HUMAN RESEARCH ETHICS COMMITTEE: (MEDICAL)

OVERALL POLICY

POL-HREC – 001*(VERSION 1)* **REVISED AND UPDATED: JANUARY 2025**

SUBJECT	**Policy regarding the University of the Witwatersrand, Human Research Ethics Committee (Medical):** ♦ **Approval of new applications for the conduct of research studies involving human participants** ♦ **Recertification of ongoing studies** ♦ **Amendments to approved Protocols and/or Participant Information Leaflets and Informed Consent Forms (PIL/ICON)** ♦ **Additional Investigators/Sites and/or Additional Research Entities/Departments** ♦ **Safety Reporting requirements including AEs and especially SAEs with particular emphasis on high risk studies** ♦ **Development and Implementation of Policies and Procedures** ♦ **Storage of documentation both electronically and hard copy** ♦ **Focus Group Discussions, Audio-recording, In-depth Interviews, Photographs, Filming** ♦ **Active and Passive Monitoring of Research Sites** ♦ **Interaction with other RECs and Regulatory Bodies**
DIVISION / SCOPE:	**University of the Witwatersrand, Human Research Ethics Committee (Medical)**
REVISION:	Ethics Secretariat
PURPOSE:	This policy aims to provide an overall description of the policies followed by the Wits HREC (Medical) relating to their responsibilities regarding the review and approval of research study applications in keeping with South African Ethics in Health Research Guidelines: Principles, Processes and Structures, 2024, 3rd Edition (NDoH 2024), South African Good Clinical Practice: Clinical Trial Guidelines. Third Edition (SA GCP 2020) and other guidelines (see references below)
PREVIOUS VERSIONS / ***(REASON FOR REVISION)***	POL-IEC-001v14 Revised and Updated
CONTENTS:	
APPROVALS:	**Signature of Chair / Co-Chair of Wits HREC (Medical)**  **Date:** 2025/01/13

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POL-HREC – 001*(VERSION 1)* **REVISED AND UPDATED: JANUARY 2025**

1. OVERALL POLICY STATEMENT

The University of the Witwatersrand, Human Research Ethics Committee: (Medical) reviews and approves research studies involving human participants, conducted under its responsibility in accordance with the following requirements:

- South African Good Clinical Practice: Clinical Trial Guidelines. Third Edition (SA GCP 2020)
- ICH Harmonised Guideline – Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice ICH – E6(R2) – Current Step 4 version dated 9 November 2016
- South African Ethics in Health Research Guidelines: Principles, Processes and Structures, 2024, 3rd Edition (NDoH 2024)
- World Medical Association, Declaration of Helsinki 2024
- International Ethical Guidelines for Health-related Research Involving Humans, Fourth Edition. Geneva. Council for International Organizations of Medical Sciences (CIOMS); 2016.
- Code of Federal Regulations: (21 Part 50) Protection of Human Subjects, (21 CFR Part 56) Institutional Review Boards, (45 CFR Part 46) Protection of Human Subjects
- OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events
- Association of British Pharmaceutical Industries (ABPI 2014)

This document will be submitted to Sponsors and Investigators who require more information about the operation of the Wits HREC (Medical).

The WHC HREC Admin Team will handle all administrative functions of the Wits HREC (Medical) for grant and commercially funded studies, while the Wits Research Office Team will handle all administrative functions for university research for degree and non-degree purposes.

1.1 APPROVAL OF NEW APPLICATIONS FOR THE CONDUCT OF RESEARCH STUDIES INVOLVING HUMAN PARTICIPANTS

All Phase I (one) including First in Human (FIH) studies, to Phase IV (four) studies that are conducted by Wits affiliated Investigators/Researchers, as well as those in Private Practice within Gauteng (where an agreement with Wits/HREC / Applicant/Sponsor and Investigator/Site has been signed regarding jurisdiction), as well as all university research involving humans for degree and non-degree purposes must be approved by the Wits HREC (Medical) prior to the enrolment of any participants.

Principal/Co-Principal and Sub/Co-Investigators will be required to sign either the Wits or SAHPRA Commitments and Responsibilities Declaration and submit this document with the study application for approval.

The requirements of the applicable ICH GCP, SA GCP 2020 Guidelines, NDoH 2024, ABPI 2014, CIOMS and FDA Code of Federal regulations will be applied in considering approval of Protocols and Participant Information Leaflets and Informed Consent Forms (PIL/ICON).

The Wits HREC (Medical) will review re-imbursements to be made to participants to ensure that they are reasonable and in line with SAHPRA's Time, Inconvenience and Expense (TIE) Compensation Model.

- **Note:** Reimbursement for healthy volunteers in Phase 1 studies, especially First-in-Human studies is still under discussion.

To facilitate the ongoing approval of the clinical investigations that were approved, follow-up reports containing the following information are required on a regular basis from the Investigator, as per SAHPRA and Wits HREC (Medical) requirements:

- Number of Participants: screened, consented, ongoing, on follow-up, withdrawn
- Summary description of participant outcomes and adverse events, especially serious adverse events
- Protocol deviations (to be categorised as Major, Minor or Critical)
- Complaints, including from whistleblowers, participants, investigators and sponsors
- Interim, End of Study and Final reports including those from iDSMC and other study committees
- Any new information obtained since the Wits HRECs most recent review

The Wits HREC (Medical) will decide on the required frequency of these reports on a per-clinical investigation basis. This decision will be based on the degree of risk to human participants, however, the minimum requirement for these reports will be on a six (6) monthly basis, however higher risk studies will require more frequent monitoring.

Three (3) monthly Progress Reports for Moderate to High-Risk Studies (especially clinical trials) and if there are any signals identified, we will request more frequent reporting.

Two (2) to Four (4) weekly Progress Reports for Very High-Risk Studies, including First In Human.

1.2. RECERTIFICATION OF ONGOING STUDIES

Re-certification Applications require formal review and renewal by the full Wits HREC (Medical) at the monthly HREC meetings.

The initial ethics approval granted for a study is valid for five (5) years. Recertification Applications will be due **5 (FIVE)** years after the initial ethics approval has expired (unless more frequent recertification is required by the Sponsor).

The Re-certification approval issued by the Wits HREC (Medical) will be valid for an additional 5 (FIVE) years (unless more frequent recertification is required by the Sponsor).

Where more frequent recertification is required by the Sponsor, it remains the responsibility of the Applicant/Sponsor and Investigator/Research Entity/Dept, to track due dates and apply for recertification.

Recertification of ongoing studies from External/Private Research Sites outside of Gauteng, will only be given for one year. Thereafter the applicant will need to obtain alternative HREC approval. This will however be considered on a case by case basis, especially for studies nearing completion.

Please refer to SOP HREC – 002 regarding Recertification of research studies.

1.3 AMENDMENTS TO AN APPROVED PROTOCOL OR PARTICIPANT INFORMATION LEAFLET AND INFORMED CONSENT FORM (PIL/ICON)

Minor amendments –changes that do not affect safety, design, analysis/results (administrative in nature).
Major amendment (technical) - changes that affect safety, design, analysis/results.
Substantive amendments requiring new clinical trial application, change in IP, change in standard of care arm, addition of study arm – including comparator or active control of arm (except approved as part of initial study), critical safety warning/s, substantive change in objectives, endpoints and rationale of the study, change in study design with significant impact on statistical analysis or the risk/benefit assessment.

Applicants to complete the Application Form for Amendments to Approved Study.

No deviations from the approved protocol, amendment/changes to the protocol/PIL/ICON/Assent, or any other written information that is provided to the participant, may be implemented prior to obtaining documented approval from the Wits HREC (Medical). The only exception is where a change is necessary to eliminate an immediate hazard(s) to participants. As soon as possible, the implemented deviation or change, the reasons for it, and if appropriate, the proposed protocol/PIL/ICON/Assent amendment must be submitted to the Wits HREC (Medical) for review and approval.

A copy of the notification to SAHPRA must accompany the submission.

The Investigator, or person designated by the Investigator, should document and explain any deviation from the approved protocol/PIL/ICON/Assent.

Please refer to SOP HREC – 006 regarding the procedure for Amendments.

1.4 ADDITIONAL INVESTIGATORS/SITES AND/OR ADDITIONAL RESEARCH ENTITIES / DEPARTMENTS

Review of additional Investigators/Sites and/or Additional Research Entities/Departments (Wits affiliated Investigators/Reseachers, as well as those in Private Practice (within Gauteng) where a Memorandum of Agreement (MoA) with Wits/HREC / Applicant/Sponsor and Investigator/Site has been signed regarding jurisdiction), would involve approval by the Chair / Co-Chair of the Wits HREC (Medical).

1.5 SAFETY REPORTING REQUIREMENTS

All Adverse Events (AEs) including Adverse Drug Reactions (ADRs), Suspected Unexpected or Serious Adverse Reactions (SUSARs) as well as Serious Adverse Events (SAEs) which may or may not be related to the Investigational Product (IP), must be reported as per the requirements of the Wits HREC (Medical) SOP HREC-005 and SAHPRA Guideline for Safety Reporting During Clinical Trials in South Africa, to ensure ongoing approval of the study.

1.6 DEVELOPMENT AND IMPLEMENTATION OF POLICIES AND PROCEDURES BY THE WITS HREC (MEDICAL)

Policies and Procedures for the Wits HREC (Medical) will be developed in accordance with the with South African Ethics in Health Research Guidelines: Principles, Processes and Structures, 2024, 3rd Edition (NDoH 2024), South African Good Clinical Practice: Clinical Trial Guidelines. Third Edition (SA GCP 2020) and ICH GCP.

For purposes of implementation of this procedure by the Wits HREC (Medical) the following points should be noted:

- The Chair and Co-Chairs of the Wits HREC (Medical) will be considered the “Head of the Division” that will be authorised to sign off all Policies and Standard Operating Procedures (SOPs) for the Wits HREC (Medical), and
- The Chair and Co-Chairs of the Wits HREC (Medical) will be responsible for ensuring that all the HREC members are familiar with the requirements of the relevant policies and procedures, and
- All Wits HREC (Medical) policies and procedures will be accessible as read-only files on the WHC and Wits web pages. Only the Chair, Co-Chairs and Ethics Secretariat will have write-access to these documents.

1.7 STORAGE OF WITS HREC (MEDICAL) DOCUMENTATION

The Wits HREC (Medical) will retain all relevant records, (e.g., written procedures, membership lists, list of occupations/affiliations of members, submitted documents, minutes of meetings, and correspondence) for a period of at least fifteen (15) years and will make them available on request to the regulatory authority/(ies). Records will be archived according to the relevant WHC procedures for archiving by the **WHC HREC Admin Team**.

1.8 FOCUS GROUP DISCUSSIONS, AUDIO-RECORDING, IN-DEPTH INTERVIEWS, PHOTOGRAPHS, FILMING

The Wits HREC (Medical) policy is a separate PIL/ICON is required for a focus group discussion and an in-depth interview.

In the FGD PIL/ICON a sentence that explains that 'although we will ask participants to maintain confidentiality there is no way to ensure this will be guaranteed' must be included.

For audio recordings, a signature line/area agreeing to this included for each form above. HPCSA regulations are to keep the audio-recordings for two (2) years after publication or six (6) years if no publication.

A separate PIL/ICON is required for Photographs, with explicit description of what will be photographed, how the photograph will be used, how confidentiality will be maintained and no identifiers e.g. tattoos, birthmarks to be shown. A separate PIL/ICON is also required for filming participants.

1.9 ACTIVE AND PASSIVE MONITORING OF RESEARCH SITES

Based on NHREC and NDoH 2024, 3rd Edition, HRECs are required to perform active and passive monitoring of research sites especially those performing high risk studies such as clinical trials.

Passive monitoring is maintained by the HREC (Medical) via regular progress reports every 2-weeks to 6 months, depending on the level of risk. In addition, the Wits HREC (Medical) plans to institute an active monitoring programme with the establishment of a Wits Research Monitoring Committee to actively evaluate research sites. This will initially be based on complaints received by whistleblowers, participants, investigators and sponsors, but will include routine visits in the future.

1.10 INTERACTION WITH OTHER RECS AND REGULATORY BODIES

In order to maintain uniformity in research ethics throughout the country, interaction between REC's should be encouraged. This includes ongoing WhatsApp groups and planned meetings. In addition, regular interaction with NHREC and SAHPRA is important.

2. DEFINITIONS AND ABBREVIATIONS

ABPI	Association of British Pharmaceutical Industries
ADR	Adverse Drug Reaction
AE	Adverse Events
CFR	Code of Federal Regulations (USA)
iDSMC	Independent Data Safety Monitoring Committee
FDA	Food and Drug Administration (USA)
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation

PIL/ICON	Participant Information Leaflet and Informed Consent
SAHPRA	South African Health Products Regulatory Authority
SAE's	Serious Adverse Events
SUSARs	Suspected Unexpected Serious Adverse Reaction
SOPs	Standard Operating Procedures
WHC	Wits Health Consortium
Wits HREC	University of the Witwatersrand, Human Research Ethics Committee

3. REFERENCES:

- South African Good Clinical Practice: Clinical Trial Guidelines. Third Edition (SA GCP 2020)
- National Health Research Ethics Council (2024) South African Ethics in Health Research Guidelines: Principles, Processes and Structures, 3rd ed
- World Medical Association, Declaration of Helsinki 2024
- ICH Harmonised Guideline – Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice ICH – E6(R2) – Current Step 4 version dated 9 November 2016
- ICH Harmonised Guideline - E2A – Clinical Safety Data Management: Definitions and Standards for Expedited Reporting
- International Ethical Guidelines for Health-related Research Involving Humans, Fourth Edition. Geneva. Council for International Organizations of Medical Sciences (CIOMS); 2016.
- Code of Federal Regulations: (21 Part 50) Protection of Human Subjects, (21 CFR Part 56) Institutional Review Boards, (45 CFR Part 46) Protection of Human Subjects
- National Health Act 2003, Government Gazette No. 36702
- Act No. 12 of 2013: National Health Amendment Act, 2013
- Constitution of the Republic of South Africa, 1996
- SAHPRA – Guideline for Safety Reporting during Clinical Trials in South Africa
- Association of British Pharmaceutical Industries (ABPI 2014)