Northern Cape Department of Health



**PROVINCIAL HEALTH RESEARCH ETHICS COMMITTEE (PHREC)**

**TERMS OF REFERENCE (TOR) AND STANDARD OPERATING PROCEDURES (SOPs)**

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# **SECTION I: PHREC TERMS OF REFERENCE (TOR)**

1. **BACKGROUND**

This document provides Terms of Reference (TOR) and Standard Operating Procedures (SOPs) for the Northern Cape Department of Health Provincial Health Research Ethics Committee (hereafter referred to as PHREC). The document has been developed with the aim to provide information that will assist researchers and the general public in terms of conducting research within the province and to ensure that their PHREC is constituted and operate in accordance with the National Department of Health (2015) Ethics in Health Research Principles, Processes and Structures guidelines**.**

* 1. According to the National Department of Health (2015), Ethics in Health Research Principles, Processes and Structures guidelines, research ethics review committee should have Terms of Reference (TOR) and Standard Operating Procedures (SOPs).
  2. This section describes the TOR for the Northern Cape Department of Health PHREC. The TOR includes the scope of the PHREC’s responsibilities, its protocol review process, its accountability responsibilities, the mechanisms for reporting and remuneration, if any, for members.
  3. The PHREC (international equivalent titles: Research Ethics Committee (REC); or Institutional Review Boards, (IRBs), or Independent Review), is an ethics review committee appointed by the Accounting Officer of the Northern Cape Department of Health to function its mandate in accordance with the revised National Department of Health (2015), Ethics in Health Research Principles, Processes and Structures guidelines.
  4. The essential purpose of the PHREC is to protect the dignity, rights, safety and welfare of all research participants in health-related research. PHREC will do this through independent ethics review of all health related research projects sought to be conducted within the province and submitted to the PHREC’s secretariat.
  5. The functions of the PHREC are in accordance with, but not limited to, the following documents and guidelines:
* The SA National Health Act. No. 61 of 2003
* The SA Department of Health (2015) Ethics in Health Research: Principles, structures and processes and (2006) South African good clinical practice guidelines
* Declaration of Helsinki (Current version)
  1. Ethics approval must be obtained before a study commences, PHREC will not consider projects for approval if it is apparent that the research has already been conducted.

# **APPOINTMENT AND MEMBERSHIP**

Membership of the PHREC should be independent, multi-disciplinary, multi-sectoral and pluralistic. In general terms, membership should include as many disciplines, sectors and professions as possible, who are appropriate mandates of the PHREC.

## **2.1. Appointment**

* + 1. PHREC members will be appointed every three years, with a letter of appointment, by the Head of the Department. Members may serve more than one term.
    2. The Chairperson and Vice Chairperson (s) will be elected by the members in the PHREC’s first meeting.
    3. All PHREC members should sign a standard confidentiality agreement on appointment to PHREC as well as in each PHREC meeting.
    4. The department will cover professional liability insurance to cover PHREC members when carrying out their mandates duties.

**2.2. Membership**

The composition of the PHREC will be in accordance with the provisions of the Department of Health (2015) Ethics in health research: Principles, structures and processes; and (2006) South African Good Clinical Practice Guidelines.

* + 1. Members of PHREC should collectively have the qualifications, experience and expertise to review and evaluate the scientific, medical, legal, psychosocial and ethical aspects of research proposals. Members drawn not only from the senior ranks, but also include culturally diverse members and an appropriate mix of males and females as well as lay persons, preferably from communities in which research is conducted.
    2. The total number of committee members must be no less than 9 and exceed 15. Include at least two lay persons who have no affiliation to the institution, at least one member who has professional training in both qualitative and quantitative research methodologies as well as at least one member who is legally trained.
    3. A Chairperson could be appointed or elected at the first meeting of the PHREC, and thereafter confirmed annually.
    4. The Deputy Chairperson should be elected by the members and be expected to assist the Chairperson with responsibilities and to step into the role of Chairperson when necessary.
    5. All members should provide the PHREC secretariat with an abbreviated CV at the beginning of their term.
    6. Members not attending 3 consecutive meetings without a valid written reason, and without submitting their reviews, will risk termination of their membership of the PHREC.
    7. PHREC members will be required to have continuous personal development in research ethics training and research integrity, as well as expected to familiarise themselves with the national and international research ethics guidelines and should have documented proof of such familiarity.
    8. The institution should provide training opportunity and refresher courses for PHREC members, at least once during a term of appointment.
    9. PHREC may co-opt expert members and other representatives as advising members as required by particular protocols.
  1. **Scope of Responsibility**

The PHREC functions on behalf of the Northern Cape Department of Health to:

2.3.1 Review human research proposal applications where the research takes place within the province.

2.3.2 Provide competent, timely review and monitoring of human research projects in respect of their ethical and scientific acceptability.

2.4.3 Determine the compliance of a human research project with the National Department of Health Ethics, principle, structure guidelines approve or decline ethical approval.

2.4.4 Provide advice to the researchers on how to promote awareness of the ethical conduct of human research.

2.3.5 Provide an independent monitoring and oversight of approved proposals

2.3.6 Report annual progress reports to the NHREC and other oversight body

* + 1. Make available the minutes and decision of the PHREC meetings to oversight body

**2.4 Accountability**

2.4.1 The PHREC is directly accountable to the Accounting Officer of the Department under which it is constituted.

2.4.2 The PHREC provides an annual report to the Accounting Officer of the Department or delegate at the end of each financial or calendar year.

2.4.3 The PHREC brings to the attention of the Accounting Officer or delegate issues of significant concern.

## **2.5. Conflict of Interest**

* + 1. PHREC members must declare any prior interest and/or involvement in any matter being discussed by PHREC to avoid conflict of interest in PHREC decision-making, including reviewing of protocols.
    2. In convened PHREC meetings, the Chair shall determine whether the member be recused for items of discussion, or be allowed to remain and address questions when asked to do so, but not vote or participate in final decision-making on the matter in question.

## **2.6. Confidentiality**

* + 1. Confidential information shall mean certain proprietary, personal, clinical or protocol-specific information which the PHREC member acknowledges to be confidential.
    2. The Confidential information may be conveyed in written or oral form

## **Quorum /Voting**

* + 1. The PHREC will make its decisions at scheduled or extraordinary meetings at which a quorum of members is present.
    2. Meetings will only be conducted when a quorum is present. A quorum will be considered present if “50% plus 1” members are in attendance.
    3. Decisions will be determined by consensus (general agreement). Where general agreement does not exist, consensus will be undermined and the decision will be arrived at by vote.
    4. Minutes taken at PHREC meetings will be of sufficient detail to show attendance at the meetings, actions taken by PHREC, if applicable, the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research, and a written summary of the discussion of disputed issues and their resolution.
    5. The PHREC has the authority from time to time, to appoint, a standing or ad-hoc subcommittee to investigate or finalise certain matters under its jurisdiction, in compliance with applicable norms, rules and regulations

1. **EXPEDITED REVIEW**

Expedited review should apply, in principle, only to research that poses no more than minimal risk of harm to research participants.

1. **RECORD KEEPING**
   1. The PHREC secretariat should keep written records of all research protocols received for review, including information sheets, consent forms and relevant correspondence, in the form in which they were approved.
   2. Electronic records are acceptable, provided that signatures, especially on the finally approved documentation, are properly documented and included in the record.
   3. The record should include at least the following:

• Name of principal investigator

• Protocol identification number

• Title of the project

• Date of approval or rejection

• Conditions of approval, if applicable

• Whether approval was expedited

• Copy of the signed final proposal or protocol approved

• Whether and how consultation occurred

1. **MONITORING** 
   1. PHREC have the right to oversight and monitor the research it approves.
   2. Researchers should provide appropriate information to the PHREC to facilitate monitoring,
   3. Where circumstances indicate that a project is non-compliant with the approved protocol and the interests of participants are at risk of harm, the PHREC may withdraw approval, after due process has been followed.
2. **COMPLAINTS**

The PHREC should have a complaints process that is accessible to researchers and other interested persons

1. **REPORTING**

7.1 The PHRECs should make relevant records available for inspection and audit by the NHREC (or its delegate) upon request.

7.2 The PHRECs must report annually on their activities

**SECTION II: PHREC STANDARD OPERATING PROCEDURES**

The PHREC Standard Operating Procedures (SOPs) set out in systematic detail how to receive and review proposals, the various procedures and considerations that should be taken into account and adhered to, as well as provide information or references to additional materials to assist with the process of review and application for ethics approval.

# **APPLICATION FOR ETHICAL REVIEW**

* 1. All researchers submitting protocols for ethics review should submit their proposal to the PHREC secretariat through the National database or directly
  2. Research proposals and all supporting documentation such as participant information sheets, consent documents, advertising and recruitment material, all instruments, questionnaires as well as research team’s current curriculum vitae (2 pages).

1. **REVIEW PROCESS AND CRITERIA**

2.1 PHRECs should have written standard operating procedures to review protocols. The Committee should review the following document/s from the researcher or principal investigator:

* Research Ethics Committee application form(s)
* Study protocol(s)
* Written informed consent form(s)
* Information sheets
* Participant recruitment procedures
* Written information to be provided to participants
* Safety information
* Information about payments to participants, if any
* Information on compensation for research related injury (insurance) for participants
* Declarations regarding conflict of interest
* Other documentation evidencing qualifications
  1. The Committee shall review all applications within a reasonable time. Ethical review should be done case-by-case deliberation.

1. **THE PROTOCOL REVIEW PROCESS FOR FULL REVIEW**
   1. All protocols for full review (non-expedited review) must be submitted to all PHREC members at least 10 working days before each PHREC meeting.
   2. Each protocol will be discussed at a convened quorate PHREC meeting at which a majority of the members of PHREC are present, including at least one member whose primary concerns are in non-scientific areas.
   3. Each non-expedited application and protocol will be reviewed in advance of a convened PHREC meeting by all PHREC members. However, a primary and secondary reviewer, and where necessary, an expert reviewer will be allocated to review each such application.
   4. The primary reviewer will, at the full PHREC meeting give a synopsis of the study together with the positive and negative aspects of the proposed research.
   5. The secondary reviewer will also report on their evaluation of the proposed research.
   6. Where a non-expedited protocol is not approved at a convened PHREC meeting and the revisions or modifications required are substantive, PHREC may require that the modifications and investigator responses are deferred to a further convened meeting of PHREC
   7. The PHREC should consists of at least nine members with a quorum being a simple majority (50 plus one).
2. **PHREC DECISION**
   1. PHREC's review of a protocol will lead to written confirmation to the applicant of either:

* Final approval
* Provisional approval conditional to modifications required by the Committee
* Rejection
  1. Reasons for provisional approval and rejection are to be furnished to the researcher in writing.
  2. PHREC must document its views in writing, clearly identifying the study, the documents reviewed, and the dates for the following:
* Approval;
* Modifications required prior to resubmission for approval;
* Rejection; and
* Termination or suspension of any prior approval.
  1. The PHREC chair will inform the researcher in writing of the PHREC decision.

## **PHREC RESEARCH PROPOSAL REVIEW CRITERIA**

Research proposals must be reviewed within the context of aforementioned regulations and guidelines. PHREC, in reviewing a protocol, must consider factors that may influence the scientific validity and ethical acceptability of the protocol. The following criteria will be used to review projects.

* 1. **Social benefit and scientific validity**: ThePHREC must consider the proposed proposal to have relevance to the community involved and/or the greater South African. PHREC must ensure that the proposed research is scientifically valid. The research does not expose research participants to potential risks and burdens.
  2. **Risk-Benefit Ratio of Project:** In order to approve research, the HREC assess and determine that all of the following requirements are satisfied:
* Risks to participants are minimised
* Using procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk
* Risks to participants must be reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result.
* In evaluating risks and benefits, PHREC shall consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies participants would receive even if not participating in the research).
* When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants.

## **5.3 Fair selection of subjects**

* + - Selection of participants should be fair and based on the study requirements.
    - PHREC shall take into account the purposes of the research and the setting in which the research will be conducted and involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
    - When some or all of the participants are likely to be vulnerable to undue influence or coercion, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these participants.

## **5.4 Informed consent processes**

* + - Informed consent will be sought from each prospective participant or the participant's legally authorized representative, in accordance with, and as required by Sections E of this document.
    - Informed consent will be appropriately documented

## **Respect for participants**

* + - The research protocol demonstrates respect for participants throughout the course of the project
    - There should be adequate provisions to protect the privacy of participants and to maintain the confidentiality and security of data.
    - Participants may withdraw from the study at any time without prejudice

## **Respect for communities and culture**

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

# **EXPEDITED PROTOCOL REVIEW PROCESS**

An expedited review procedure consists of a “fast track review” of research proposal involving human participants by three members of PHREC allocated to the study by the PHREC Chair, meaning the study will be reviewed before the full PHREC meeting and a decision will be given to the researcher.

* 1. . Expedited review should apply, in principle, only to research that poses no more than minimal risk of harm.
  2. Research proposals may be considered for expedited ethical review process only if it involves minimal risk (the probability and magnitude of harm or discomfort anticipated in the research, is not greater in and of themselves than those ordinarily encountered in daily life, or during the performance of routine physical or psychological examinations or tests.)
  3. Expedited review procedure for minimal risk research may be used, at the discretion of the PHREC chairperson, or any other person delegated this responsibility by the chairperson.
  4. The chairperson, or a PHREC member appointed by the chairperson, will review the research study and provide the chairperson with a written report. The chairperson will at his discretion:
* **Approve** the study.
* **Request modifications** prior to approval.
* **Defer approval** -i.e. refer the study to a full sitting of the PHREC for consideration.
  1. If modifications are requested, then all requested changes must be made before a final letter of approval will be issued.
  2. The researcher may start the project only once an approval letter has been received.
  3. The approval report of reviewers and all written comments by the chairperson will be made available to all committee members in the following meeting.

# **PHREC MEETING REVIEW**

* 1. The PHREC will convene on quarterly basis, to review and consider proposals.
  2. New applications must be received at least 10 working days before a meeting.
  3. An administrative review should be completed by the secretariat who may request additional information.
  4. The chairperson may, at his/her discretion, co-opt an external expert for a particular protocol, if he/she feels the committee does not have the necessary expertise to adequately evaluate all aspects of a particular protocol.
  5. Copies of the application form, study synopsis and patient information and consent form will be made and distributed to all committee members at least one week prior to the meeting as part of the meeting “Agenda” file.
  6. Reviewers will make written comments available to the chairperson, prior to each meeting, if they are unable to attend the meeting.

# **COMMUNICATION OF REVIEW DECISIONS**

* 1. Decisions taken at the PHREC meeting, or via an expedited review process, are communicated in writing to the applicant.
  2. Only once the requirements are satisfactorily fulfilled, will a formal letter of approval be issued.
  3. On occasion, where the requirements are not satisfactory a research study may be rejected completely.
  4. Researcher should direct all queries of the PHREC through secretary who will attempt to resolve problems and liaise with the chairperson when necessary.
  5. It is the responsibility of the investigator to comply with all requests and return the requested documentation with a covering letter responding to the points raised, to the PHREC as soon as possible but not later than 3 months from the date of issue.
  6. The application will be cancelled if no feedback is received by 3 months.

# **INFORMED CONSENT**

* 1. No researcher may involve a human being as a participant in research covered by this policy unless the investigator has obtained the legally effective informed consent of the participant or the participant's legally authorized representative, where appropriate.
  2. An investigator shall seek such consent only under circumstances that provide the prospective participant or their representative with sufficient opportunity to consider whether or not to participate and that minimise the possibility of undue influence or coercion.
  3. The information that is given to the participant or the representative shall be in language understandable to the participant or the representative.
  4. Written informed consent should always be obtained unless an alternative process is clearly justifiable.
  5. The process of recruitment and documentation of informed consent must be clearly described in the study protocol.

## **BASIC ELEMENTS OF INFORMED CONSENT**

The following information shall be provided to each research participant in the study:

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

## **DOCUMENTATION OF INFORMED CONSENT**

* 1. Informed consent shall be documented by the use of a written consent form approved by PHREC and signed by the participant or the participant's legally authorized representative. A copy shall be given to the person signing the form.
  2. The written consent document must include the elements of informed consent required. This form may be read to the participant or the participant's legally authorized representative, but in any event, the investigator shall give either the participant or the representative adequate opportunity to read it before it is signed. If the participant is unable to read or write there shall be an independent witness to the oral presentation who must verify in writing that the informed consent process was valid and in accordance with the requirements of this SOP document.
  3. PHREC may waive the requirement for the investigator to obtain a signed consent form for some or all participants if it finds either:
     1. That the only record linking the participant and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.
     2. That the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context.
     3. In cases in which the written documentation requirement is waived, HREC may require the investigator to provide participants with a written statement regarding the research.
     4. Once the participant has agreed to participate, at least 2 copies of the signed form will be made. The original is to be kept by the principal investigator. One copy may be kept in the participant’s medical records when appropriate; and one copy will be given to the participant.

**12. RECORD KEEPING**

12.1 PHREC secretariat should keep written records of all research protocols received for review, including information sheets, consent forms and relevant correspondence, in the form in which they were approved. Note that electronic records are acceptable, provided that signatures, especially on the finally approved documentation, are properly documented and included in the record.

12.2 The record should include at least the following:

• Name of principal investigator

• Protocol identification number

• Title of the project

• Date of approval or rejection

• Conditions of approval, if applicable

• Whether approval was expedited

• Copy of the signed final proposal or protocol approved

• Whether and how consultation occurred

1. **MONITORING** 
   1. PHRECs have the right to monitor the research it approves
   2. Researchers should provide appropriate information to the PHREC to facilitate monitoring,
   3. PHRECs may recommend and adopt any additional appropriate mechanism for monitoring, including random inspection of research sites, welfare monitoring sheets, data and signed consent forms, and records of interviews. Information and consent materials should indicate that such monitoring may take place.
   4. PHRECs should request regular, at least annual, reports from principal investigators on matters including but not limited to

* progress to date, or outcome in the case of completed research
* current enrolment status (numbers, active or closed)
* whether participant follow-up is still active or completed
* information concerning maintenance and security of records
* evidence of compliance with the approved protocol
* evidence of compliance with any conditions of approval
* list all adverse events in the past 12 months
* list all amendments made in the past 12 months.

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

**14. COMPLAINTS**

14.1 PHREC should have a complaints process that is accessible to researchers and other interested persons

**15. REPORTING**

15.1 PHRECs should make relevant records available for inspection and audit by the NHREC (or its delegate) upon request.

15.2 PHRECs must report annually on their activities, including

• membership and membership changes

• the number of meetings held

• confirmation of participation by required categories of members

• the number of protocols presented, the number approved and the number rejected

• monitoring and related matters

• complaints received and action taken.

**16. PROPOSAL**

The following information will be required for the consideration of research proposals.

* 1. TITLE OF THE PROPOSED RESEARCH
  2. DATE
  3. NAME AND ADDRESS OF ALL THE INVESTIGATORS, COLLABORATORS, AND/OR SUPERVISORS (starting with the principal investigator). Indicate which parts of the protocols each investigator will be responsible for. Who will actually carry out any procedure participants, and if appropriate, what training they have had.
  4. SITE(S) OF RESEACH (Attention should be paid to the facilities available for participants’ comfort, and availability of emergency procedures in the event of an unanticipated occurrence).
  5. NUMBER OF RESEARCH PARTICIPANTS TO BE ENROLLED
  6. PROPOSED DURATION OF STUDY
  7. A SUMMARY OF THE PROPOSED STUDY – Not more than 250 words and should include:
     1. The hypothesis and scientific basis or justification for the study
     2. The usefulness and significance of the study
     3. An assessment of the benefits (to participants and/or groups in the community or the entire community) and the risks
     4. An outline of the study design
     5. An indication of steps taken to ensure and maintain confidentiality

* 1. THE PROJECT PROPOSAL – To include:
  + An introduction and background information on the research topic
  + A clear statement of the objectives of the research proposal
  + The justification for the research (This should include review of the current knowledge from the literature on the topic, with an explanation of why this project is necessary, and how it will contribute to the overall knowledge in this area)
  + Materials and methods. These include:
    - Details of procedures to be performed
    - Choice of research respondents, inclusion/exclusion criteria, and number (and, where appropriate, a justification for that number) any controls, etc.
  + Procedures to be performed on human subjects, if any. This should indicate:
    - Details of data collection and analysis methods
    - The citing of relevant references (i.e. literature etc.)
  + A copy of any questionnaires to be administered
  + A table of contents with all pages numbered
  + All abbreviations should be explained

* 1. FAIR SELECTION OF RESEARCH RESPONDANTS

Researchers/investigators should be cognizant of the special problems of research involving vulnerable populations such as children, prisoners, pregnant women, mentally and physically challenged persons, or economically or educationally disadvantaged persons.

* 1. COPY OF THE INFORMED CONSENT FORM

This must include:

* Statements outlining in lay language the purpose of the research, what will be done in the study, and indicating that this has been explained orally and in writing to the participant (or the participant’s parent or legal guarding if a child) who understands at will be done. These must be countersigned by participant or his/her legally authorized representative;
* Explicit statement about any risk or discomfort to the participant, with an assessment of the degree of risk, and viable alternatives;
* A statement that the subject’s participation is voluntary, and that refusal to participate, or (if after having agreed to participate) withdrawal from the study at any time not affect the participant’s access to care or affect the type of care to which she/he is entitled;
* The name, address, telephone and fax numbers, and e-mail address, if any, of a contact person;
* A statement confirming that time was given for the participant to consider his/her involvement;
* Statement that the participant or his/her legal guardian has read the informed consent form or that it has been read to him/her. And that she/he understands its content; that a copy will be given to the participant; and that the signature of the participant or the legal guardian indicated that she/he has freely agreed to participate;
* The consent procedure should bear the signature of a witness who is not connected to the research protocol