RNEC

PAC-02 **Version number (1.0)** **Effective date (01 Jun 2026)**

Review and Approval of Protocol Amendments and Modifications

Definitions

- **Protocol Amendment**: Any change to an RNEC-approved protocol or related documents, including consent forms, procedures, recruitment, eligibility, data handling, or study personnel.
- **Administrative Amendment**: Changes that do not affect study design, risk, or participant experience (e.g., staff changes, contact details).
- **Minor Amendment**: Changes that do not increase risk and do not substantially alter study objectives or methods.
- **Major Amendment**: Changes that may affect participant safety, risk level, scientific validity, or informed consent.
- **Protocol Modification**: Any adjustment to study procedures, whether minor or major, requiring notification to and review by RNEC.

1. Purpose

This SOP describes procedures for submission, review, approval, and implementation of protocol amendments to ensure that any changes to approved research maintain scientific integrity and participant protection. No amendment may be implemented prior to RNEC approval, except where necessary to eliminate immediate hazards to participants.

2. Scope

This SOP applies to:

- All amendments to RNEC-approved research protocols
- Administrative changes (e.g., PI contact details, site staff)
- Scientific and ethical changes, being minor, or major amendments (e.g., eligibility criteria, new arms).
- Amendments reviewed through expedited or full committee procedures
- Consent-related changes (e.g., revised consent forms, waiver updates).

3. Responsibilities

(1) Principal Investigator (PI) shall:

- Submit amendment requests with supporting documents prior to implementation
- Provide justification and tracked changes
- Update participant documents as required
- Re-consent participants if applicable
- Report urgent safety amendments within **48 hours**

RNEC Secretariat shall:

- Receive amendment submissions and screen for completeness
- Log amendments and forward to Chairperson to assign review pathway
- Track timelines, communicate decisions and maintain records

(2) RNEC Chairperson shall:

- Categorize amendments (administrative, minor, major)
- Determine review pathway (expedited, or full committee)
- Assign reviewer(s)
- Endorse decisions

(3) Reviewer(s) shall:

- Assess scientific and ethical impact, evaluate risk changes
- Review consent updates
- Complete Amendment Assessment Form
- Recommend outcome

4. Procedures

Step 1. Submission

- PI completes the Protocol Amendment Application
- Pays amendment fees and submit proof of payment.
- All amendments submitted via the RNEC Online Platform.

Step 2. Administrative Screening

- Secretariat verifies completeness, version control and signatures.
- Secretariat acknowledges receipt within **5 working days**.
- Incomplete submissions returned

Step 3. Categorization

Chairperson categorizes amendment:

(A) **Administrative amendments**:
Reviewed and approved by Chairperson. The administrative amendments may include:

- Corrections recommended by the regulatory authority
  Recommeded cganges by the Rwanda FDA.
- Corrections to typos or formatting
  Minor edits that do not change meaning, such as fixing spelling or grammar, updating section numbering, correcting non-substantive inconsistencies.
- Updates to contact information
  New phone number or email for the PI or study coordinator, updated institutional address, revised emergency contact details, as long as the study team and responsibilities remain the same
- Changes in study personnel without change in roles
  Adding or removing research assistants, updating CVs or training certificates, replacing staff in non-key roles.
  If the PI or co- investigator changes, that becomes a major amendment, not administrative.
- Updates to study documents that do not affect participants
  Revised version numbers, updated institutional logos, formatting changes to recruitment materials without altering content
- Administrative updates to study timelines
  Extending the study end date when no additional procedures occur, adjusting internal milestones, updating expected enrollment dates.
  If the timeline change affects participant burden or procedures, it becomes a major amendment.
- Updates to funding or grant numbers
  New grant ID, updated sponsor administrative details, change in internal cost center.
  If the funding source changes in a way that affects conflict of interest, it may require a higher-level review.
- Administrative updates to study sites
  Updating site addresses, adding a site that is already RNEC-approved under a master protocol, removing a site that never enrolled participants.
  Adding a new site requiring new oversight is a major amendment.
- Updates to data management details that do not affect privacy
  Changing file naming conventions, updating storage location within the same secure system, adding administrative data fields.
  If identifiability or privacy risk changes, it becomes a major amendment.

The minor amendment should be reviewed by designated reviewers or Chairperson. Thus, the decision should be within maximum **14 days** from the submission to decision making on the amendment.

(B) **Minor amendments**:
Reviewed via expedited procedure. The minor amendments may include:

- Minor changes to consent forms
  Small edits that do not introduce new risks or procedures, such as clarifying wording, adding non-substantive explanations or updating formatting.
- Minor changes to recruitment materials
  Updating a phone number or email
  Adding a newspaper ad using the same approved language
  Slight wording adjustments without changing meaning
- Minor revisions to surveys or interview instruments
  Allowed when changes stay within the scope of the original study.
  Wordsmithing or adding clarifying questions

Adding questions similar to those already approved
Deleting non-essential questions

- Addition or removal of non-key study personnel
  Adding/removing research assistants.
  Updating training documentation.
  Changing the PI is not minor.
- Minor changes to study documents
  Updating brochures, questionnaires, or participant materials without altering procedures
  Clarifying instructions
- Minor adjustments to inclusion or exclusion criteria
  Only when they do not affect risk or the risk-benefit ratio.
- Minor changes to data collection procedures
  Adding or removing a measurement that does not increase risk
  Adjusting timing of data collection without increasing burden
  Changes in the logistical arrangements for storing or transporting samples
  Changing tool for recording study data without changing questionnaire, hosting server or sharing agreements
- Minor changes to study title or administrative details
  Title change or clarifications to protocol text
- Minor updates to participant numbers
  Only when the change does not increase risk or alter study design.
- Minor updates to study dates or timelines
  Adjusting start or end dates
  Extending timelines without adding procedures

The minor amendment should be reviewed by designated reviewers or Chair. Thus, the decision should be within maximum **21 days** from the submission to decision making on the amendment.

(C) **Major amendments**: Reviewed by RNEC full board. Major amendements include whatever procedural changes alter the risk which participants are exposed to, or the potential benefit, constitutes a major amendment. Examples include:

- Changes that affect participant safety or risk profile
  Increasing drug dosage, exposure, or duration of treatment
  Adding or removing safety tests or monitoring procedures that could alter risk-benefit balance
  New toxicology or pharmacology data requiring modification due to changed risk assessment
  Addition of serious unexpected adverse events or newly identified risks requiring protocol changes
- Major changes to study design or methods of the study
  Changing the primary or secondary endpoints in a way that affects scientific validity or safety
  Adding or removing a study arm or placebo group
  Any change to study design that significantly impacts statistical analysis or risk–benefit assessment
- Changes to study population
  Significant changes to inclusion/exclusion criteria (e.g., age range, adding vulnerable populations)
  Adding a new population not previously approved (e.g., adults lacking capacity)
- Changes to consent or participant-facing materials
  Significant revisions to consent forms or participant information sheets (new risks or procedures)
  Changes to recruitment or consent procedures (e.g., switching from in-person to digital consent)
  Changes in questionnaires, letters of invitation, letters to other clinicians/scientists
- Changes to study procedures
  Adding new tests, procedures, or interventions not previously approved
  Changing type, volume, or frequency of biological sample collection (e.g., adding lumbar puncture)
  Changing length or number of study visits in a way that affects burden or risk
- Changes to study sites or investigators
  Adding or removing study sites (especially if site qualifications differ)
  Changing the chief investigator or principal investigator
  A change of sponsor (s), or sponsor's legal representatives
  Significant changes to site selection or investigator training requirements
- Changes to participant compensation or financial arrangements
  Increasing payments or incentives that may influence voluntariness or create conflict of interest
  Changes to insurance or indemnity arrangements for the trial
- Temporary halts or restarts
  Temporary halt of the trial or a trial site, or restart after a halt (often due to safety concerns)
- Changes to data identifiability or privacy protections
  Switching from anonymous to identifiable data collection or vice versa
  New data linkages that increase identifiability or privacy risk
- Any change that alters the study primary purpose or scientific value
  Changing the main or specific objective of the research (e.g., shifting from safety to efficacy)

Adding new research questions that fall outside the original scope
Introduction of additional genetic or biological studies, or background information affecting the scientific value.

The major amendment must be reviewed by full RNEC board at next meeting. Major amendments are requested on an approved protocol and CAN NOT be combined with Annual Renewal Application. Decision provided within **7 days** after the review meeting.

Step 4. Ethical and Scientific Review

Reviewer evaluates:

- Impact on objectives
- Methodological validity
- Risk–benefit balance
- Participant burden
- Consent adequacy
- Data protection

Reviewer submits written recommendation.

Step 5. Decision

- Possible outcomes:
  - Approved
  - Approval with minor modifications
  - Require major revisions
  - Disapproved (Reasons documented)
- Chairperson endorses decision.

Step 6. Communication

- Secretariat issues written decision including approved changes, effective date and conditions (if any)
- Decision is notified within **7 working days** after the review meeting or reviewers feedback in case of minor

Step 7. Implementation

- PI may implement amendment only after written RNEC approval, except for urgent safety changes.

Step 8. Documentation

- Secretariat archives amendment requests, reviewer assessment, decision letter, and final approved documents.
- Records retained for minimum **10 years**.

5. Urgent Safety Amendments

If immediate changes are required to protect participants:

- PI implements change immediately
- PI notifies RNEC within **48 hours**
- RNEC reviews retrospectively

6. Required Documents

Amendment submissions must include:

- Protocol Amendment Request Form.
- Summary of changes and rationale (included in the amendment request form).
- Protocol with highlighted changes (with tracked changes)
- Revised protocol (clean version)
- Updated informed consent forms (if applicable).
- Revised data collection tools (if applicable)
- Updated recruitment materials (if applicable)
- Updated Investigator Brochure/ product info (if applicable).
- Risk–benefit assessment of changes (included in the amendment request form).
- Any new supporting documents (insurance certificate, site approvals).

Incomplete submissions shall be returned.

7. Timelines (Indicative)

Steps	Timeline
Administrative amendments	Within 7 working days after submission
Minor amendments	Within 15 working days after submission
Major amendments	Next RNEC meeting

8. Compliance

- Failure to obtain approval before implementation may result in suspension, termination, and/or institutional notification
- All major amendments must undergo full board review before implementation.
- Emergency safety modifications may be implemented immediately, but PI must notify RNEC within **48 hours**.

9. Quality Assurance

RNEC shall:

- Periodically audit amendment decisions
- Review SOP every 3-5 years
- Train investigators, staff and reviewers

10. References and Ethical Framework

(1) Law N° 015/2022 of 29/06/2022 relating to research on a human being (View/Download).
(2) Ministerial Order N° 002/MoH/2023 of 21/03/2023 relating to Rwanda National Research Ethics Committee on a human being (View/Download).
(3) Law N° 003/2018 of 09/02/2018 Establishing the Rwanda Food and Drugs Authority, and Determining its Mission, Organization and Functioning (View/Download).
(4) Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Participants (2024) (View/Download)
(5) CIOMS - International Ethical Guidelines for Health-related Research Involving Humans (2016) (View/Download)
(6) ICH - Guideline for Good Clinical Practice E6 (R3) View here
(7) WHO Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants (2011) (View/Download)
(8) RNEC Ethical Guidelines (View/Download)

11. Revision History

Version	Date	Summary of changes
1.0	**11-05-2009**	First RNEC SOP for Review and Approval of Protocol Amendments and Modifications