed for scientific rigor of the methodology. Only once the proposal has been approved at Faculty level does the protocol escalate to REC-H for human ethics review.
5. For any study serving at REC-H, at least two REC-H members will review the submission in depth and lead relevant discussions at a meeting. All other REC-H members will participate in discussions and have access to all documentation.
6. Formal feedback to researchers is in the form of a resolution (NOT APPROVED, RESUBMISSION, APPROVED WITH MAJOR MODIFICATIONS, APPROVED WITH MINOR MODIFICATIONS, APPROVED WITH NO CORRECTIONS) supported by detailed anonymised mandatory and advisory feedback (form RECH-REV-01 Review Criteria and Feedback). In the case of provisional approval of an application with minor or major corrections, a REC-H member is nominated as the liaison for the study to see it through to final approval. To be approved, all mandatory feedback is required to be addressed within a maximum period of 3 months from date of serving at a REC-H meeting. Neglecting to finalise the approval of a study timeously results in the protocol being recorded as withdrawn and the process must commence all over again. Advisory feedback is intended to be considered at the discretion of the Faculty, PRP and PI.
7. See related section on 'Human Research Ethics Committee: Composition and Documentation of Activities' for more information on the Committee's decision- making process.

13 APPEALS PROCESS

13.1 GENERAL

1. Researchers have the right to appeal decisions made by the Faculty PGSC or the REC-H or may have concerns regarding the administration process.
2. All appeals will be treated confidentially, as far as possible.
3. In summary: appeals may be submitted via email by the principal investigator through the REC-H Administrator who will forward it to the Chairperson of the REC-H, copied to the Chairman of the FPGSC, who will discuss it with REC-H Chairman.
4. The Ethics Committee reference number must be included on the correspondence.
5. There must be a clear motivation for the appeal.
6. The REC-H Chairperson or delegated member(s) may then seek outside consultation about the research project. This will then be reported back to the REC-H members along with recommendations regarding the appeal.
7. The REC-H committee will then reconsider the entire protocol with the new motivations and a decision will be made.

8. The decision after the appeals process is final.
9. This document describes the procedures for appealing a determination by the REC-H.

13.2 Policy

1. The REC-H may determine that some or all of a proposed research activity cannot be approved, or may require the researcher to make changes to the research in order to obtain approval. REC-H requirements and disapprovals that are consistent with regulations and policies may not be reversed by any official or agency, including another similar committee.
2. A researcher may appeal to the REC-H to do a formal re-review of a decision. The only grounds for requesting an appeal are when -
    a. there have been multiple unsuccessful efforts by the researcher and the REC-H to resolve a disagreement, and
    b. the researcher believes that the REC-H's decision is due to -
        i. inadequate or inaccurate information,
        ii. REC-H non-compliance with REC-H policy, national and/or international regulations.
3. The REC-H Chair has the authority to determine whether an appeal request will be accepted.
4. Only one appeal will be allowed on a given matter. The concluding determination made by the REC-H regarding the appeal is final and not subject to further appeal.
5. Complaints about REC-H-related business must be directed to the REC-H in the first instance. If the matter remains unresolved, it may be escalated to an appeal committee appointed by the RTI committee for a decision and then to the National Health Research Ethics Council (NHREC) for further adjudication.

13.3 Procedures

1. The appeal must be requested by the researcher within 30 calendar days of the date of the most recent REC-H review letter to the researcher concerning the decision that is being appealed.
2. The appeal request consists of sending the following to REC-H Administration:
    a. A cover letter outlining the basis for the appeal.
    b. Any supplemental documentation that supports the appeal.
    c. Within three business days of receipt, the REC-H Administration: Provides the REC-H Chair with a copy of the materials; and sends the researcher an acknowledgment of receipt of the appeal request.
3. The REC-H Chair reviews the appeal request to determine whether an appeal is appropriate, as defined above. This may include consultation with the researcher, REC-H Administration, the initial REC-H reviewer(s) and others, as needed.
4. REC-H Administration informs the researcher by email if the appeal request has been accepted.
5. The appeal is heard at an REC-H meeting. This may be a regularly scheduled REC-H meeting, or it may be a meeting convened specifically for this purpose.
6. The researcher is required to attend the REC-H meeting and to present the appeal to the REC-H members. REC-H Administration works with the REC-H and the researcher to schedule a mutually acceptable review date as soon as possible.
7. REC-H Administration follows standard procedures to identify the REC-H 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.
8. During the REC-H meeting:
    a. The REC-H 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.
    b. The researcher is invited to present information and rationale to the REC-H.
    c. The researcher's colleagues (if present) are invited to present.
    d. There is a question-and-answer session with the researcher and colleagues.

e. The researcher and colleagues leave the meeting room.
f. The REC-H members and other meeting attendees discuss the appeal.
g. The REC-H moves and then votes whether to take one of the following actions -
    i. approve the appeal and modify the original decision;
    ii. disapprove the appeal and uphold the original determination; or
    iii. defer the appeal and obtain additional information or consultation to make a final decision.

9. REC-H Administration communicates the REC-H's appeal determination, and any considerations or requirements associated with it, to the researcher in a letter within 7 business days of the REC-H's determination. If appropriate, the determination may also be communicated by email or telephone call with follow-up email, by the REC-H Chair.
    a. All REC-H correspondence must be addressed to the principal investigator or delegated signatory unless dictated by particular circumstances.
    b. REC-H Administration works with the REC-H Chair and/or the primary reviewer to draft the letter.

14 COMPLAINTS PROCESS

14.1 TYPES OF COMPLAINTS

1. The REC-H may receive complaints about researchers, the conduct of research, or about the conduct of the REC-H. Complaints may be made by participants, researchers, staff of the institution, or others. All complaints should be handled promptly and sensitively.
2. Possible complaints cover a broad spectrum from 'inadvertent technical deviations' from established protocols to allegations of scientific misconduct or fraud. The primary concern in response to any complaint is the extent to which research participants are endangered. There may also be concerns about the degree to which researchers are fulfilling their responsibilities, questions around culpability for misconduct and misleading reports being published by a researcher accused of misconduct or fraud. Often the REC-H will be the most appropriate body to consider complaints in the first instance, although ultimately, the responsibility lies with Nelson Mandela University.

14.2 PROCEDURES FOR RECEIPT OF COMPLAINTS

1. A complaint should be lodged with the REC-H Administrator. The REC-H Administrator will forward the complaint on to the REC-H Chairperson.
2. Submissions from whistle-blowers will be confidential and can be made to the REC-H Chairperson.
3. The Chairperson of the REC-H will receive the complaints; he/she may delegate this responsibility to a member of the REC-H. All complaints will be dealt with and may require the assistance of other persons (not necessarily members of the REC-H).
4. Should any person feel that the response of REC-H is inadequate, a complaint can be escalated to the DVC: RII at dvc-rii@mandela.ac.za, and thereafter the National Health Research Ethics Council (NHREC), to which REC-H is affiliated.

14.3 PROCEDURES FOR RESPONDING TO COMPLAINTS

1. The Chairperson would consider the complaint - including, where necessary, reference to original protocol, contact with researchers, or contact with complainants.
2. The Chairperson will respond urgently when there is any suggestion of harm to research participants, researchers, or any other person. In extreme circumstances, an immediate demand to suspend a research study may be necessary while concerns are adequately investigated. In other cases, prompt action may be

required to rectify or remove the cause of concern. Having determined the urgency of the need for action, the Chairperson should take any, and possibly all, of the following steps according to the circumstances:

a. Make a clear and full written record of the complaint.
b. Seek further information from all relevant parties.
c. Notify the PI and PRP of the complaint and request a written response, which will serve at the next meeting of the REC-H or at an urgent meeting of the REC-H, which will be convened if necessary.
d. If necessary, confer with the highest level of management and authority within the relevant institution.
e. Advise the complainant of the response.

14.4 PROCEDURES FOR INVESTIGATING COMPLAINTS

1. Where initial investigations reveal a situation that requires further investigation and review, the following procedures are recommended, at the discretion of the REC-H Chairperson:
   a. Table the investigation report at the next REC-H meeting.
   b. In addition to the written response from the researcher, invite the researcher(s) to explain the situation to the REC-H and to demonstrate why the project should not be discontinued and ethical approval withdrawn.
   c. Advise researcher(s) that they may be accompanied by one or more colleagues.
   d. Reconsider the original research proposal and seek additional information from the researcher(s) in relation to the conduct of the study, or any other relevant factors, before making a final decision whether to **revise** or **reconfirm** the original decision to approve the project.
   e. Having considered the matter, the committee may:
      i. **withdraw approval** resulting in suspension of the project,
      ii. **require amendments** to the original research proposal or to the conduct of the research, or
      iii. allow the project to continue without amendment.
2. The REC-H will inform the principal investigator/research in writing of the decision of the REC-H explaining the reasons for the recommendations. It may be necessary to inform research participants that the research they have been participating in has been modified or discontinued. In this instance, the REC-H will take advice from the researcher(s) about the wording of the notice to participants.
3. An appeal against a decision can be made and should be referred to a mediator independent of the REC-H and related activities.
4. Advise the complainant of the response. Where the complainant is not satisfied with the actions taken, the complaint could be referred to the DVC: RII.

14.5 ALLEGATIONS AND COMPLAINTS OF SERIOUS RESEARCH MISCONDUCT

1. Research misconduct includes any of the following:
   a. Fabrication, falsification, plagiarism, or deception in proposing, carrying out, or reporting results of research.
   b. Deliberate, dangerous, or negligent deviations from accepted practice in carrying out research. This includes failure to follow established protocols if this results in unreasonable risk or harm to human beings, animals, or the environment and also the facilitating of misconduct by collusion in, or concealment of, such actions by others.
   c. Failure of informed consent.
   d. Breaches of confidentiality.
   e. Deception in research process.
   f. Misrepresentation or falsification of credentials.

2. Misconduct does not include honest error or honest differences in the design, execution, interpretation, judgment in evaluating research methods or results of misconduct (including gross misconduct) unrelated to the research process.
3. Where there has been an allegation of serious misconduct, the institution should ensure the following:
    a. Protection of participants.
    b. Appropriate confidentiality (in case the allegation proves to be groundless).
    c. Protection of 'whistle-blowers'.
    d. Natural justice for those who are the subject of any allegations or complaints.
4. Confidentiality, protection for complainants and natural justice for the person complained about will be dealt with by the review process outlined as follows:
    a. Determine whether the allegation falls within scientific misconduct.
    b. Determine whether there is prima facie evidence of scientific misconduct.
    c. Institute a formal investigation to evaluate all relevant facts to determine whether scientific misconduct has been committed and, if so, by whom, as well as the seriousness of the misconduct. The integrity of the research data must be evaluated, and all appropriate groups advised if inaccurate, misleading or invalid data have been published or submitted to other agencies.

14.6 Complaints concerning REC-H review processes

1. Most complaints received by REC-H concern the review process itself or the manner in which researchers and their projects have been considered and dealt with. For example, researchers may complain when the REC-H has rejected a proposed project, when a committee is perceived to be taking undue time considering a proposal, or when conflict has arisen between a committee and researchers. In many situations, the problem may simply be one of inadequate communication between the committee, its administrators, and the complainant(s).
2. The Chairperson will attempt to deal with the concern or complaint without formal investigation where possible.
3. If the matter remains unresolved, the principle investigators may lodge a formal complaint with the Deputy Vice-Chancellor: RII.
4. If the complainant is dissatisfied with the decision of the Deputy Vice-Chancellor: RII, an appeal may be lodged with the Vice-Chancellor. The decision of the Vice-Chancellor is final and binding.

15 Monitoring/Continuing Review

1. Nelson Mandela University researchers (staff and/or students) of currently active studies making use of human participants are required to complete and submit a progress report on an annual basis.
2. Failure to do so may result in the immediate suspension or termination of all data collection activities linked to the study. In the case of currently active studies which require renewal/extension of data collection activities and/or amendments to the study, the relevant form should be completed and accompany the submitted progress report.
3. Researchers are advised to familiarise themselves with the Documentation prior to completing and submitting a progress report for review. Failure to do so might result in a delay in the review and approval of the progress report, thereby impacting on the ability of the study to continue (if applicable).

15.1 Policy

1. The mandate of the Human Research Ethics Committee is to protect human research participants. Continuing review of ongoing research is one aspect of this commitment. Continuing review must be

substantive and meaningful focussing on whether the balance of risks and benefits for a particular study has changed, whether there are unanticipated findings involving risks to participants and/or others, and whether any new information regarding risks and benefits should be provided to participants. Review must occur within one year of the last approval date, unless the Committee determines that review should occur more frequently. The South African Health Products Regulatory Authority (SAHPRA) requires six monthly progress reports for clinical trials under its jurisdiction. Progress reports using the SAHPRA format are acceptable to the Human Research Ethics Committee. Continuing review is additional to the review required for all amendments, serious adverse events and unanticipated problems.

2. For protocols initially reviewed by the full committee, the Committee must decide whether ongoing reviews/approvals require full-committee or expedited review. The Chair or a designee will perform expedited continuing reviews. These are detailed in this standard operating procedure.
3. When conducting continuing review, the Human Research Ethics Committee should start with the working presumption that the research, as previously approved, does satisfy the prescribed criteria. The Committee should focus on whether there is any new information provided by the investigator, or otherwise available to the Committee, that would alter the Committee's prior determinations, particularly with respect to its prior evaluation of the potential benefits or risks to participants. The Committee should also assess whether there is any new information that would necessitate revision of the protocol and/ or the informed consent document.

15.2 PURPOSE

1. The purpose of this policy is to provide guidance on the continuing review process as required by NMU. The policy also clarifies the consequences for an investigator failing to submit an annual progress report.

15.3 PROCEDURES

1. Department of Health Guidelines

a. According to the Department of Health's Research Ethics Guidelines (2015), the Human Research Ethics Committee must monitor the ongoing conduct of approved research. The frequency and type of monitoring should reflect the degree of risk to participants. The Committee must receive, at least annually, reports from principal investigators on the following issues:
   i. Progress to date, or outcome of completed research.
   ii. Information concerning maintenance and security of records.
   iii. Evidence of compliance with the approved protocol.
   iv. Evidence of compliance with any conditions of approval.

b. Further, a research ethics committee may conduct random inspections of research sites, data and signed consent forms and records of interventions (with prior consent and knowledge of participants). As a condition of approval of each protocol, researchers must report:
   i. Serious or unexpected adverse effects on participants.
   ii. Proposed changes in the protocol.
   iii. Unforeseen events that might affect continued ethical acceptability of the study.
   iv. If a study is stopped before the expected date of completion and provide reasons.

2. Continuing Review

a. Continuing review is a broad term that covers a range of possible procedures depending on the level of risk inherent in a study. For example, depending on the level of risk, the Human Research Ethics Committee may request:
   i. More frequent, than annual, continuing review.
   ii. Sequential continuing review, for instance after the enrolment of a few participants.
   iii. Independent monitoring of the consent process and rigorous evaluation of participants' understanding of the protocol and of being a research participant.

b. The Human Research Ethics Committee must determine at the time of the initial and at the time of each continuing review whether it is necessary for future continuing reports to be submitted more frequently.
    i. Criteria which may be used to determine whether continuing review should occur more frequently include:
    ii. Magnitude of risks.
    iii. Participants' vulnerability.
    iv. The experience of investigators in conducting research.
    v. The Committee's previous experience with the investigators (e.g., compliance history, previous problems with the investigator obtaining informed consent, or prior complaints from participantsabout the investigator).
    vi. Magnitude of adverse events which may be irreversible, life threatening or disabling (the more so when there are no off-setting direct benefits to participants).
    vii. The type and magnitude of a risk is unknown, for instance in proof of concept research involving initial attempts to find out if a laboratory discovery or hypothesis with potential clinical applicability works as expected when used in humans. The risks cannot be fully described until they are tested in humans and may be irreversible.
    viii. Previous experience indicating that the frequency of adverse events is a potential concern.
    ix. There have been non-compliance concerns which warrant more frequent monitoring.
    x. A protocol raises ethical concerns about research design or implementation for which there is no consensus or where available ethical or regulatory guidance is ambiguous or contradictory, for example using placebos in studies when there is a known effective treatment for a condition such as hypertension.
    xi. The projected rate of enrolment.
    xii. Whether the research involves novel interventions.

c. When the Human Research Ethics Committee is concerned about the levels of risk in a study, in addition to specifying a time interval between continuing reviews, it may specify a participant enrolment number as a threshold for determining when continuing review is to occur. For example, at the time of initial review and approval of a high-risk clinical trial, the Committee might require that continuing review occur either in 6 months or after 5 participants has been enrolled, whichever occurs first. The minutes of full committee meetings should clearly document the approval period (continuing review interval).

15.4 Documentation for Continuing Review

1. The principal investigator is responsible for timely submission of a protocol summary and status report on the progress of the research which includes:
    a. Number of participants enrolled.
    b. Number of participants who withdrew.
    c. Number of participants lost to follow-up.
    d. A summary of any complaints about the research since the last Committee review.
    e. A summary of any relevant recent literature, interim findings, and amendments or modifications to the research since the last Committee review.
    f. Any relevant multi-centre trial reports.
    g. Any other relevant information, especially about risks associated with the research. (Have risks and benefits been consistent with those originally anticipated?)
    h. Information regarding requests for changes.
    i. Changes in sponsors or funders.
    j. Changes in research personnel.

k. A copy of the current informed consent documents, including Afrikaans and Xhosa translations if applicable.
l. Any newly proposed consent documents.
m. A summary of any unanticipated problems and available information regarding adverse events. In many cases, such a summary could be a brief statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document and any investigator's brochure.

2. If the Chair or designees has determined that a protocol requires continuing review at a full committee meeting then, two weeks before the convened meeting, all members must receive and review an electronic protocol summary and a status report on the progress of the study, and at least one member must receive the complete protocol. The following materials are sent to the main reviewer:
   a. A summary containing the relevant information required to determine whether the protocol continues to fulfil the criteria for approval.
   b. A status report on the progress of the research, including any changes previously approved by the Committee.
3. When reviewing the informed consent document(s), the Committee must ensure that:
   a. The currently approved or proposed consent document is still accurate and complete; and
   b. Any significant new findings that may relate to the participant's willingness to continue taking part are given to participants.
4. To efficiently accomplish its continuing review workload, the Chair summarises the progress of a study; a typical summary might include the following information:
   a. The research is proceeding according to the Human Research Ethics Committee-approved protocol.
   b. The rate of participant enrolment is as expected.
   c. There have been no unanticipated problems.
   d. The rate and pattern of adverse events are as expected.
   e. No participants have complained about the conduct of the research or withdrawn from the research.
   f. There is no new published or unpublished information that would alter the Committee's prior determinations, particularly with respect to the Committee's evaluation of the potential benefits and risks to participants and the informed consent process.
   g. No changes to the protocol or informed consent documents are needed.
5. In the absence of the Chair raising any concern about the research, the Committee should be able to complete its continuing review deliberations for such a project within a brief period of time.
6. On the other hand, the following continuing review of a randomised control trial is likely to raise concerns which need more lengthy deliberation:
   a. The rate of serious adverse events occurring in participants is significantly higher than expected.
   b. A completed research project recently reported in the literature identified previously unrecognised risks for the same experimental intervention being tested in the clinical study undergoing continuing review.
   c. The investigator is proposing several substantive revisions to the protocol in response to the new risk information, including the addition of new exclusion and new safety monitoring procedures for participants.
   d. The investigator is proposing substantive changes to the informed consent document which include a description of the new information regarding reasonably foreseeable risks.
7. In these circumstances, the Human Research Ethics Committee needs to spend significantly more time carefully reassessing whether the risks to participants are sufficiently minimised and reasonable, given the new information presented and informed consent document proposed by the investigator, or whether additional changes should be required.

8. The protocol must be approved by a majority of the core (or alternative) members present. After the meeting the investigator is notified in writing of the action taken. Written notification will include the signed annual progress report form The Committee's conditions, if any, must be met before continuing approval may be granted.
9. When approving research with conditions at the time of continuing review, the Committee must specify whether any conditions need to be satisfied before an investigator can continue particular research activities related to those conditions.
10. Expedited review of annual progress reports by the Chair or designee follows the substantive approach outlined above.
11. As a rule, initial approval for a research study is for one-year only, with approval expiring on the one- year anniversary date of the original approval date. The continuing review date is set according to the date on which final approval is granted, either by full-committee or expedited review. [Note: this does not apply to US federally-funded or supported research – see below for separate guidance.]
12. Principal investigators are responsible for ensuring that annual progress reports are submitted with enough time for continuing review to take place before the expiry date of the study. The Human Research Ethics Committee does not have the resources to notify investigators when their studies require annual renewal. If an annual progress report is not submitted prior to the expiry date, a study's approval will lapse, and no data may be collected or used during the period of lapsed approval. Where no applications for renewal are forthcoming, a study may be closed.
13. If the full committee (or Chair or designee) does not approve the continuation of a study, it must inform the principal investigator in writing, with reasons for its decision. The principal investigator is invited to respond in person or in writing providing justification for revising the decision or a proposal to change the protocol. The fact that an appeal by the principal investigator is on-going does not change the expiry date of prior approval or the consequences of a lapse in such approval. If the principal investigator appeals the decision the Committee must ensure there is a fair hearing of the appeal.
14. No Human Research Ethics Committee member may undertake or participate in a continuing review of a study in which he/ she has a conflict of interest, except to provide information requested by the Committee.

15.5 Setting the Continuing Review Due Date

1. Note: The US Office for Human Research Protections (OHRP) provides a detailed explanation for determining the effective date of initial IRB approval and the date for continuing review in its Guidance on IRB Continuing Review of Research, November 10, 2010, pp. 30-47:

   > '*Except when an expedited review procedure is used, the protocol continuing review date is set according to the date of approval by a full committee meeting. Of note, IRB review of an amendment to a research project during the period for which approval is authorised does not constitute continuingreview of the project as a whole, and thus does not extend the date by which continuing review must occur (e.g. beyond one year from the effective date of the initial approval or the most recent continuingreview approval). In order for the research to be approved by the IRB at a convened meeting, it must receive the approval of a majority of the core (or alternative) members present at the meeting (45 CFR46.108(b)). (Put simply, review of amendments does not alter the date by which continuing review must occur because continuing review examines the full protocol, not simply a change to it.)*'

2. Determining the first continuing review date for research reviewed by the Committee at a convened meeting at the time of initial review and approved for one year

3. When the Committee reviews and approves research without conditions at a full committee meeting
    a. When the Committee conducts the initial review of a research project at a convened meeting and approves the research for one year without requiring either (a) changes to the protocol or informed consent document(s), (b) submission of clarifications or additional documents, the effective date of the initial approval is the date of that Committee meeting. In such circumstances, the expiry date of the initial approval period and the date by which the first continuing review must occur may be as late as one year after the Committee meeting at which the research project was initially approved (See OHRP Guidance for an example, p. 41).
4. When the Committee reviews and approves research with conditions at a full committee meeting without requiring further review at a subsequent convened meeting
    a. A much more common scenario is when the Committee conducting the initial review of a research project at a convened meeting takes the following set of actions:
        i. Approves the project for one year
        ii. As a condition of approval, requires (a) changes to the protocol or informed consent document(s), or (b) submission of confirmations of specific assumptions or understandings on the part of the Committee or additional documents, and
        iii. Directs that the Committee Chairperson (or other individual(s) designated by the Committee) to review and determine on behalf of the Committee whether the changes, clarifications, and/ or additional documents to be submitted by the investigator(s) are satisfactory.
    b. Under this scenario, further review by the Committee at a subsequent convened meeting is not necessary for the initial approval to become effective, and the effective date of the initial approval is the date on which the Committee Chairperson (or other individual(s) designated by the Committee) has reviewed and accepted as satisfactory all changes to the protocol or informed consent documents, or any other responsive materials, required by the Committee from the investigator. In such circumstances, the expiry date of the initial approval period, which is the date by which the first continuing review must occur, may be as late as one year after that effective date of initial Committee approval. The OHRP notes that the first continuing review in these circumstances may occur earlier; for example, for logistical reasons the Committee may choose to set the expiry date of the initial approval period at one year from the date of the Committee meeting at which the research project was initially approved with conditions.
    c. The Committee records must include documentation of the date when the Committee Chairperson (or other individual(s) designated by the Committee) determined that all conditions of Committee approval have been satisfied and the approval becomes effective, and the expiry date of the initial Committee approval.
5. Determining the date for the second and all subsequent continuing reviews for research reviewed by the Committee at convened meetings and approved for one-year intervals, including how to maintain a fixed anniversary date for the expiry of annual Committee approvals
    a. The Committee must conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. Given this requirement, it is important to recognise that the use of the 'effective date' of Committee approval (i.e. the date on which the Committee Chairperson or other individual(s) designated by the Committee has determined that the conditions of approval have been satisfied) – as opposed to the date of the convened meeting at which the Committee approved a research study with conditions – to determine the latest permissible date for continuing review only applies to the first continuing review. For all subsequent continuing reviews of a research study, since there will be an ongoing approved study, the date of the convened meeting when the Committee conducts continuing review and approves the study (with or without conditions) determines the latest permissible date of the next continuing review.

6. Anniversary dates for approvals
    a. Given the logistical advantages of keeping the expiry date of the Committee approval period constant from year to year through-out the life of a project, when (a) the Committee grants approval for one year at the time of each continuing review, and (b) the Committee performs continuing review and re-approves (with or without conditions) the research within 30 days before the Committee approval period expires, the Committee retains the anniversary of the expiry date of the initial approval as the expiry date of each subsequent one-year approval period. For example, if the Committee conducts the initial review of a research study and approves it without conditions on October 1, 2022 for one year, the Committee may conduct its first continuing review anytime between September 1 and October 31 2023, and re-approve the research for another one-year period that expires on October 1, 2024. The same timing can be applied to each subsequent continuing review until the research activities involving human participants are completed. (See OHRP Guidance for examples, p. 42-45).
    b. Ultimate responsibility rests with the principal investigator to monitor and track approval periods and to ensure continuing reports are filed in time for Human Research Ethics Committee review, in particular where review by the full committee is needed.
    c. If an investigator fails to provide continuing review information to the Human Research Ethics Committee or the committee has not reviewed and approved a study by the specified continuing review date, the research must stop, unless the committee finds that it is in the best interests of individual participants to continue taking part in the research interventions or interactions. Enrolment of new participants, participant follow-up and data collection may not occur after a study has expired. When continuing review of a study does not occur prior to the end of the approval period specified by the Committee, the Committee's approval expires automatically. Depending on its administrative capacity, the Human Research Ethics Committee will send a letter informing the principal investigator of the suspension but the responsibility rests with the researcher to suspend enrolment.
    d. The determination regarding whether it is in the best interests of already enrolled participants to continue to participate in the research after Committee approval has expired may be made initially by the investigator, possibly in consultation with the participants' treating physicians (if the investigator is not the treating participants' physician, but the investigator as soon as possible must submit a request for confirmation that the Committee agrees with the determination. The determination by the Committee may be made by the Committee Chairperson, by another Committee member or group of Committee members designated by the Committee Chairperson, or at a convened meeting of the Committee Furthermore, this determination maybe made for all enrolled participants as a group or for each individual participant. If the investigator or Committee determines that it is not in the best interests of already enrolled participants to continue to participate, investigators must stop all human participants research activities, including intervening or interacting with participants and obtaining or analysing identifiable private information about human participants.
    e. When Committee approval of an ongoing research project lapses and the Committee subsequently re-approves the project, the Committee may approve the project for one year and establish a new anniversary date for the expiry date of subsequent approval periods, or it may re-approve the project for a period of less than one year so as to retain the original anniversary date on which prior approval periods expired.
    f. When continuing review of a research project does not occur prior to the end of the approval period specified by the Committee, Committee approval expires automatically. The OHRP does not consider such an expiry of Committee approval to be a suspension or termination of Committee approval. Therefore, such expiries of Committee approval do not need to be reported to the OHRP as suspensions or terminations of Committee approval under the Common Rule.

g. However, if the Committee notes a pattern of non-compliance with the requirements for continuing review (e.g., an investigator repeatedly or deliberately neglects to submit materials for continuing review in a timely fashion or the Committee itself is frequently not meeting the review dates), the Committee should determine whether such a pattern represents serious or continuing noncompliance that needs to be reported to appropriate institutional officials, the Health and Human Services Agency that supported the research, and the OHRP (45 CFR 46.46.103(b)(5).

h. Additionally, researchers who allow a lapse of an annual renewal or who fail to respond to feedback regarding a proposed amendment or adverse or unanticipated event, may be informed that their funding has been frozen, that other proposals will not be reviewed, or that they have triggered a higher level of continuing review, such as an internal audit process.

15.6 Communicating the Human Research Ethics Committee's Continuing Review Determination to Investigators and the Institution

1. The Committee must notify the investigator and the institution in writing of its decision to approve or disapprove proposed research or of modifications required to secure Committee approval of the research. If the Committee decides to disapprove the research, it must include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing. The OHRP recommends that the Committee notifies any sponsor or co-ordinating centre of a study (possibly through the investigator) of any decision to disapprove the research and the reasons for its decision.
2. The REC-H's written notification of approval must state:
   a. The period of time for which the project is approved
   b. Any conditions of the IRB's approval
   c. The date by which the next continuing review must occur.
   d. Written notification includes the return of the signed Annual Progress Report Form.

15.7 Suspension or Termination of HREC Approval of Research or Disapproval of Research at the Time of Continuing Review

1. The Committee has the authority to suspend or terminate approval of research that is not being conducted in accordance with the Committee's requirements or that is associated with unexpected serious harm to participants (45 CFR 46.113). A suspension or termination of Committee approval of research may occur at any time during the period for which Committee approval has already been given.
2. For a multicentre research project for which many or all institutions engaged in the research project choose to rely on their local Committees' review of the project, a local Committee's decision at one institution to suspend or terminate its approval of the research only applies to the conduct of the research project at that institution.
3. The Committee must promptly report any termination or suspension to the investigator, appropriate institutional officials, the Health and Human Services (HHS) agency that supported the research and the OHRP (45 CFR 46.103(b)(5) and 46.113). Such reports must include the reasons for the Committee's action (45 CFR 46.113).
4. **Committees must follow written procedures for ensuring such reporting (45 CFR 46.108(a)). When reporting the suspension or termination of Committee approval of a research project to the OHRP, the OHRP recommends that the report include the following information:**
   a. The name of the institution (e.g. university) conducting the research
   b. The title of the research project and the title of any related grant, contract or cooperative agreement
   c. The name of the principal investigator for the research project
   d. The REC-H REF number and the number of HHS award(s) (e.g. grant, contract)

e. The actions the institution is taking or plans to take to address the suspension or termination (e.g., investigate alleged non-compliance, educate the investigator, educate all research staff, and require monitoring of the investigator or the research project).

5. When the Committee (a) suspends or terminates its approval during the period for which the Committee approval has already been given or (b) disapproves a research project at the time of continuing review, the Committee should establish procedures to ensure the rights and welfare of currently enrolled participants are protected, participants are not put at risk, and participants receive appropriate care, if indicated, during the period of suspension or following the cessation of the research. This is particularly important in the context of clinical trials. For example, the Committee, in consultation with the principal investigator and the participants' physicians, may need to determine whether it is in the best interests of currently enrolled participants to:

a. Continue receiving the interventions that were being administered to participants under the research project
b. Be transferred to another institution engaged in the research so that participants' participation in the research can continue
c. Be transitioned to medical management outside the research context.
d. Continuation of participants on interventions that were being administered under the research project may be appropriate at least temporarily, for example, when those interventions hold the prospect of direct benefit to participants or when withholding those interventions poses increased risk to the participants. If the Committee decides that already enrolled participants should continue to receive the interventions administered during the research, data collection (especially safety information) should also continue for such participants.

15.8 Identifying the Point when Continuing Review is No Longer Necessary

1. Continuing review and re-approval of a research project at least annually is required so long as the research involves human participants. The OHRP considers a research project to continue to involve human participants as long as the investigators conducting the research continue to obtain:
   a. Data about the participants through intervention or interaction with them
   b. Identifiable private information about the participants in the research.
2. With respect to obtaining identifiable private information, the OHRP considers this to include obtaining identifiable biological specimens originating from living individuals. This includes:
   a. Collecting or receiving identifiable private information (including identifiable biological specimens) from any source (i.e., not already in the possession of the investigator)
   b. Collecting identifiable private information by observing or recording private behaviour without interacting or intervening with human participants
   c. Using, studying or analysing identifiable private information (including identifiable biological specimens), even if the information was already in the investigator's possession before the research begins. This includes using, studying or analysing any of the following:
      i. Identifiable private information obtained by interacting or intervening with human participants
      ii. Identifiable private information stored in documents, records, photographs, images, video recording or audio recordings provided to the investigators from any source
      iii. Identifiable private information stored in documents, records, photographs, images, video recording or audio recordings already in the investigator's possession before the research begins
      iv. Identifiable private information obtained about an individual by interviewing other people
      v. Identifiable biological specimens provided to the investigators from any source
      vi. Identifiable biological specimens already in the investigator's possession before the

research begins

3. A research project no longer involves human participants once the investigators have finished obtaining data through interaction or intervention with human participants or obtaining identifiable private information about the participants, which includes using, studying or analysing identifiable private information. Once all such activities described in the Committee-approved protocol are finished, the project no longer needs to undergo continuing review. For example, when the only remaining activity of a research project involves the analysis of aggregate data sets without individual participant identifiers, no further continuing review is necessary. At that point, the Committee can formally close its file for the project and advise the investigator of that action. Similarly, maintaining individually identifiable private information without using, studying or analysing such information is not human participants' research and thus does not require continuing review.

15.9 Study Closure or Final Report

1. A study is considered active or ongoing until a study closure or final report is submitted to the Human Research Ethics Committee. This is also consistent with FDA regulations (21 CFR 56.108) which require prompt reporting to the Committee of any changes in research activity, and completing a study is considered a change in activity.
2. The principal investigator can voluntarily close a study when completed and Human Research Ethics Committee approval is no longer required, when all participant accrual is completed and/or all data (including study follow-up data) pertaining to participants have been collected and when no further interaction with participants is planned for research purposes. In multi-centre commercial trials, the principal investigator must provide confirmation from the sponsor that all participants have completed their final visits and follow-up at the local site (i.e. Mandela University) is complete.
3. To formally close a study, the principal investigator must submit a final report specific to that study. Final reports will be reviewed and approved by an expedited process. The principal investigator will be sent written notification of the study's closure, including a signed original copy of the Final Closure Report. If a study is not closed but is allowed to expire as a lapse in approval, an administrative suspension letter may be sent to the principal investigator.
4. If a principal investigator terminates employment with the University, he or she must submit a final report to the Human Research Ethics Committee or transfer the protocol to another principal investigator via an amendment which requires Committee approval. If the principal investigator is unwilling or unable to provide such an amendment, the Committee may choose to administratively close the study.

15.10 Verification of No Material Changes since Prior Human Research Ethics Committee Review

1. The Human Research Ethics Committee or other agents designated by the Committee may determine at any point during the period of approval for a particular protocol that the protocol requires verification from sources other than the investigator that no material changes have occurred since prior Committee review.
2. The nature of the study will determine from which source verification is to be requested. The decision will be made on a case-by-case basis using, among others, the following sources of verification:
   a. Pharmacy distribution records
   b. Data Safety Monitoring Boards
   c. Sponsors
   d. Research participants' records
   e. Hospital medical records

3. A request for verification that no material changes have occurred since prior Human Research Ethics Committee review may be made by, among others:
    a. The Human Research Ethics Committee based on information in the continuing review form.
    b. The Chair, a Committee member, the Committee's administrative staff.
    c. An investigative subcommittee or an independent audit team.
4. Examples of criteria which might alert the Human Research Ethics Committee to the need for such verification include:
    a. Randomly selected projects.
    b. A potential incident of non-compliance raises concern.
    c. Complex projects conducted by investigators who previously have failed to comply with research ethics guidelines or determinations of the Committee.
    d. Projects where concerns about possible material changes occurring without Committee approval have been raised based on information in the continuing review reports or from other sources.

16 STUDY EXTENSION

1. Extensions of low-risk faculty-approved protocols may also be approved by the Faculty Ethics Committees, and not at REC-H. The following conditions must be adhered to:
    a. Extension of medium and high-risk protocols must serve at REC-H.
    b. Original ethics approval is granted for one-year. Thereafter, two extensions may be approved bringing the total period of the ethics approval to three years.
    c. If data collection for a study is required to continue after the three-year period, a new application for ethics approval must be submitted and approved.
    d. An extension of ethics approval cannot be granted on a lapsed protocol. If the original ethics approval period has expired, a new application for ethics approval must be submitted and approved. Data collection may not commence or continue if ethics approval has lapsed.
    e. A progress report must be submitted together with the application for extension. All documentation must be retained for audit by the National Health Research Ethics Council (NHREC).
    f. All extensions approved at faculty level must be submitted to RECH for noting, together with all new applications approved at faculty level.
    g. All medium and high-risk protocols need to be approved by REC-H, and all low risk which were originally approved via RECH needs to come back to RECH for approval of an extension.
    h. If a study requires an extension beyond the three years permitted (and ethics has not lapsed), the PI is to submit a progress report under the old application – but only if the study requires a time extension. If the project needs to be amended as well, then a new application must be submitted.
    i. An extension can be approved from the date of the original expiry.
    j. All extensions will be for a one-year period.

17 AMENDMENTS REVIEW

17.1 DEFINITIONS

1. Minor Amendments

a. A minor amendment is defined as a change that does not materially affect the balance of risks and benefits in a study or does not substantially change the specific aims or design of the study. Examples of minor amendments include:
b. Administrative or informational amendments:

i. Changes in research staff.
ii. Change in telephone numbers.
iii. Changing the study title (e.g. just a reshuffling of words).
iv. Addition or removal of qualified investigators, study sites.
v. Revision of format of consent documents, recruitment materials or questionnaires.
vi. Correction of typographical errors.

c. Procedural amendments
i. Drawing slightly different amounts of blood.
ii. Changing frequency at which blood is drawn.
iii. An increase or decrease in proposed number of participants supported by a statistical justification.
iv. Narrowing the range of inclusion criteria.
v. Broadening the range of exclusion criteria.
vi. Changing the amount of compensation, within reasonable limits.
vii. Revisions to the informed consent documents to improve clarity, to include missing elements or to revise lay language.
viii. Decreasing drug dosage or frequency of administration.
ix. Decrease in number of study visits provided such a decrease does not affect collection of relevant safety-related data.
x. Minor adjustments in the duration of the study for retrospective reviews

2. Major Amendments

a. Such amendments involve significantly increased risk to participants and often reflect changes in the direction of a study that may substantially change its purpose or goal. Changes that alter the overall purpose or objective of a study may require a new study submission.

b. Examples of changes that may affect the balance of risks and benefits include:
i. Change of study title
ii. Adding a new activity that may increase risk to participants.
iii. Changing drugs or medications as well as dosages.
iv. Changing levels of radiation exposure.
v. Adding a vulnerable population.
vi. Adding or changing invasive procedures.
vii. Adding a research arm to the study.
viii. Substantially extending the duration of exposure to the test material or intervention.

c. To obtain Human Research Ethics Committee approval for amendments, the principal investigator must submit an amendment application form describing all proposed modifications. This applies to the protocol and the informed consent forms. In addition, 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.

17.2 Requesting an Amendment

1. Nelson Mandela University researchers (staff and/or students) of currently active studies making use of human participants who require an amendment to a currently active study in terms of data collection activities are required to complete and submit a request for the review and approval of such an amendment PRIOR to implementing the amendment, except where it is essential to prevent and/or exclude immediate hazards and/or risks to currently enrolled participants (in case of the latter situation, please alert Imtiaz.Khan@mandela.ac.za for advice on the required procedure to follow). Failure to

request an amendment prior to implementation thereof may result in the immediate suspension or termination of all data collection activities linked to the study.

2. Amendments to studies include but are not limited to changes in research protocol, written/oral information/consent documents and/or data collection instruments. If the amendment involves only a change to the primary responsible person (PRP), primary investigator (PI) or any other researchers collaborating with the study, the following procedure detailed at https://rd.mandela.ac.za/Research-Ethics/Research-Ethics-Committee-Human-(REC-H)/Request-for-Change-in-Study-Researchers must be followed.
3. Unless there are extenuating circumstances, continuous applications for amendments to a particular study will not be viewed in a favourable light. This procedure described below is NOT for requesting approval for an extension/renewal of a previously approved protocol (for this purpose please refer to https://rd.mandela.ac.za/Research-Ethics/Research-Ethics-Committee-Human-(REC-H)/Extension-of-a-Study

17.3 Minor Amendments

1. Minor amendments to a currently active study are subject to expedited approval. Minor amendments are restricted to the following:
   a. Any modification that would not significantly affect the assessment of the risks and/or benefits of the study.
   b. Any change that does not significantly affect the aims and/or design of the protocol for the study.
   c. A decrease/increase in sample size, supported by relevant statistical motivation.
   d. Administrative changes such as researcher contact details, the removal/addition/replacement of research personnel and/or study sites.
   e. Reducing the inclusion criteria.
   f. Increasing the exclusion criteria.
   g. Modifying data collection points or volume of data collected as long as any safety regulations/constraints are retained.
   h. Changes in compensation and/or reimbursement with adequate rationale.
   i. Any editorial modifications that serve to clarity but not alter the existing meaning of a document.
   j. Any translations of documents previously reviewed and approved by REC-H.

17.4 Procedure for requesting a Minor amendment

1. The procedure for requesting approval for a minor modification is by means of written communication on a signed letterhead to Imtiaz.Khan@mandela.ac.za citing the study reference number and providing a detailed description of each change, supported by a rationale for each change as well as any and all relevant revised documentation for each change.
2. One copy of each amended study document which clearly highlights the changes must be submitted (highlighting of changes can be implemented by means of tracked changes, striking through “old text” and showing the “new text” in bold, underlined or in italics, or similar).
3. Additionally, one clean copy of the each amended document should accompany the written request.
4. Failure to submit both copies of modified documents and/or rationale for proposed modifications will delay the review and approval process.

17.5 Major Amendments

1. Major amendments to a currently active study are subject to full REC-H review. Examples of major amendments include but are not limited to the following:
   a. Increasing the inclusion criteria.

b. Reducing the exclusion criteria.
c. Emergence of new and/or serious and/or significant risks to either participants and/or researchers.
d. Requirement for new and/or additional study documentation to be distributed to or viewed by
e. participants that include information and/or data collection items significantly different to that in materials previously approved by REC-H.
f. Any other change that does not qualify as a minor amendment (see list above).

2. Researchers are advised to familiarise themselves with the Amendment Guidelines prior to completing and submitting a request for a major amendment.
3. Failure to do so might result in a delay in the review and approval of the amendment request, thereby impacting on the ability of the study to continue.

18 UNANTICIPATED PROBLEMS REPORTING

Nelson Mandela University researchers (staff and/or students) of currently active studies making use of human participants who experience an unanticipated or adverse event during the data collection activity are required to immediately suspend data collection activities and to please alert Imtiaz.Khan@mandela.ac.za for advice on the required procedure to follow.

18.1 POLICY

1. In line with local and international ethical and regulatory requirements, the RECH mut have written procedures to ensure timely reporting to the committee, sponsors and appropriate regulatory agencies unanticipated problems, including serious adverse events, which might place human research participants at a greater risk of physical, psychological, economic or social harm.

18.2 PURPOSE

2. The purpose of this policy is to outline requirements and timelines for reporting and reacting to internal and external reports of unanticipated problems, including adverse events in research with human participants.

18.3 DEFINITIONS

1. Unanticipated problems
   a. An 'unanticipated' problem is any ***internal*** incident, experience or outcome that meets all the following three criteria:
      i. 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 Human Research Ethics Committee or to participants such as in initial protocol applications, any amendments, investigator brochures, scientific literature, product labelling, package inserts and Human Research Ethics Committee-approved informed consent documents or any existing documentation regarding the research conducted to date under the protocol;
      ii. 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);
      iii. Suggests that the research places participants or others at a greater risk of physical, psychological,economic or social harm than was previously known or recognised.
   b. In summary, an unanticipated problem is:

i. **Unexpected** – not in the consent form, investigator's brochure, protocol package insert or label; or unexpected in its frequency, severity or specificity;
ii. **Related to the research** – caused by, or probably caused by, or associated with a device;
iii. **Harmful** – caused harm to participants or others, or placed them at increased risk of physical, psychological, economic or social harm.

c. Examples of unanticipated problems include:
i. Loss of a laptop computer containing confidential information about participants or others.
ii. A spouse physically abused by his or her partner for taking part in the study.
iii. 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.
iv. Finding that laboratory reports on blood or other samples were in error.

2. Adverse Events
a. An adverse event is defined as any untoward or unfavourable medical or psychological occurrence ina participant, including any abnormal laboratory finding, symptom or disease. An adverse event doesnot necessarily have a causal relationship with the research, or any risk associated with the research.
b. **Unexpected adverse events**. Unexpected adverse events are those in which any of the following applies:
i. The specificity or severity is not consistent with the current Investigator's Brochure.
ii. The event is inconsistent with the risk information in the current protocol application.
iii. The event is occurring more frequently than anticipated.
iv. For example, liver failure due to diffuse hepatic necrosis in a participant without any underlying liver disease if the protocol did not identify liver disease as a potential adverse event. In contrast, prolonged neutropenia and opportunistic infections in participants given an experimental chemotherapy regimen as part of an oncology trial would be examples of expected adverse events if the protocol described prolonged severe neutropenia and opportunistic infections as common risks for all participants.

c. Internal Adverse Event
i. Internal adverse events are those experienced by participants enrolled at a site under the jurisdiction of the Nelson Mandela University.

d. External Adverse Event
i. External adverse events are those experienced by participants enrolled at other institutions or in a study for which Mandela University is not the coordinating centre.

e. Serious Adverse Event (SAE)
i. A serious adverse event is any adverse event in research that results in any of the following:
a. Death.
b. A life-threatening incident (places the participant at immediate risk of death from the event as it occurred).
c. Hospitalisation (initial or prolonged).
d. Disability.
e. Congenital abnormality.
f. 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).
g. Inadvertent disclosure of confidential information if this presents an immediate risk to a participant such as from spousal or child abuse.

18.4 TIMELINES FOR REPORTING

1. Reporting Unanticipated Internal Problems or Adverse Events
2. Unanticipated Problems
    a. Principal investigators must report to the Human Research Ethics Committee within seven calendar days after the investigator first learns of their occurrence all unanticipated problems that increase the risk of harm to participants or others.
3. Fatal and Life-threatening, Unexpected Adverse Drug Reactions
    a. Principal investigators must report to the Human Research Ethics Committee as soon as possible but not later than seven calendar days after the investigator first learns of their occurrence all fatal and life-threatening adverse drug reactions in clinical trials.
4. Serious and Unexpected Non-fatal Adverse Drug Reactions
    a. Principal investigators must report to the Human Research Ethics Committee as soon as possible but not later than fifteen calendar days after first learning of their occurrence all serious unexpected drug reactions that are not fatal or life-threatening.
5. Expected Adverse Drug Reactions
    a. Principal investigators must notify the Human Research Ethics Committee within fifteen calendar days after the investigator first learns of their occurrence all adverse drug reactions that are expected but are judged to be occurring at a significantly higher frequency or severity than expected. The basis forthese assessments must be included in the investigator's report.
6. Serious and Unanticipated Adverse Device Effects
    a. Principal investigators must **report** to the Human Research Ethics Committee and to the sponsor (if applicable) as soon as possible but not later than seven calendar days after first learning about their occurrence all unanticipated adverse device effects. The sponsor shall immediately conduct an evaluation of the unanticipated adverse device effect.
7. New Information that might Impact the Conduct of a Clinical Trial
    a. Principal investigators must report to the Human Research Ethics Committee within three calendar days of first learning about their occurrence 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. The report could include individual case reports or a major safety finding from other sources.
8. Reporting External Serious Unexpected Adverse Drug Reactions
    a. Principal investigators must report to the Human Research Ethics Committee as part of the six-monthly progress report in a line listing format all serious unexpected adverse drug reactions originating from other South African or international sites.

18.5 HOW ARE INTERNAL REPORTS SUBMITTED?

1. Investigators typically learn about internal adverse events from participants, another collaborating investigator or the participant's health care provider. If the investigator judges that the event represents an unanticipated problem or adverse event that requires timely reporting as described above, the principal investigator shall use the standard SAE reporting form to notify the Human Research Ethics Committee and the sponsor as required under a monitoring plan described in the Committee-approved protocol. The standard internal reporting form must be completed regardless of whether other forms (e.g., sponsor, CIOMS, Medwatch) have already been completed. Information such as a summary of the event, or drug company reports may be attached and submitted with the form.
2. Reports of unanticipated problems, including serious adverse events, submitted to the Human Research Ethics Committee must include the following:
    a. Appropriate identifying information for the research protocol, such as title, investigator's name, and Human Research Ethics Committee reference number.

b. A detailed description of the adverse event, incident, experience or outcome.
c. An explanation of the basis for determining that the adverse event, incident, experience or outcome represents an unanticipated problem.
d. A description of any changes to the protocol or other corrective actions taken or proposed in response to the unanticipated problem.

3. The investigator must independently determine and comment on whether the event was thought to be related, possibly related, unrelated or the relationship is unknown. The Human Research Ethics Committee therefore relies on the principal investigator's expertise to assess the causality of the problem or event, its seriousness and whether it was expected. Investigators must also recommend whether a change in the protocol is needed to minimise risks to participants, whether the consent form should be revised to reflect this risk and whether participants in the study should be re- consented in light of this risk.
4. All adverse event reports are acknowledged with an official Human Research Ethics Committee stamp and returned to the principal investigator. A copy of the stamped original is placed in the protocol file.

18.6 Investigation and Evaluation of the Reports

1. The Human Research Ethics Committee Chair or a designee is responsible for reviewing adverse events.
2. If there are immediate risks to participants, the Chair or designee may take one or more of the following actions:
   a. Suspend Human Research Ethics Committee approval to ensure the ongoing safety of participants.
   b. Call an emergency Human Research Ethics Committee meeting to act on the report.
   c. Request additional information from the principal investigator or others.
3. If the investigator determines that an adverse event is not an unanticipated problem, but the monitoring body subsequently determines that the event does represent an unanticipated problem (for example, due to an unexpectedly higher frequency of the event), the monitoring body should report this finding to the investigator and such reports must be promptly submitted to the Committee.
4. Reportable events that are not serious and do not require immediate action are reviewed by the Human Research Ethics Committee Chair or designee using an expedited procedure. At the Chair's discretion, reports will be reviewed at convened Human Research Ethics Committee meetings. The Chair or full committee may request further information or require the following remedial actions:
   a. Revise the protocol.
   b. Modify inclusion or exclusion criteria to mitigate the newly identified risks.
   c. Suspend enrolment of new participants.
   d. Suspend procedures in currently enrolled participants.
   e. Modify informed consent documents to include a description of newly identified risks.
   f. Provide additional information about newly recognised risks to previously enrolled participants.
   g. Suspend approval.
   h. Terminate approval.
5. Any proposed changes to a research study in response to an unanticipated problem, including serious adverse events, must be submitted as amendments, and approved by the Human Research Ethics Committee before being implemented, except when necessary to eliminate apparent immediate hazards to participants.
6. At the time of continuing review, principal investigators must submit a summary of serious problems and serious adverse events that occurred at the investigator's site (i.e. internal), are study-related and that have occurred since the last continuing (or initial) review of the study.
7. In most cases, an appropriate summary would be a statement that there have been no unanticipated problems and that serious adverse events have occurred at the expected frequency and level of severity as documented in the protocol, the informed consent form and the investigator's brochure, where applicable. The principal investigator must also summarise in the continuing review report all internal non-

serious adverse events that have occurred since the last continuing (or initial) review of the study. For multi-centre studies, the principal investigator shall include the following documents with the continuing report:

a. Most recent copy of the sponsor's analysis of adverse event reports, if applicable.
b. Most recent copy of the DSMB report, if applicable.
c. Summary of all external serious adverse events presented in the context of the entire multi-centre study, if possible.

19 DEVIATIONS FROM APPROVED STUDY PROTOCOL

19.1 POLICY

1. Research ethics and regulatory guidance requires that any changes to an approved protocol must receive prior HREC approval before implementation unless the change is to eliminate an immediate harm to a research participant. Sometimes changes are noted or recognized after they occur. All changes no matter how minor should be reported to the REC-H whether they are planned or noted after the fact.
2. Such incidences may result in the permanent suspension of the study.
3. Retrospective approval for deviations from approved study protocol is not possible.

19.2 PURPOSE

1. The purpose is to define protocol deviations and to outline procedures for reporting deviations to the HREC. Protocol deviations will also be distinguished from other protocol modifications.

19.3 DEFINITIONS

a. Protocol amendment
    i. A protocol amendment is a permanent, intentional action or process that amends or revises a previously approved protocol. There is documented approval from the Human Research Ethics Committee, and sponsor.
b. Protocol or study exception
    i. A protocol or study exception is a one-time intentional action or process that departs from the HREC approved protocol.
c. Protocol deviation
    i. A protocol deviation is an unplanned or unforeseen failure of the PI or other study personnel to follow the specified procedures approved by the HREC. 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.
    ii. It is the PI's responsibility to categorise a protocol deviation as major or minor.

19.4 MAJOR PROTOCOL DEVIATIONS

1. Major protocol deviations are deviations which affect a participant's safety, condition or status, the integrity of the study data, pose a significant risk of harm and change the balance of risks and benefits and a participant's willingness to continue participation.
2. If a deviation meets any of the following criteria it should be classified as major (the list is not exhaustive):
    a. The deviation has harmed or posed a significant or substantive risk of harm to a participant:
        i. A participant received the wrong treatment or incorrect dose.
        ii. A participant met withdrawal criteria during a study but was not withdrawn.

iii. A participant received an excluded related medicine.

b. The deviation compromises the scientific integrity of the study data:
   i. A participant was enrolled but does not meet the protocol's eligibility criteria.
   ii. 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).
   iii. Changing the protocol without HREC approval.
   iv. Inadvertent loss of samples or data.
c. The deviation is willful or knowing breach of ethical or regulatory policies or guidelines:
   i. Failure to obtain informed consent
   ii. Falsifying research or medical records
   iii. Performing tests or procedures beyond the investigator's professional scope
   iv. Failure to follow the safety monitoring plan
d. The deviation involves serious or continuing non-compliance with institutional or regulatory policies:
   i. Working under an expired professional license.
   ii. Repeated minor deviations.

19.5 Minor Protocol Deviations

1. Minor protocol deviations are deviations which do not affect a participant's safety, compromise the integrity of the study data or affect a participant's willingness to continue taking part in the study.
2. Examples of minor deviations include:
   a. Missing pages of a completed consent form
   b. Inappropriate documentation of informed consent such as missing signatures
   c. Using an expired consent form that has not changed significantly
   d. Participant did not receive a copy of the signed consent form (but on discovery, a copy is given to the participant)
   e. Study procedure conducted out of sequence.
3. Often making a distinction between major and minor deviations is a matter of degree; for example, signing an expired/invalid consent form that has not changed significantly is likely to be categorized as a minor deviation, whereas signing an expired/invalid consent form which has since added or deleted study procedures to a new consent form would be considered a major deviation.

19.6 Documenting and Reporting Protocol Deviations

1. As soon as a protocol deviation is identified in a study, it must be reviewed, documented and categorized by the PI. Documentation must include the following:
   a. PI's name and study title
   b. Date deviation occurred
   c. |Date deviation identified
   d. Has sponsor been notified, where applicable.
   e. Has sponsor agreed to allow participant to remain in the study, where applicable
   f. Description of deviation
   g. Explanation of why deviation occurred
   h. Corrective follow-up action taken
   i. Preventative measures implemented, where applicable.
   j. Investigator's assessment of whether deviation is major or minor, with reasons.
   k. PI's signature and date
2. Deviations may be recorded as a summary log or a note in the study records.

3. The PI of currently active studies making use of human participants who deviate from the approved study protocol are required to immediately suspend data collection activities and report major protocol deviations within seven calendar days of first hearing of the incident to Imtiaz.Khan@mandela.ac.za for advice on the required procedure to follow.
4. The Chair or a designee will review all protocol deviations. As part of the review the Chair will determine whether the deviation constitutes an unanticipated problem that involves risks to participants or others, or serious or continuing non-compliance which requires further action. Once the review is complete and the Chair is satisfied that appropriate follow-up action has occurred, an official acknowledgement will be sent to the PI.
5. If the PI 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 progress report.

20 STUDY SUSPENSION AND TERMINATION

20.1 POLICY

1. According to the Department of Health, where a research ethics committee is satisfied that such circumstances have arisen that a research project is not being conducted in accordance with the approved protocol and that, as a result, the rights and welfare of participants are not or will not be protected, the research ethics committee may withdraw approval. The research ethics committee shall also inform the researcher and the institution of its action and shall recommend that the research project be discontinued or suspended. Where ethical approval has been withdrawn, a researcher must discontinue the research and comply with any special conditions required by the research ethics committee.

20.2 PURPOSE

1. The purpose of this policy is to outline the procedures for suspending or terminating research.

20.3 PROCEDURES

1. The REC-H may suspend or terminate a study based on a report or allegation of:
    a. Unanticipated problems involving risks to participants or others.
    b. Serious or continuing non-compliance.
    c. Findings in the continuing review or monitoring process.

20.4 SUSPENSION

1. A suspension occurs when the REC-H Committee or Chair places a temporary hold on research that has been previously approved so that no new participants may be accrued, no research interventions may occur unless necessary for currently enrolled participants' safety and welfare, and no follow-up may be conducted unless it is in the best interest of participants and approved by the Committee.
2. Note: The word 'suspension' in this section refers to suspensions as a result of the REC-H decision but can also refer to suspensions that occur automatically due to a lapse of Committee approval. *A suspension due to lapse of Committee approval will be referred to as an 'administrative closure' which will automatically occur when the Committee approval period expires.*
3. The REC-H Chair will notify the PI of the suspension or termination in writing, providing reasons. The Chair will inform the PI of steps to be taken as a result of the suspension or termination of the research study.

20.5 Termination

1. Termination of a previously approved protocol occurs when the REC-H withdraws approval and stops all research activity permanently. No new participants may be enrolled, and no further research interventions can occur. Where indicated, follow-up visits may be conducted with Committee approval to monitor participants' safety and welfare.
2. The REC-H Chair will notify the PI of the suspension or termination in writing, providing reasons. The Chair will inform the PI of steps to be taken as a result of the suspension or termination of the research study.

20.6 Steps to be Taken

1. Steps could include:
    a. Drafting a plan to withdraw participants which protects their safety and wellbeing.
    b. Notifying current participants, by phone, email or in person, that the study has been suspended or terminated and providing reasons for the action.
    c. Notifying participants of any follow-up procedures, assessments or referrals which are necessary and permitted by the REC-H for their safety. This may require a gradual withdrawal, if an abrupt discontinuation is likely to put participants at risk.
    d. Temporary or permanent transfer of responsibility for the study to another PI.
    e. Reporting any adverse events or outcomes to the REC-H and sponsor which happened during follow-up.
2. All written communication from the investigator to the participants requires REC-H approval prior to distribution.
3. The PI may appeal against the decision to suspend or terminate a study within seven calendar days of receiving written notification. The written appeal to the REC-H needs to include a plan for ensuring that the rights and welfare of currently enrolled participants are protected and a plan to ensure that future participants will be protected if the study receives Committee approval.

20.7 Investigator-Initiated Voluntary Suspension or Termination (Discontinuation)

1. An investigator may choose to voluntarily suspend or terminate some or all activities of an approved protocol.
2. The investigator must notify the REC-H Chair and provide reasons for the suspension or termination.
3. The committee may request any additional information in order to make an independent determination.
4. Researchers (staff and/or students) of currently active studies who determine that the discontinuation of study is imminent for whatever reasons, are required to complete and submit a notification for the discontinuation/closure of the study.
5. For the discontinuation of a study and therefore the data collection for which ethics approval was granted, the discontinuation/closure report should be submitted no later than 1 month after reaching such a conclusion.

20.8 Records

1. The date that the research is suspended, terminated, or voluntarily suspended or terminated must be noted in the protocol file and the database.
2. All correspondence relating to these actions will be filed with the protocol.

20.9 Administrative Closure of a Protocol or Suspension due to Lapse of Ethics Committee Approval

1. If a continuing review of an active study is not approved prior to the expiry date, the REC-H approval will automatically end, and the study will be suspended. It is the responsibility of the PI to monitor approval periods and to ensure that continuing review reports are filed in time to allow expedited of full committee review.
2. Whilst the committee will try to send our letters informing PIs of a suspension for lapse of approval, PIs remain responsible for suspending all research activities.
3. For the imminent closure of a study, a closure report may be submitted on conclusion of data collection activities as long as it is known that no further interaction with participants will be conducted. An updated progress report must be submitted with the closure report. A suspension due to lapse of Committee approval will be referred to as an 'administrative closure' which will automatically occur when the Committee approval period expires.
4. For a study where ethics approval has lapsed.
    a. A new ethics application is required, which will undergo the full review process for new applications. If a low-risk study, the applicant submits their project through the Department/Faculty committee, and it will subsequently be ratified at the REC-H. If a medium/high risk study, it must serve at a convened meeting of the REC-H. A new ethics reference number will be allocated. Information on previous ethics clearances obtained for the previous (lapsed) study should be included in the new application.
5. Researchers are advised to familiarise themselves with the Closure/Discontinuation of a Study guidelines and instructions prior to completing and submitting a relevant request for study termination/suspension. Failure to do so might result in a delay in the review and approval of the request.
6. Researchers (staff and/or students) of currently active studies who determine that the closure of study is imminent for whatever reasons, are required to complete and submit a notification for the discontinuation/closure of the study.

21 Guidelines for Umbrella Projects

1. Umbrella projects may be defined as large (un)sponsored, national/ international research projects including Honours and/or undergraduate group research projects, in which humans are the subjects of research. Engagement with the chairperson is suggested if further clarity is required.
2. An umbrella research project:
    a. Is a broad research project under which a number of smaller, independent research projects fall.
    b. Is a project in which a number of individual Masters (treatise and research) and Doctoral students collaborate, with each individual Masters and Doctoral student conducting research to realise at least one objective of the umbrella research project. It is understood that the names of the Masters and Doctoral students involved in the project may not be available at the time of application. An application for an umbrella research project (form RECH-003/U) is required.
    c. Requires that the individual Masters and Doctoral students submit independent ethics applications (attached to form RECH-003/S[1], sub-studies) for their parts of the umbrella project (i.e. independent proposal, data collection instruments etc.). This could therefore happen concurrently with or after approval of an existing umbrella project.
    d. Is also advised for groups of undergraduate, PGDip and/or Honours students undertaking small research projects. An application for an umbrella research project (form RECH-003/U) is required.

[1] Completion and submission of RECH-003/S merely serves for the purpose of obtaining an independent ethics number per student

In this case, individual sub-studies must be submitted for approval on a form RECH-003/S as supporting documentation for form RECH-003/U, either individually or as a group submission of sub-studies (only if data collection procedures and instruments of such studies are significantly similar).

3. Researchers are advised to familiarise themselves with the New-Umbrella-Project-Ethics-Application guidelines and instructions prior to completing and submitting a relevant request for an umbrella or associated sub-study. Failure to do so might result in a delay in the review and approval of the request.

22 Reference Material (Form Templates)

1. Researchers are advised to familiarise themselves with the (REC-H) forms, guidelines and instructions prior to completing and submitting a relevant request for a study.
2. Failure to do so might result in a delay in the review and approval of the request.
3. It is the responsibility of the user of the documentation to ensure that the current version of the documentation is being used.

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