|  |
| --- |
| **HREC (MEDICAL)**  **CHECKLIST AND GUIDING**  **INFORMATION FOR**  **FULL APPLICATION FORM** |

**APPENDIX 1 - SUBMISSION REQUIREMENTS:**

**1. REQUIRED UPFRONT FOR THE FULL HREC APPLICATION TO BE ACCEPTED:**

**ANY INADEQUATE SUBMISSION WILL BE REJECTED**

1. Completed and signed **Full HREC Application Form**.

* All sections must be completed correctly.
* Realistic duration of study (section 4.3.2) – usually start date should be 6 weeks or more after scheduled HREC (Medical) meeting date.
* Section 11 must be signed by PI, Supervisor(s) and Academic HoD.
* Degree and non-degree studies must be signed by PI and HoD other than PI, if PI is HoD. This includes Wits affiliates i.e. academic staff, entities, public government institution and NGOs affiliated with Wits.

1. Clean **Research/Study Proposal**. Compulsory for all applications/submissions (non-degree, undergraduate and postgraduate degree).
2. **Ethics training certificates** for all investigators and supervisors (not >3 years old); GCP training is not sufficient.
3. University Protocol Review Committee Postgraduate Approval Letter – required for PhDs.
4. Study design **research tools** as required. Must be attached as separate annexures not nested in proposal with document title, version number and date. Wits Templates available on ethics website page <https://www.wits.ac.za/research/researcher-support/research-ethics/ethics-committees/>

* **Participant Information Leaflet/Informed Consent Form/s (PIL/ICON)** – for adults and legal guardians, plus A**ssent Form** for minors >7 years.
* **Data Collection Sheet**, where appropriate.
* **Questionnaire**, where appropriate.
* **Interview topics** – individual or Focus Group Discussion (FGD), where appropriate.

**2. Required before final approval (ethics clearance):**

Documents to be submitted together with amendments after receiving outcome of ethics application. Submit together with ethics corrections.

1. Relevant permission from study site/s (e.g. hospital CEO, etc) and other entities.
2. SAHPRA approval (if health product - including medicine, medical devices, or kits).
3. University Protocol Review Committee (Undergrad) or Postgrad Approval Letter.
4. Data Transfer Agreement/Material Transfer Agreement (DTA/MTA) if data or samples are to be taken outside of Wits for analysis.
5. An Independent Ethics Committee (IEC) certificate(s) for an area outside WITS’ jurisdiction - must be NHREC accredited if in South Africa. Country IEC or an Institutional Review Board (IRB) if international collaboration.

**3. Can be post-clearance:**

1. Registrar’s approval, where University of the Witwatersrand students are concerned.

**NB: NOTE: STUDY SITES WITH INSUFFICIENT DOCUMENTATION MAY BE REJECTED WITHOUT AFFECTING THE APPROVALS OF OTHER SITES**.

**APPENDIX 2 – LIST OF POSSIBLE APPROVALS AND DOCUMENTS (if applicable):**

1. **SAHPRA.**
2. **University Protocol Review Committee or Postgrad Approval Letter.**
3. **University Registrar/School authority.**
4. **Research Ethics Training Certificate for all Investigators and Supervisors (not more than three years old) and GCP Training Certificate** (if applicable).
5. **Gatekeeper or database keeper permission for secondary data analysis** (plus a list of the data to be recorded must accompany this application; omit all identifiers on the data collection sheet – name, address, contact details, date of birth, etc.; use a study number to identify individuals where necessary).
6. **South African National Clinical Trials Registry (SANCTR).**
7. **National Health Research Database (NHRD) registration.**
8. **NHLS approval for access to Bio samples: AARMS registration.**
9. **Hospital CEO or Representative.**
10. **HoD.**
11. **District Manager.**
12. **Provincial or National Department of Health**
13. **Other Independent Ethics Committees/Institutional Review Board (IRBs).**

**APPENDIX 3 - RESPONSIBILITIES:**

1. Please note that it is the responsibility of the Principal Investigator and the Supervisor (if applicable) in an application to ensure that he/she has received the final HREC (Medical) Clearance before commending any research. This is signified by, and only by, the issuing of a Clearance Certificate, which will be headed as such.
2. Please indicate clearly, where correspondence should be sent; failure to do this may cause delays. Please provide the PI and the supervisor’s email address (where applicable) for sending copies of correspondence.
3. Please provide a protocol detailing the background to the research, the design of the investigation and all procedures, is submitted with the application.
4. Researchers with syndicates in the Wits Health Consortium – please read the home page at [www.witshealth.co.za](http://www.witshealth.co.za) regarding the requirement that the syndicate must be based in a Wits academic department, or recognised research entity.
5. Please note: No late online applications will be accepted after the submission date listed at: <https://www.wits.ac.za/research/researcher-support/research-ethics/ethics-committees/>, chose HREC (Med), see “Downloads”. Applications received after this date will be carried forward to the following meeting: incomplete applications will not be accepted.
6. For any assistance, please contact the WRO Ethics Secretariat to the Human Research Ethics Committee (Medical) at 011 717 2700/1234/2656 or email: [Hrec-Medical.ResearchOffice@wits.ac.za](mailto:Hrec-Medical.ResearchOffice@wits.ac.za)
7. No data may be collected before ethics clearance certificate is issued by the HREC (Medical). In no circumstance will retrospective clearance be given.

**WITS PLAGIARISM POLICY:**

1. The University’s policy on plagiarism is set out at: <https://intranet.wits.ac.za/exec/registrar/Policies/Policy%20%20Plagiarism.pdf#search=plagiarism>
2. Applicants seeking ethics clearance are required to be familiar with this policy.

**BIOBANKING (IF APPLICABLE):**

If any human tissue samples are stored for future secondary/unrelated and/or commercial use, then it is considered to be biobanking. Biobank Ethics applications are dealt with by the Biobanks Ethics Committee (BEC), a Subcommittee of the HREC (Medical).

BEC requires application forms to be submitted for:

* BEC 1 Form: Approval of a Biobank for sample storage or for
* BEC 2 Form: Storage/Retrieval/Transfer of HBM in a BEC approved Biobank.

(Please follow the link below for the latest list of approved biobanks)

**If yes,** please submit a parallel submission to BEC. Please contact Tanya Coetzee or Rhulani Mkansi ([Tanya.Coetzee@wits.ac.za](mailto:Tanya.Coetzee@wits.ac.za) or [Rhulani.Mkansi@wits.ac.za](mailto:Rhulani.Mkansi@wits.ac.za) 011 717 2816/1234) for more information on the directives, guidelines and procedures of BEC.

Please follow the link below for submission requirements to the BEC:

<https://www.wits.ac.za/research/researcher-support/research-ethics/ethics-committees/>

**APPENDIX 4 - STORAGE OF BLOOD AND/OR TISSUE SAMPLES:**

The policy of the ethics committee is:

* If, blood or tissue specimens are to be stored for future analysis and/or it is planned that analysis may be done outside Wits, then the specimens must be stored at Wits with release of sub-samples only once projects have been approved by the local Research Ethics Committee applicable to where the research will be done, as well as by the Wits Human Research Ethics Committee: (Medical);
* A separate information sheet and consent form for this is required. Please see the Standard Operating procedure at [www.witshealth.co.za/Services/Research-Ethics](http://www.witshealth.co.za/Services/Research-Ethics)
* For information on Biobanks and the Biobank Ethics Committee within the Wits Human Research Ethics Committee, please go to <https://www.wits.ac.za/research/researcher-support/research-ethics/ethics-committees/>, choose HREC (Med), see “Downloads”, see “Biobanks Ethics Committee”
* Only approved analyses may be done;
* Specimens may not be shared with anyone, unless approved by the Wits Human Research Ethics Committee (Medical); usually, an inter-institutional Materials Transfer Agreement (MTA) will be pre-requisite.

**APPENDIX 5 – Participant Information Leaflet and Informed Consent Form (PIL/ICON):**

1. The **Wits HREC (Medical)** and **The National Health Research Ethics Council (NHREC)** requires a Participant Information Leaflet and Informed Consent Form written in language understandable to the participant (or parent/legal guardian) detailing what the participant will be told. This should include the following:
   1. Please ensure to INVITE the participant to take part in the study; please include a greeting and introduce yourself.
   2. Participation is voluntary, and refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled.
   3. The participant may withdraw consent for the study at any time without penalty or loss of benefits.
   4. A brief description of the research, its duration, procedures, study intention, participation and what the participant may expect and/or be expected to do.
   5. Any foreseeable risks, discomforts, adverse effects or potential benefits, including those for placebo and standard of care.
   6. Disclosure of approved alternatives available to the participant.
   7. Emergency contact name and 24-hour telephone number.
   8. Explanation that medical treatment will be provided in the case of an adverse event (especially serious adverse event).
   9. Compensation for trial related injuries will be in accordance with the ABPI 2014 guidelines.
   10. A separate PIL/ICON for blood / tissue samples taken for future testing unrelated to the study.
2. The **Informed Consent Form** should include a clear statement that the participant is consenting to involvement in research, and not to specific treatment, which will not necessarily provide personal benefit. Any potential personal benefit should be mentioned when this is possible. In a trial **involving a placebo**, the participant must be made aware that, although the potential risks and benefits of all the investigational products have been explained, none of the active investigational products may be administered and it will not be possible for the researcher to reveal whether an active investigational products or placebo is being administered. An important piece of information is that the participant is free to withdraw from the study at any time without prejudicing any treatment that is required for existing or future medical conditions.
3. Minors over 7 years of age need to sign an Assent Form together with Parents/Legal Guardian Consent.

**APPENDIX 6:**

1. **SOUTH AFRICAN NATIONAL CLINICAL TRIALS REGISTRY (SANCTR):**

The South African Cochrane Centre (SACC), in partnership with the National Department of Health (DoH) and the Cochrane Infectious Disease Group, has established a South African Registry for all clinical trials conducted in South Africa

The South African National Clinical Trials Registry (SANCTR) is a South African initiative to support clinical trial registration within the Republic of South Africa. The SANCTR is an official registry and member of the World Health Organization (WHO) Network of Primary Registers. The SANCTR provides data to the central WHO International Clinical Trials Registry Platform (ICTRP) through the regional register - PACTR, so that trials registered in the SANCTR are represented in global searches (WHO ICTRP search portal URL: <http://apps.who.int/trialsearch>)

1. **THE NATIONAL HEALTH RESEARCH DATABASE (NHRD) REGISTRATION:**

This is essential for Provinces to be aware of, and evaluate studies being done in their hospital’s districts or clinics, etc.

**APPENDIX 7 - CHECKLIST – HREC APPLICATION 2024 – SUBMISSION:**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **PLEASE TICK** | **CHECKLIST** |  |
|  |  | **South African National Clinical Trials Registry (**SANCTR) Registration– Attach SANCTR “Proof of capture” form to Ethics Application Form – **VIEW** – https://sanctr.samrc.ac.za/ | Date of Issue |
|  |  | The National Health Research Database (NHRD) registration. | Date of Issue |
|  |  | Covering Letter (One page) | Date |
|  |  | Completed HREC 2024 Application Form |  |
|  |  | Protocol including Synopsis | Version:  Date: |
|  |  | Patient Information Leaflet and Informed Consent Documents + Assent Forms  Not Applicable | Version:  Date:  Language: |
|  |  | Patient Information Leaflet and Informed Consent Document for Collection and Storage of Genetic Material for Future Use  Not Applicable | Version:  Date:  Language: |
|  |  | Patient Information Leaflet and Informed Consent Document for Blood or Tissue Collection and Storage for Future Use  Not Applicable | Version:  Date:  Language: |
|  |  | SAHPRA Approval Letter / Letter of Application / Notification | Date Of Letter: |
|  |  | Insurance Certificate (if applicable)  Valid | From: |
|  |  | Patient Questionnaire(s) And/or Diary Cards;  Not Applicable | Version:  Date: |
|  |  | Advertisement(s); Please list mediums to be used:        Not Applicable | Version:  Date: |
|  |  | **Protocol Review Application Form**  To be signed by Applicant, Principal Investigator, Supervisor (if applicable) and Head of Department  (Please Note: If trial is being conducted in Provincial Health facilities approval from Hospital CEO/Clinical Manager/District Research Committee (whichever is applicable) must be obtained by Sponsor/Investigator AFTER ethics approval)  Approval Document:  Not Applicable | Province: |

**APPENDIX 8 - HREC (MEDICAL) SCORING SYSTEM:**

|  |  |
| --- | --- |
| Category |  |
| 1. Approved unconditionally. |  |
| 1. Approved subject to minor revisions delegated to the secretariat to complete. |  |
| 1. Pending Approval subject to response to comments provided by the reviewers, to be resolved by the original reviewers. |  |
| 1. Not approved as requires major revision and/or reviewer comments to be resolved. Will require review at the next HREC meeting. |  |
| 1. Not approved in the current form. Must be resubmitted and will receive a new application number and review timeline. |  |
| 1. Rejected due to substantive ethical concerns, will not be reviewed again. |  |

**APPENDIX 9:**

**Select DAIDS Risk/Benefit Category (If NIH Sponsored):**

**Subpart D – Additional Protections for Children Involved as Participants in Research:**

**X Category Description**

45 CFR 46.404 Research not involving greater than minimal risk.

45 CFR 46.405 Research involving greater than minimal risk but presenting the prospect

of direct benefit to the individual subjects.

45 CFR 46.406 Research involving greater than minimal risk and presenting no prospect

of direct benefit to individual subjects, but likely to yield generalizable

knowledge about the subject’s disorder or condition.

45 CFR 46.407 Research not otherwise approvable which presents an opportunity to

understand, prevent, or alleviate a serious problem affecting the health or

welfare of children.

45 CFR 46.408 Requirements for permission by parents or guardians and for assent by

children.

45 CFR 46.409 Wards.

**The Ethics Assessors will select a DAIDS Risk/Benefit Category for NIH Sponsored studies that include minors.**

**APPEDIX 10 – RISK TABLE:**

**HREC (Medical) Risk level categories definitions (May 2019)**

In South Africa, as elsewhere, it is necessary to assess the level of risk involved in undertaking research. The risk may be to research participants or patients, to communities, to institutions, or even to the researchers themselves. This is to ensure that responsible investigators have applied their minds and, in so doing, put in place whatever measures may be required to prevent or minimize unintended or negative outcomes.

This table identifies broad categories of risk. Schools/Departments can provide specific examples of these categories that are specific to that particular discipline, or the types of data collection methods or participant groups that are most common in that discipline.

|  |  |  |  |
| --- | --- | --- | --- |
| **Risk category** | **Definition** | **Example** | **Notes** |
| No risk | No contact with identifiable individuals, *e.g.* when study involves anonymized information | *In vitro* laboratory study using commercially-available cell lines, bacterial cultures, etc  Review of anonymized information in the public domain | These studies usually qualify for an ethics waiver |
|  |  |
| Minimal risk | Where the likelihood and magnitude of possible harm are no greater than those imposed by daily life in a stable society, or are to be found in routine clinical testing | Questions about participant’s everyday lives, activities and opinions*,* without detailed identifiable information. Student opinion surveys would, for example, usually fall into this category  No sensitive questions or topics  No vulnerable participant categories; participants may be experts, officials, professionals |  |
| Low risk | Where the only foreseeable risks is that of temporary discomfort, or where there may be some sensitivity involved in terms of the questions asked | Questions about participant’s everyday lives, activities and opinions, which may include biographical information and some potentially sensitive questions and/or topics  Taking of blood samples may cause minor discomfort  Questions about a participant’s HIV status or sexual behavior can be sensitive  No vulnerable participant categories |  |
| Medium risk | Where there is a possible risk of some harm for participants and/or the researcher, but where appropriate steps can be taken to mitigate or reduce risk | Sensitive topics and/or questions that may have potential for trauma and emotional distress  Drug trial, pre-general release to the market  May include vulnerable participant categories or marginalized groups.  There is a clear justification to undertake the research using this participant group and/or using the proposed instruments, because likely benefit exceeds likely risks | Support/counselling services must be provided for participants, when appropriate  A distress protocol should be given, when appropriate |
| High risk | Where there is a real and foreseeable risk of harm, which may lead to serious adverse consequences if not managed in a responsible manner | Clinical procedures in which a successful outcome cannot be guaranteed, but where non-intervention is likely to result in harm to the individual  Highly sensitive topics, e.g. experiences of inter-partner violence, rape, mistreatment of children, etc  Vulnerable or marginalized participant groups, or where multiple vulnerabilities exist  Research involving deception of the participants  Where the participants place themselves at risk of harm if they participate  Where the researcher/s may place themselves at risk of harm  Where the researcher/s may place themselves at risk of breaking the law, or may be legally required to report what they find, e.g. child abuse or neglect. In such instances, the researcher should consult a competent person or agency, as to whether referral to the Police or Social Welfare is warranted  Where the research may reveal information that may place the participant or others at risk (e.g. victims of abuse, violence, crime), requiring intervention from state institutions  There is a clear justification to undertake the research using this participant group and/or using the proposed instruments, despite the potential risks | Remedial interventions by external professionals can be taken should harm occur  External support/counselling services must be provided for participants and/or for the researcher  A distress protocol and debriefing strategy should be given, if appropriate  Research involving orphans under the age of 18, who have no formal Guardian, may only proceed if a court order is handed down by the High Court |

**NOTES:**

**(1) Definitions of terms**

**Discomfort** refers to a sensation of uneasiness, disturbance or mild pain.

**Risk** refers to (i) the likelihood of exposure to a particular negative consequence, and/or (ii) the magnitude of the possible consequences of exposure, and/or (iii) the possibility that research could result in harm.

**Harm** refers to damage incurred (which may include physical, psychological/emotional, social, economic or legal harm) as an outcome of an action, or through emotional distress.

**(2) Discussion of risk**

Individuals who may be at increased risk include:

• Those who are dependent/reliant on the institution/person who provides/mediates access to researchers;

• Those who are involved in illegal activities or who are criminalized by the state, e.g. drug dealers, sex workers, undocumented migrants.

NB: it is essential to consider the individual – not an aggregated group – when assessing risk.

**(3) Discussion of vulnerability**

Vulnerability can stem from: a lack of capacity or impaired ability to provide voluntary informed consent; health status; social pressures that may impact on the ability to make a free and informed decision; any inability to protect one’s interests in research. Vulnerability may be considered as dynamic and specific to a particular context, and may also arise as a result of power asymmetries between participants and researchers/institutions. There may be layers of vulnerability that function and interact within a participant’s circumstances. Being vulnerable does not necessarily imply that harm or exploitation will occur, but it does increase the risk of harm or exploitation through research.

In addition to those in vulnerable categories, vulnerability may also include individuals whose ability to provide informed consent may be reduced where:

* Their decision-making capacity is limited due to individual mental health status;
* They are physically impaired to the extent that they are largely or wholly dependent on others to function from day to day;
* Their decision-making capacity is limited due to the environment in which they live/work, e.g. prisoners/detainees, residents of drug rehabilitation centres;
* They exist in a hierarchical structure which constrains their freedom of operation, *e.g.* members of the armed forces, certain religious orders;
* They are under 18 years of age;
* They are dependent on the state to maintain a legal status, e.g. documented asylum seekers, documented refugees.

NB: it is essential to consider the individual – not an aggregated group – when assessing vulnerability.

The researcher needs to minimise the risk of harm, ensure that the consent process supports a truly informed decision, and put in place additional measures to ensure ethical involvement of vulnerable groups. Where necessary, applications should include details of steps to be taken to facilitate data collection across language barriers (e.g. interpretation or translation) and/or in cases of illiteracy.

It is important for researchers to consider the inconvenience or cost to participants taking part in their research so that appropriate travel costs or refreshments are provided. Loss of income and absence from work needs to be avoided or compensated appropriately.

Useful references:

Bracken-Roche, D., Bell, E., Macdonald, M.E. and Racine, E. (2017). The concept of ‘vulnerability’ in research ethics: an in-depth analysis of policies and guidelines. *Health Research Policy and Systems*, 15 (1), 8, doi:10.1186/s12961-016-0164-6.

Horn, L., Sleem, H. and Ndebele, P. (2014). Research vulnerability. In: M. Kruger, P. Ndebele and L. Horn (Eds.), *Research ethics in Africa: A resource for research ethics committees*. Stellenbosch: SUN Press, pp. 81-90.

**(4) Distress protocol**

A ‘distress protocol’ is a procedure to follow in emergency situations where, for example, a participant becomes clearly distressed during an interview. Under such situations, the interview is terminated and the distress protocol is enacted. Researchers may need to consider:

1. The possible distress experienced by the participant: e.g. questions that address issues of abuse, abandonment, previous negative sexual experiences, or traumatic memories that may induce distress. A distress protocol must include the name and contact details of an appropriate provider who can provide support, at no cost to the participant. This may include counselling services or access to legal services; specific contact details of such services must be included.

2. The possible distress experienced by the researcher: this may include provisions for how the safety of the researcher will be supported, and should be discussed with supervisor and the name and contact details for counselling services provided if needed