Health Research Ethics

Wits/Aberdeen University 2-day Training

Mpumalanga Health Research Committee, Mpumalanga Department of Health

Maria van der Merwe BDiet MNutr
Lucia D'Ambruoso BSc (Hons) MSc PhD FHRA FRSPH

August 2022

Module III
Research governance, RECs

UNIVERSITY OF ABERDEEN | UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | vapar | AGINCOURT 30 | health MPUMALANGA PROVINCE REPUBLIC OF SOUTH AFRICA

1

What does this training cover?

Module I: Health research, ethical principles

Module II: Norms, standards, and criteria

Module III: Research governance and RECs

Module IV: Contemporary issues

Module V: Monitoring research conduct

Not specifically covered: Biological materials/Human tissue; Clinical/medical ethics, therapeutics; Genetics/genomics research but principles apply

vapar

2

UNIVERSITY OF ABERDEEN

Module 3

Research governance: REC

3

Module III Learning Outcomes

a) Outline research governance considerations
b) Describe key aspects of RECs: mandates, roles, structures
c) Understand core functions of RECs (ethical review)
d) Orient to guidance for submission of documents for ethical review

Plenary: REC for PHRC – bridging policy and practice

4

3a | Research governance

Providing a conducive environment for the coordination and conduct of health research

- Articulation of a vision for health research
- Setting research priorities
- Coordination of actors' interventions and investments
- Ensuring ethical standards
- Building research partnerships

WHO/AFR research strategy major components of research governance

- Availability of valid health research policies, strategic plans, and priority lists
- Legislation on health research
- National or institutional RECs
- Scientific review committees
- Strong institutional capacity to coordinate (focal person and a designated unit to coordinate health research)

Source: Nabyonga-Orem et al 2021

5

African research governance in context

Among the challenges of healthcare decolonization … are: weak institutional capacity for supporting locally generated research and innovations; legal and bureaucratic frameworks that 'other' and impede the advancement of traditional healthcare; disproportionately higher investment in biomedical healthcare than basic public healthcare.

African researchers and innovators constantly have to align their work to priorities to HIC funders in order to be able to access funding…researchers feel more accountable to funders, who set priorities, than to the specific needs of their local populations Atuire & Rutazibwa, 2021

6

Governance must be adaptive

An adaptive governance structure to embrace new developments in medicine … to guard against weakness in regulating research on new interventions…It is thus imperative that outdated or narrowly scoped laws be updated ..to respond to both the challenges and opportunities presented by technological and methodological advancements impacting on or driven by health research Nabyonga-Orem et al 2021

7

3b | RECs: mandate, role, structure

*The Declaration of Helsinki highlights the need for ethical review by an **independent and appropriately constituted** REC. The committee must be **transparent** in its functioning, must be **independent** of the researcher, the sponsor and any other undue influence, and must be duly **qualified**.*

*It must take into consideration the **laws and regulations** of the country or countries in which the research is to be performed as well as applicable **international norms and standards**.*

*The committee must have the **right to monitor** ongoing studies including information about any serious adverse events. At the end of the study, a final report should be submitted to the committee including the study's findings and conclusions* Thurtle et al 2021

8

Mandate and role

The primary role of the REC is to protect the interests (rights and welfare) of the research participants who volunteer to take part in scientifically sound research. Consequently, the primary responsibility of each REC member is to decide independently whether the proposed research protects the interests of participants adequately and keeps to exemplary standards in research activities.

RECs must review 'health research' proposals and protocols to ensure that the research will promote health, contribute to prevention of communicable or non-communicable diseases or disability or result in cures or alleviation of suffering caused by communicable or non-communicable diseases or disability (NHA s 73(2)(a)). (1.6.3)

Source: NDoH, 2015

9

Structure

All REC members should have documented proof of research ethics training, refreshed at least once within appointment period

Independent, multi-disciplinary, multi-sectoral and pluralistic. Multiple perspectives:

- **scientific expertise** behavioural/social sciences; health care providers; members who have legal/ethics expertise;
- **ethnically and culturally diverse** members and an appropriate mix of males and females
- **lay persons**, preferably from communities in which research is conducted
- **Independence** members not affiliated with organizations that sponsor, fund, or conduct research reviewed by the REC

i. at least 9 members with a quorum being a simple majority

ii. where the number of members is more than 15, the quorum may be 33%

iii. at least 1 layperson

iv. at least 1 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

v. at least 1 member with professional training and experience in qualitative research methodologies

vi. members with professional training and experience in quantitative research methodologies

vii. a member with expertise in bio-statistics

viii. a member with expertise in research ethics

ix. at least 1 member who is legally qualified

Sources: WHO, 2011; NDoH, 2015

10

3c | Core functions of RECs: ethical review

- Conduct rigorous **ethics review** of research proposals (main responsibility of REC)
- Ensure welfare and other interests of participants, researchers 'used' in research properly protected
- Research conducted in accordance with required ethical norms and standards

NHREC firmly supports ethical practice research should reflect **core values of respect, scientific merit and integrity, justice and beneficence**.

Of highest priority are

- **refinement of ethics guidelines,**
- **establishment of research ethics committees, and**
- **strengthening of review processes**

to protect the rights, safety and welfare interests of individuals involved

Source: NDoH, 2015

11

Ensuring ethical and scientific standards

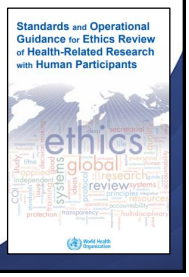
- protect participants from harm **weighing** risks of harm against the likelihood of benefit by minimising risks of harm to the extent possible and then by **balancing** risk of harm relative to the likelihood of benefit
- **hold researchers accountable for the research activities**
- **promote important social and ethical values**
- Thorough and inclusive process of discussion and deliberation
- Seeking external input where necessary
- Consensus-building process of decision-making

Sources: WHO, 2011; NDoH, 2015

12

Written procedures & policies: TORs, SOPs

- **Definitions as appropriate, standards/guidelines**
- Committee membership and governance, institutional authority and responsibility, independent consultants
- Activities and processes: frequency of meetings, preparation of agenda and minutes, registers for meetings, expectations and time-lines for reviewers
- REC procedures for expedited and full REC review
- Quorum requirements
- Decisional analysis guidance
- Conflict of interest and confidentiality
- **Protocol review process: submission of documents**
- Communicating decisions
- **Monitoring, continuing review and re-certification**
- Protocol amendment procedures
- Adverse events/unanticipated problems
- Protocol deviations and protocol violations
- Non-compliance consequences
- Suspension and termination
- Compliance checks and audits
- **Informed consent**
- **Privacy, confidentiality**
- **Research involving minors**
- **Research involving vulnerable persons**
- Data collection/storage, documentation/archiving
- Biological materials collection, storage
- Databases, registries and repositories
- Complaints procedures
- Whistle-blower protection



Sources: WHO, 2011; NDoH, 2015

13

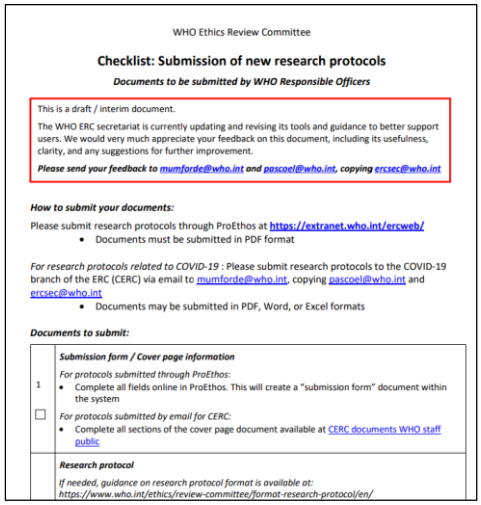
Resources

1. **Support staff,** adequate in number and training to enable the REC to carry out its technical and administrative responsibilities;
2. **Adequate resources** to fulfil assigned functions: office space and equipment and supplies (e.g. computers, stationery, telephones, shredding machine) to conduct business, store committee files, and keep documents secure and confidential;
3. **Access to appropriate space** for the committee to meet and adequate means for members to communicate as needed between meetings;
4. **Adequate financial resources** for committee to produce high-quality work;
5. **Compensation for REC members** if necessary and unless they are already being compensated for their time and effort through other means

Sources: WHO, 2011

14

3d | Guidance for submission of documents for ethical review



WHO Ethics Review Committee

Checklist: Submission of new research protocols

Documents to be submitted by WHO Responsible Officers

This is a draft / interim document.

The WHO ERC secretariat is currently updating and revising its tools and guidance to better support users. We would very much appreciate your feedback on this document, including its usefulness, clarity, and any suggestions for further improvement.

Please send your feedback to mumforde@who.int and pascoel@who.int, copying ercsec@who.int

How to submit your documents:

Please submit research protocols through ProEthos at **https://extranet.who.int/ercweb/**

- Documents must be submitted in PDF format

For research protocols related to COVID-19 : Please submit research protocols to the COVID-19 branch of the ERC (CERC) via email to mumforde@who.int, copying pascoel@who.int and ercsec@who.int

- Documents may be submitted in PDF, Word, or Excel formats

Documents to submit:

1	☐	***Submission form / Cover page information*** *For protocols submitted through ProEthos:* • Complete all fields online in ProEthos. This will create a "submission form" document within the system *For protocols submitted by email for CERC:* • Complete all sections of the cover page document available at CERC documents WHO staff public
		Research protocol *If needed, guidance on research protocol format is available at: https://www.who.int/ethics/review-committee/format-research-protocol/en/*

- **Submission of new research proposals**
- Submission of response to the ERC review
- Submission of proposals for 'continuing review'
- Requesting an 'amendment to an approved protocol'
- Project closure

Source: WHO Research Ethics Review Committee (ERC)

15

Recommended research protocol format: Part 1

- Project summary
- General information
- Rationale & background information
- References (of literature cited in preceding sections)
- Study goals and objectives
- Study design
- Methodology
- Safety considerations
- Follow-up
- Data management and statistical analysis
- Quality assurance
- Expected outcomes
- Dissemination and publication policy
- Duration
- Problems anticipated
- Ethical considerations
- Informed consent

Source: WHO Research Ethics Review Committee (ERC)

16

Recommended research protocol format: Part 2

- Budget
- Other support for project
- Collaboration with other scientists or research institutions
- Links to other projects
- Curriculum Vitae of investigators
- Other research activities of the investigators
- Financing and insurance

Source: WHO Research Ethics Review Committee (ERC)

17

3e | Review process

- Documents required for review
- Review procedures, and decision-making
- Communicating a decision
- Follow-up reviews and monitoring of proposed research
- Documentation and archiving

Source: WHO, 2011

18

Submissions, documents required for review

Applicant instructions:

- Name and contact details of REC secretariat to whom application should be submitted
- Written documentation to be submitted as part of application
- Format of submission
- Languages in which documents are to be submitted
- Number of copies to be submitted
- Deadlines for submission
- Means of submission acknowledgement and other correspondence
- Expected time for notification of decision following review
- Time frame to be followed if additional documentation or revision is requested
- Fee structure
- Procedure for seeking amendments to protocol or documents
- Required format for recruitment material, information to be given to prospective research participants, and informed consent
- Checklist for the above

Source: WHO, 2011

19

Submissions, documents required for review

Documents required:

- Signed and dated application form
- Research protocol
- Summary in non-technical language
- Ethical considerations
- Previous research that supports / justifies the proposal
- Safety data. when applicable
- Current CV of primary investigator
- Data collection forms
- Forms and other materials for recruitment of participants
- Informed consent forms (local languages)and process
- Measures to ensure privacy and confidentiality
- Statement on remuneration or other services / goods to participants
- Insurance coverage, if applicable
- Disclosure of previous decisions pertaining to the proposal
- Statement of agreement to comply with ethical guidelines

Source: WHO, 2011

20

Review procedures

Written procedures:

- specify process by which REC will decide which projects should be reviewed by full convened committee and which projects may be reviewed through expedited procedure
- address who will have responsibility of making this determination, number of reviewers required for expedited review, how reviewers will be selected
- state procedures for coordinating with and/or relying on reviews and decisions of other domestic RECs or RECs in other countries

The Chair regularly notifies REC members of expedited reviews that have been conducted between convened REC meetings.

Source: WHO, 2011

21

Decision-making

Decision making procedures to clearly describe:

- ethical guidelines on which the REC will rely to make its decisions
- manner in which the project documents will be presented to committee for discussion
- process by which project will be discussed, who may remain in the room during various components of the discussions and/or decision-making
- quorum requirements for making a decision
- pre-defined method for arriving at decision, who may take part in decision-making
- clear options for decisions; criteria for each outcome described, as should any specific follow-up procedures associated with each option, including specific procedures for re-review, as applicable.

Source: WHO, 2011

22

Communicating a decision

a) Specific identifying information about the project
b) A clear statement of the decision reached
c) Signature (dated) of the Chair (or another authorised person) of the REC.
d) Mechanisms for researchers to request reconsideration of REC decisions, either by REC itself or by other entities.
e) Mechanisms for informing public about REC decisions (e.g., bulletin board or internet postings, newsletters, or use of registries).

Source: WHO, 2011

23

Follow-up reviews and monitoring

Considerations:

a) documents to be reviewed
b) quorum requirements and communication procedure for follow-up reviews
c) intervals for follow-up reviews, determined by the nature of the research project - generally at least once a year
d) circumstances that will trigger follow-up reviews, in addition to those that are regularly scheduled
e) decision resulting from a follow up review should be issued and communicated to the applicant, indicating either that the original decision is still valid or that there has been a modification, suspension, or withdrawal of the REC's original decision.

Source: WHO, 2011

24

Documentation and archiving

All REC documentation and communication to be dated, filed, and archived according to the committee's policies and written procedures.

Consistent with any relevant local laws or institutional policies.

Records may be kept in hard copy, electronically, or both – with sufficient safeguards.

Members of staff to be sufficiently trained to understand their responsibilities related to record keeping, retrieval, and confidentiality.

Procedures outline who is authorised to access committee files and documents.
a) Committee-related documents

b) Project-related documents

25

Key procedures

Secretariat

- Online submission portal
- Initial screening
- Review types:
  - Full committee review
  - Expedited /Accelerated
  - Exemptions
  - Continuing
- Review meeting
  - 2 primary reviewers

  Protocol discussion with PI
- Disputes
- Recommendations
  - Approved as submitted
  - Conditional approval: amendments/clarifications
  - Not approved: rewriting/additional information
  - Rejected
- Communicating outcomes
- Timeframes (monthly meeting)

26

Applications & Feedback

- Monitoring
- Addressing gaps
- Complaints/appeals
- Research repositories

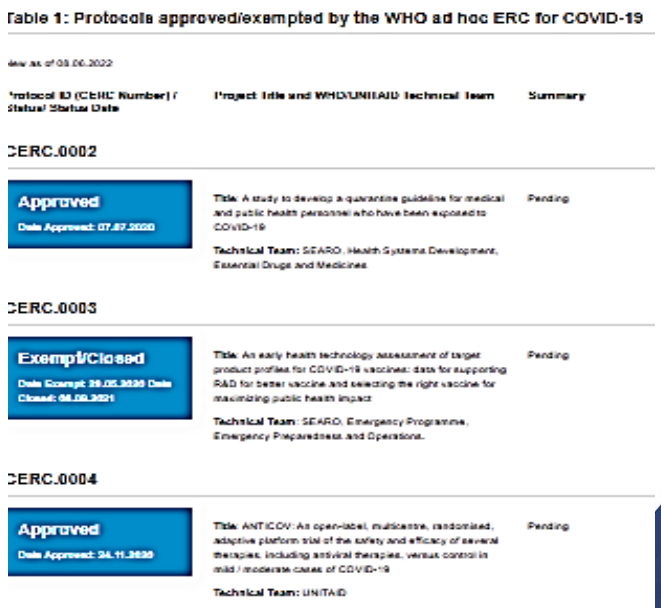


Table 1: Protocols approved/exempted by the WHO ad hoc ERC for COVID-19

Protocol ID (CERC Number) / Status/ Status Date	Project Title and WHO/UNITAID Technical Team	Summary
CERC.0002		
Approved	Title: A study to develop a quarantine guideline for medical and public health personnel who have been exposed to COVID-19 Technical Team: SEARO, Health Systems Development, Essential Drugs and Medicines	Pending
CERC.0003		
Exempt/Closed	Title: An early health technology assessment of target product profiles for COVID-19 vaccines: data for supporting R&D for better vaccine and selecting the right vaccine for maximizing public health impact Technical Team: SEARO, Emergency Programme, Emergency Preparedness and Operations.	Pending
CERC.0004		
Approved	Title: ANTICOV: An open-label, multicentre, randomized, adaptive platform trial of the safety and efficacy of several therapies, including antiviral therapies, versus control in mild / moderate cases of COVID-19 Technical Team: UNITAID	Pending

Source: WHO Research Ethics Review Committee (ERC)

27

Review Tools

World Health Organization

Research Ethics Review Committee (WHO ERC)

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – HTTP://INTRANET.WHO.INT/HOMES/RPC/ERC – HTTP://WWW.WHO.INT/RPC/RESEARCH_ETHICS

SECTION 1
PROTOCOL (SCIENTIFIC AND TECHNICAL ISSUES)

The ethical integrity of research depends substantially on its design and methodology. Consequently, the following section includes key questions on scientific and technical issues that should be included in the research protocol. This section does not provide guidance on how to design a study, but rather raises key technical and scientific issues that need to be well explained in study protocols. For guidance on how to design a research study, please consult the following link:
http://www.emro.who.int/publications/pdf/healthresearchers_guide.pdf

The ERC website also has additional guidance documents on writing research protocols and informed consent forms, available at the following link:
http://www.who.int/rpc/research_ethics/format_rp/en/index.html

Background information

1. Is the rationale for the study clearly stated in the context of present knowledge? ☐
2. Have you included a review of literature with references? ☐
3. Have you described the study setting? ☐

Goals and objectives

4. Are the objectives and/or hypothesis to be tested clearly stated? ☐

Source: WHO Research Ethics Review Committee (ERC)

28

RECs and Community engagement

- Has the study clearly defined both the research and the broader community, are proposed engagement mechanisms appropriate?
- What should the direct benefits of the research be for the community involved?
- Does the research question answer a community priority?
- How will the findings be translated into action to address the identified priority area?
- How will possible individual and community harm be minimised?
- Will the research conduct stakeholder analysis, are there independent sources from which relevant information can be obtained?
- Will the research establish a CAB, or is there a CAB already present in the area? If one still needs to be established, what process has to be undergone for establishing the CAB, and will the anticipated process be both inclusive and democratic?
- How will study explore power dynamics among different community stakeholders to ensure true representation of community?

Source: Kruger, Ndebele and Norn, 2014

29

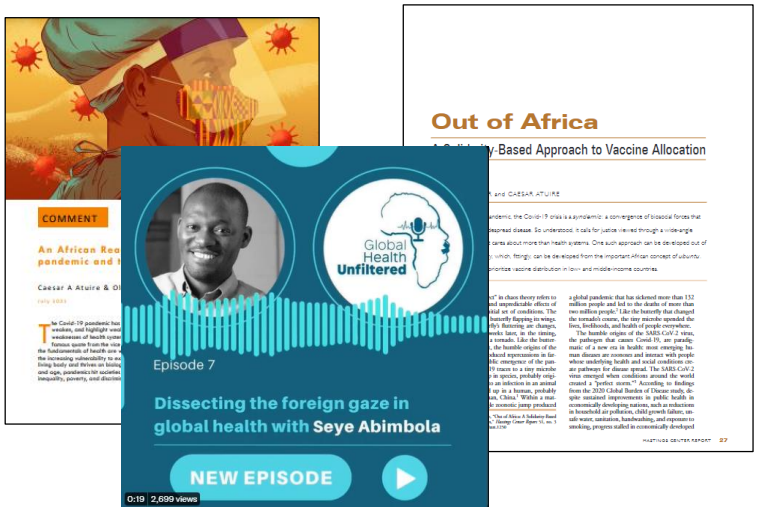
RECs and Community engagement (cont.)

- Are the responsibilities of researchers towards the participants, the wider community and the CAB clearly defined?
- How will community consultation and partnership building be sustained throughout the research project's life cycle?
- Will researchers concerned be guided by a communications plan in the process and the end-of-study results dissemination?
- Has the committee taken note of project documents related to community engagement that have yet to be developed in full and presented to the committee for ethical approval? (Such documents could include: the communications plan; the community engagement plan; the related standard operating procedures (SOPs); and the information, education and communications (IEC) materials pertaining to the study.
- Will the research project recruit staff from local or central government health institutions, and, if so, will this compromise or weaken the community health system involved?

Source: Kruger, Ndebele and Norn, 2014

30

Governance structures must be adaptive



An adaptive governance structure to embrace new developments in medicine … to guard against weakness in regulating research on new interventions…It is thus imperative that outdated or narrowly scoped laws be updated ..to respond to both the challenges and opportunities presented by technological and methodological advancements impacting on or driven by health research Nabyonga-Orem et al 2021

31

	Indicator	Achieved	In progress	Not initiated
1	Existence of legally binding instruments for health-related research with human participants in alignment with international guidelines	Argentina, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, Mexico, Panama, Peru, and Uruguay	Bolivia, El Salvador, Guatemala, Haiti, Honduras, Jamaica, Nicaragua, Paraguay, and Venezuela	Trinidad and Tobago
2	Existence of a national body responsible for the oversight of research ethics committees	Argentina, Brazil, Chile, Costa Rica, Cuba, Ecuador, El Salvador, Mexico, Panama, Paraguay, Peru, and Uruguay	Bolivia, Colombia, Dominican Republic, Guatemala, Haiti, Honduras, and Venezuela	Jamaica, Nicaragua, and Trinidad and Tobago
3	Existence of policies that support research ethics training for investigators and ethics review committees	Argentina, Colombia, Costa Rica, Cuba, Panama, Peru, and Venezuela	Bolivia, Brazil, Chile, Dominican Republic, Ecuador, El Salvador, Guatemala, Mexico, Paraguay, and Uruguay	Haiti, Honduras, Jamaica, Nicaragua, and Trinidad and Tobago
4	Existence of the requirement of the prospective registration of clinical trials in accordance with WHO standards	Cuba	Argentina, Brazil, Chile, Colombia, Costa Rica, Ecuador, Guatemala, Haiti, Mexico, Panama, Peru, and Uruguay	Bolivia, Dominican Republic, El Salvador, Honduras, Jamaica, Nicaragua, Paraguay, Trinidad and Tobago, and Venezuela
5	Existence of policies on the responsible conduct of research	Peru	Colombia and Panama	Argentina, Bolivia, Brazil, Chile, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Paraguay, Trinidad and Tobago, Uruguay, and Venezuela
6	Existence of established procedures to do thorough accelerated ethics review of research during emergencies	Panama	Brazil and Peru	Argentina, Bolivia, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Paraguay, Trinidad and Tobago, Uruguay, and Venezuela

Table 2: Countries per indicator and its compliance

Research ethics systems in Latin America and the Caribbean: a systemic assessment using indicators

Bernardo Aguilera, Sarah Carracedo, Carla Saenz

32

Plenary: REC for PHRC
Bridging policy and practice

- Identify policy/practice gaps:
  - structural; organisational; feasibility of compliance; feasibility of adaptive governance (power/control); resource implications
- Build strategies to address gaps
- Codesign (web resources, other?)

33

Module III Learning Outcomes

a) Outline research governance considerations
b) Describe key aspects of RECs: mandates, roles, structures
c) Understand core functions of RECs (ethical review)
d) Orient to guidance for submission of documents for ethical review

Plenary: REC for PHRC - bridging policy and practice

34