HUMAN RESEARCH ETHICS COMMITTEE: (MEDICAL)

STANDARD OPERATING PROCEDURE

COMPLIANCE QUERIES, DEVIATIONS/VIOLATIONS

SOP-HREC–004 *(VERSION 1)* **REVISED AND UPDATED : JANUARY 2025**

SUBJECT:	**Procedure for management of compliance queries, protocol deviations/violations that occur at Wits HREC (Medical) approved sites**
DIVISION / SCOPE:	**University of the Witwatersrand, Human Research Ethics Committee (Medical)**
AUTHOR: **REVISED BY:**	Ethics Secretariat
PURPOSE:	This procedure describes the process to be followed by the Wits HREC (Medical), through the Ethics Secretariat, relating to compliance queries, protocol deviations/violations regarding studies that are conducted at Wits HREC (Medical) approved sites.
PREVIOUS VERSIONS / ***(REASON FOR REVISION)***	SOP-IEC-004-v10 Revision
CONTENTS:	1. Statement 2. Categories of Protocol Deviations/Violations 3. Critical Deviations/Violations identified by Wits HREC (Medical) 4. Critical Deviations/Violations identified by Sponsor/Applicant 5. Reporting Requirements 6. Whistleblowing 6. Definitions And Abbreviations 7. References 8. Template: Reporting Protocol Deviations/Violations
APPROVALS:	**Signature of Chair / Co-Chair of Wits HREC (Medical)** Paul Ruff **Date:** 2025/01/13

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1. Statement

The Investigator / Entities / Research Departments should conduct the study in compliance with the principles and guidelines of good clinical practice, as well as the protocol agreed to by the Sponsor/Applicant and which was given approval/favourable opinion by the Wits HREC (Medical).

The Investigator should not implement any deviation from, or changes of the protocol without agreement by the Sponsor/Applicant and prior review and documented approval/favourable opinion from the Wits HREC (Medical) of an amendment, except where necessary to eliminate an immediate hazard(s) to study participants, or when the change(s) involves only logistical or administrative aspects of the study (e.g., change in monitor(s), change of telephone number(s)).

As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) should be submitted:
(a) to the Wits HREC (Medical) for review and approval/favourable opinion,
(b) to the Sponsor for agreement and, if required,
(c) to SAHPRA (if applicable)

The Investigator, or person designated by the Investigator, should document and explain any deviation from the approved protocol and promptly report to the Wits HREC (Medical):

(a) Deviations from, or changes of, the protocol to eliminate immediate hazards to the study participants.
(b) Changes increasing the risk to participants and/or significantly affecting the conduct of the study.
(c) New information that may adversely affect the safety of the participants or the conduct of the study.

2. Categories of Deviations/Violations

Critical: Evidence that the participant/patients' safety, rights and/or confidentiality either have been or have significant potential to be critically compromised or serious doubts about the accuracy and/or credibility of data. Critical deviations/violations may lead to suspension of the Site and/or Investigator(s). Numerous major deviations/violations may result in a critical finding.
Major: A major non-compliance with applicable regulations and guidelines effecting the safety, rights and/or confidentiality of study participants or the accuracy/credibility of the data that may not have developed into a critical issue, but which may have the potential to do so unless addressed. Numerous minor non-compliances within on system may also result in a major finding.
Minor: A minor non-compliance with applicable regulations and guidelines that have no or minimal effect on participants' safety, rights or confidentiality but need to be addressed in order to have sustained confidence in the work of the site/investigator/organisation. These are predominantly administrative in nature.

3. Critical Deviations/Violations identified by Wits HREC (Medical)

Deviations/violations that might significantly affect participant's safety and well-being and/or reliability of the study data will be examined by the Chair and/or Co-Chairs, **and if necessary**, will be put before the HREC (Medical) for action that may include, but not be limited to, disqualification as an Investigator and/or Site requiring rehabilitation before being accepted as an Investigator in other/future studies as an Investigator/Site in future studies.

The Chair of the Wits HREC (Medical) or their representative, together with a representative from the Ethics Secretariat, may meet with the Sponsor/Applicant to discuss the deviation/violation, and jointly formulate an action plan before meeting with the Investigator(s) and taking any action.

Where deemed necessary by the Wits HREC (Medical) and the Sponsor/Applicant, the Wits HREC (Medical) will appoint and send independent auditors / Wits HREC monitors to the problem site for an audit/monitoring visit dependent on the nature of the potential problem. The audit/monitoring visit findings will be reported to the Wits HREC (Medical). Upon receipt of the findings, the HREC may set up meetings with the appropriate Sponsor/Applicant to discuss correctional measures to be implemented.

Depending on the severity of the deviation/violation, Investigators must either attend a meeting with their Head of Department/Research Entity, the Chair and/or co-Chairs of the Wits HREC (Medical) and a representative from the Ethics Secretariat or be required to address the full Wits HREC (Medical). The Sponsor/Applicant will, as a matter of course, be informed of the meeting and may also attend the meeting if they choose to do so.

Should it be deemed necessary, a Site and/or Investigator may be disqualified from future clinical research until appropriate rehabilitation has taken place.

4. Critical Deviations/Violations identified by Sponsor/Applicant

Should a Sponsor/Applicant identify a critical violation at a Wits HREC (Medical) approved site, this should be communicated to the Ethics Secretariat as soon as possible after identification, who will then refer the matter to the Chair and/or co-Chairs. The communication will be examined by the Chair and/or co-Chairs and if necessary, will be put before the Ethics Committee for noting and/or further action.

The Wits HREC (Medical) may appoint and send independent auditors or Wits HREC (Medical) monitors to the problem site for an audit or monitoring visit, depending on the severity of the reported problem. The audit/monitoring findings will be reported to the Ethics Secretariat and the Wits HREC (Medical) in writing. Upon receipt of the audit/monitoring findings, the Ethics Secretariat acting on behalf of the Wits HREC (Medical) will set up a meeting with the appropriate Sponsor/Applicant to discuss correctional measures.

Depending on the severity of the deviation/violation, Investigators must either attend a meeting with their Head of Department/Research Entity, the Chair and/or co-Chairs of the Wits HREC (Medical) and a representative from the Ethics Secretariat, or be required to address the full Wits HREC (Medical). The Sponsor will be notified of the meeting and may attend it if they choose to do so.

Should it be deemed necessary, a Site and/or Investigator may be disqualified from future clinical research until appropriate rehabilitation has taken place. This may include a PI having to work as a SI under a new PI for a number of studies, as well as doing further Ethics and GCP training.

5. Reporting Requirements

Investigators are urged to review and classify all deviations/violations as minor, major or critical.

1. All **major and critical deviation/violations** where participant/patients' safety, rights and/or confidentiality have either been or have significant potential to be compromised or serious doubts about the accuracy and/or credibility of data, need to be notified to the Wits (HREC**) immediately once known**. We have provided a template on which to report this.

2. **All major and critical deviations/violations** must also be submitted in a **line listing** format, as attachment to the **six-monthly progress report**.

3. **Minor deviations/violations** must be reported in a six-monthly line listing format, as a separate communication, at the same time as the six-monthly progress report.

Example of what to include in line listing of deviations/violations:
Protocol Number:
Site ID:
Participant ID:
Severity Classification: (Critical/Major/Minor):
Date of deviation/violation:
Deviation/Violation Description:
Corrective Action:
Preventative Action:

6. Whistleblowing

Any person within or without the University is encouraged to use the Wits Integrity Hotline to report any alleged infringement, misconduct or offence committed by a Principal Investigator, National Principal Investigator, Sub-Investigator, Co-Investigator, Supervisor, Site Personnel, or any University personnel linked to Research, as well as by Participants or their Families, or any or any other person that may have committed such a potentially relevant offence.

https://www.wits.ac.za/media/wits-university/research/documents/Ethics%20complaint%20structure.pdf

Whistle-blowers should use the dedicated email address (wits.integrity@wits.ac.za) or by calling the hot line (082 938 45 59/69). The matter will be dealt with confidentiality as per the University's Whistleblowers Policy. The report will remain anonymous as far as possible in law. The DVC: R&I will consult with the University's representatives to find a way forward to process such report and to resolve such report.

7. Definitions And Abbreviations

DVC	Deputy Vice Chancellor
GCP	Good Clinical Practice(s)
HREC	Human Research Ethics Committee
ICH	International Council for Harmonisation
R&I	Research and Integrity
SOPs	Standard Operating Procedures
WHC	Wits Health Consortium
WITS	University of the Witwatersrand

8. References

The University of the Witwatersrand, Human Research Ethics Committee: (Medical) aims to manage any queries, protocol deviations/violations regarding studies identified at Wits HREC (Medical) approved sites, in accordance with the following guidelines

- 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 and
- Wits HREC-Medical SOP, Draft 3 Approved by UR&IC 23 Oct 2023
- SAHPRA'S Guideline for Safety Reporting During Clinical Trials in South Africa, October 2022

TEMPLATE: NOTIFICATION REGARDING CRITICAL / MAJOR DEVIATIONS / VIOLATIONS

PART 1: ADMINISTRATIVE *(Blocks will expand to contain the information required, no extra references or pages should be added)*	
Ethics Reference Number:	
Study Title:	
Phase of study:	
Protocol/Project/Study Number:	
Approved Version/No. and Date:	
Health product being studied (if applicable):	
Funder/Donor:	
Sponsor:	
Applicant:	
Contact Person:	
Address:	
Cell No.:	
E-mail address:	
Date of Notification:	

PART 2	DETAILS OF DEVIATION/VIOLATION
1. Department/Research Entity:	
2. Site:	
3. Investigator(s): (PIs Co-Is and/or Sub-Is	
4. Date:	
5. Description:	
6. Classification (Critical/Major):	
7. Root Cause:	
8. CAPA:	
9. Implementation Date:	
10. Effective date of resolution:	
11. Evaluation/Follow-up:	
12. Comments:	

I, the undersigned, agree to conduct/manage the above-mentioned study under the conditions as stated in this application	
Applicant/Principal Investigator: Signature: ……	Date ……