NATIONAL INSTITUTE FOR MEDICAL RESEARCH

MEDICAL RESEARCH COORDINATING COMMITTEE

NATIONAL HEALTH RESEARCH ETHICS SUB-COMMITTEE

GUIDELINES FOR REVIEWING HEALTH RESEARCH PROTOCOLS

July 2022

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Introduction

One of the core functions of the National Institute for Medical Research carried out through the Medical Research Coordinating Committee (MRCC), is to review and approve health research protocols that apply for ethics clearance in the Country. Members of the scientific community are engaged in the review process due to their scientific and ethical expertise in the areas of the protocols. This undertaking, under the supervision of the National Health Research Ethics sub-Committee (NatHREC), is central to safeguarding research integrity and the safety of Tanzanian citizens, particularly those participating in health research. This document is set to guide reviewers through the process and to standardise the reviews for all types of applications.

Section A: Validation of the Protocol

3. Validation of the applications will be done by the NatHREC Secretariat upon receipt in the Research Ethics Information Management System (REIMS) as follows:
    a. For new applications: The person who validates the documents will check all submitted documents for completeness against the standard application checklist. This includes checking for:
        i. Full protocol.
        ii. Filled MRCC application form.
        iii. Cover Letter: Should be on official letterhead, signed and submitted by PI as specified in the NatHREC Standard Operating Procedures. The letter must be recent and relevant to the application.
        iv. Institutional Commitment and Support Letters.
        v. Letter from Student supervisors
            - Must be on official letterhead(s)
            - Supervisors writing support letters for students must be affiliated with academic institutions in Tanzania.
        vi. Data collection tools and information and consent forms (ICFs).
        vii. IRB approvals (where applicable).
        viii. Material Transfer Agreement (MTA) and/or Data Sharing and Transfer Agreement (DSTA) (where applicable).
        ix. Ethical clearance fee payment receipt.

The Secretariat will inform the applicant to submit the missing documents or information if there is missing information. The Secretariat may allow the initiation of the review process at their discretion while the applicant processes submission of the missing documents.

b. For protocol amendments: apart from documents specified in the checklist, applications for protocol amendments must also include:
    i. A detailed summary specifying each amendment either on the cover letter or a separate summary in table format.
    ii. An amended protocol with highlighted and tracked changes.

The reviewer can communicate to the Secretariat to confirm that missing documents will be submitted or highlight additional missing documents. This information will be communicated between the reviewer and secretariat through the communication channel in REIMS.

Section B: Review of New Protocols (Non-Clinical Trials)

1. General approach – The recommended flow in reviewing a study protocol is to follow the following sequential steps:
    a. Check all submitted materials for completeness as indicated in the Protocol submission checklist (duly filled application form, Principal Investigator's (PI) cover letter, institutional commitment letter(s), support letter(s), protocol and appendices.
    b. Use a word document for writing comments (to be recorded clearly for each relevant sub-section).
    c. Read the cover letter from the PI, Institutional Commitment Letter(s), Support Letter(s) and Letter from supervisor (in case the applicant is a student).
    d. Review the abstract/summary.
    e. Review the MRCC Application Form.
    f. Review the protocol.

g. Review appendices [CVs of investigators, data collection tools, consent and assent forms, certificates of ethical clearance from other ethics committees, Material Transfer Agreement (MTA) and Data Sharing and Transfer Agreement (DSTA) where appropriate, etc.].
h. Synthesise and submit the comments online through Research Ethics Information Management System (REIMS).

2. Detailed review of individual sections.
    a. Cover Letter
        a. Should be on official letterhead, signed and submitted by PI as specified in the NatHREC Standard Operating Procedures.
        b. Should contain sufficient relevant information to the applicant's current submission.
    b. Institutional Commitment, Support Letters and Letter from supervisor
        a. Should be on official letterhead(s).
        b. Supervisors writing support letters for students must be affiliated with academic institutions in Tanzania.
        c. The letters should indicate available resources (infrastructure and human resource) required to undertake the proposed research.
    c. Title
        a. Should be clear and descriptive.
        b. Should be the same in the application form and protocol.
        c. Must align with problem statement, objectives and methodology.
        d. Theme must be culturally appropriate in the Tanzanian context.
    d. Abstract

        Should contain essential elements of the protocol summarised in a clear and succinct manner. These elements include:
        a. Background – short, indicating the magnitude of the problem and rationale.
        b. Broad/General objective (Aim) – clear and to the point.
        c. Specific objectives – These have to be 'SMART'[1].

[1] SMART means Specific, Measurable, Attainable/achievable, Realistic/Relevant and Time-bound

e. Methodology – covering study type/design, study areas and population, Sampling approaches and sample size (where applicable), data collection, analysis plan, and study duration.
f. Budget – amount (with currency), funder, funding mechanism and duration.

3. MRCC Application form

The MRCC application form is a summarised version of the entire protocol that gives a snapshot. All sections must be duly filled; refer to the "Application for Ethical Approval form" in the Applicant Resources section of REIMS.

a. The front page should have the following:
   i. Full names, academic qualifications, and institutional affiliation(s) of the PI should be provided.
   ii. PI's signature and contact information.
   iii. If the Main PI is not a Tanzanian, the name and contact information of the Local PI who is Tanzanian must be provided. S/he must be affiliated with a registered academic or research institution in Tanzania.
   iv. Names of other Co-investigators should be provided.

b. Content:

   This should have the following items reflected:

   i. Statement of the problem that is clear and concise, rationale, duration, location/study site(s) and significance of the study.
   ii. A narration of how the local government official(s) in the proposed/identified study areas will be (or have been) contacted.
   iii. A clear scientific justification of sampling approaches whereby issues of area selection, sample size determination, recruitment methods, inclusion and exclusion criteria, and study endpoints are presented.
   iv. A concise description of data collection techniques and management includes data entry and cleaning processes, analysis and storage procedures.
   v. Attachments of Institutional Research Ethics Review Board/Committee's clearance certificates. This applies to both protocols submitted by applicants from institutions available in Tanzania and those done in collaboration with researchers from institutions outside Tanzania.

vi. A fully packaged but straightforward consent-seeking process, whereby issues of study objectives, duration, benefits, potential risks and non-coercive participation approaches, including the freedom to participate or withdraw from the study after consenting, are presented. In line with these points, a justification to ensure study participants, especially the vulnerable populations, are protected is to minimise harm to participants and safeguard participants' privacy and confidentiality in the short and long term.

vii. A narration of plans for PI and co-investigators on protecting human research participants and ethics relating to health research.

viii. Justification for transfer of data and/or materials outside Tanzania and plans for local capacity-building in data analysis. Hand in hand with these is a submission of Material Transfer Agreement (MTA) in case materials are to be taken abroad or brought in from outside Tanzania. A Data Sharing and Transfer Agreement (DSTA) shall be filled if the study involves foreign investigators or institutions.

ix. Details of the funding body (name, address and amount).

4. Protocol

i. Must conform to the standard format, including sub-sections with subheadings summary/abstract, background/introduction and literature review, statement of the problem, rationale, objectives/aims, methodology and references[2].

ii. Information given (from title to content) must match those in the abstract and MRCC application form.

iii. Should provide additional details not accommodated in the application form, specifically in the literature review, methodology and ethical procedure(s) sub-sections.

iv. Background – should be brief but informative.

v. Problem statement and rationale – should state what necessitates the conduct of the study in the target population and what will be the possible utilisation of the generated findings.

[2] The length of each identified subsection will depend on the study sponsors/funder or academic institution requirement and available literature resource(s).

vi. Objectives/aims – should be linked to the problem statement and rationale. Specific objectives must be related to the main/broad objective and be SMART (specific, measurable, achievable, relevant/realistic, and time-bound).

vii. Literature review – must flow logically, covering all the known and unknown in each objective and finishing with gaps in the available evidence.

viii. Methodology

a. Study Design

- Evaluate if the study type/design is appropriate for the study objectives. Particular attention should be paid to special groups such as children and pregnant women, indigenous populations and other high-risk groups.

b. Sampling

- Sample size must be statistically justified for quantitative data purposes. For qualitative data, the sample size should be justified and show how data saturation will be reached.
- The inclusion and exclusion criteria must be scientifically sound, fair and unambiguous, and justification for selecting the intended sampling population/study sites (geographical distribution of the problem under study, accessibility, facilities etc.).

c. Data collection

- Tools used in data collection must be appended and described in detail, and their validity and reliability should be addressed where appropriate. Training of data collectors should be described.
- Studies involving the collection of biological samples such as blood and blood products, the amount of the samples to be collected should be well justified.
- Particular attention should be paid to sample collection from new-borns, neonates, infants and children. Less invasive options should be sought whenever possible.

d. Data analysis
    - Statistical tests should be justified and aligned with the study variables and objectives.
    - Plans for processing, analysis and storage of samples and data should be presented. Equipment, software, and other facilities to be used should be specified and appropriate.

e. Data management
    - Safeguards on privacy and confidentiality of data and samples collected must be stated clearly. This includes, among other things, data anonymisation, limitation of access and destruction of audio/video recordings after analysis unless it was stated in advance that they could be stored for future research or academic-related processes.

f. Other areas for review include the following:
    - Incentives or compensation: justification in case money or other incentives will be given to participants. They must be justifiable and reasonable,
    - Dissemination plan: Researchers must disseminate findings to the study areas and other relevant stakeholders where applicable. Dissemination plans should be described.
    - Study limitations.
    - Budget: must be presented with sufficient details identifying the individual line items and their monetary values in standard international currency. Justification provided must be reasonable and acceptable. The exchange rate used is dated from the Bank of Tanzania, where local currencies are presented.
    - Workplan or study timelines: must give realistic milestones for the study in line with study duration and funding. Must include all activities planned in the study.
    - References – should be current (although historical perspectives may be acceptable) and must follow a standard format (Vancouver, Harvard or other styles). Use of any of these styles must be uniform

throughout. All cited literature must be included and match the text's citation.

g. Appendices

These include curricula vitae, data collection tools, consent forms, MTA, DSTA, ethics clearance certificates, and receipts for payment of ethical clearance fees)

- Curricula Vitae (CV). Must be provided for PI, Local PI and all Co-investigators. Each must narrate the investigator's educational qualifications, training background and experience related to the proposed study's nature. To keep the CV concise, the presented information should be relevant to demonstrate the competence of the respective study/applicant. It is expected that the investigators must cover all the scientific and technical expertise expected to complete the proposed research successfully. In case of shortcomings, comment should be given to PI to consider adding into the team a Co-investigator with expertise in the area that is not covered.
- Data collection tools (questionnaires, data collection matrices etc.). Must bear investigators' institutional logo. Must be in English and Kiswahili as appropriate (being an accurate translation of each other), using language that is easy for the targeted study population to understand. If the tool proposed is not standard, plans must be given for pre-testing/piloting before use. Must be adequate in coverage of all specific objectives. For tools involving interviews of group discussion, the length of the tool should not be excessive to prevent fatigue/exhaustion on the part of respondent(s)/participant(s). Should not contain questions or data elements that are outside the scope of the study or are not culturally appropriate. Investigators using online data collection tools such as Open Data Kit (ODK) which can be linked to servers outside Tanzania in real-time, must obtain DSTA approval before embarking on data collection in the field.
- Consent forms (for participants aged 18 years and above) and assent forms (for children from 10 years to 17 years of age) who can read

and write as well as understand the description of the study - in addition to parental consent/permission). Consent and assent forms must be included and should cover all groups of research participants unless investigators are requesting for. Waiver of informed consent - such as in retrospective studies where it is not possible to go back and consent participants, and the study has no more than minimum risk. Verbal consent with waiver of documentation of consent – such as in studies of sensitive nature where breach of confidentiality is a principal risk, and documentation of consent links participants to the study. Waiver of parental consent/permission for emancipated minors – such as married adolescents living in their households. Must bear investigators' institutional logo. Must both be in English and Kiswahili (being an accurate translation of each other), of reasonable length, written in a language that is easy to understand, and must cover a general description of the study, why the participant is asked to participate, voluntariness, right to refuse participation or withdrawal from the study without impact on care or any other benefit, what will participants be expected to do in the course of the study, cost of participating, benefits to participants as well as risk to participants and their mitigation (including plans for ensuring confidentiality and privacy, such as timelines for disposal of identifying information such as video and audio recordings). The consent form must provide contact information (24/7 reachable landline or hotline/mobile phone numbers, emails) of the Local PI and NatHREC for participants to use in case of study-related questions. Should end with a "*consent statement"* (example, "I agree to participate/I allow my child to participate in the study") that will be signed, or thumb printed by the participant/parent/guardian who agrees to participate in the study and the investigator administering consent. Where there is a need for using photographs, sharing samples and or data with other investigators, or using stored DNA for future unforeseen studies, the consent statement must include a clause permitting this. Electronic consent (e-consent) may be

acceptable for studies where data collection is done entirely online (for example, using online questionnaires or telephone interviews).

- MTA and DSTA. The NIMR-approved versions of the MTA and DSTA forms must be used in their actual form without addition or omission of any item. Any breach of this guideline will result in the application being rejected and the applicant being penalised for violation. If applicable, the duly completed MTA and DSTA forms should be appended/attached at the time of submission for ethical clearance for any study seeking to transfer materials and data.
- Ethical clearance certificates. Valid and current certificates of ethical approval of the study from research ethics committees at collaborating institutions outside Tanzania should be attached. Similarly, certificates issued by other research ethics committees within Tanzania should also be attached.

5. The reviewer will summarise on REIMS recommendation for one of the following:
    a. **Recommended for approval as presented** - for adequately presented submissions with no need for changes or clarifications in any component.
    b. **Recommended for approval after minor revisions** – in case minor clarifications or documentation are needed and generally involve minor concerns that do not affect the understanding, appropriateness and alignment of the problem statement, study questions, objectives, rationale and methodology, including ethical procedures. Examples include but are not limited to unclear study title; incompletely filled MRCC form (such as missing signatures or responses to some items); abstract missing some components such as total budget; grammatical or typographical errors in any section; improperly sequenced objectives; inconsistencies in reported figures between the MRCC form and protocol; missing logos, and minor clarifications needed for the informed consent process or consent form (such as the right to withdrawal from study or contact information of the PI), and required clarification for investigators who are not PI's (such as their missing CV's).
    c. **Recommended for approval after major revisions** - in case any number of clarifications or documentation are needed in areas which are critical for

evaluating the ability of the PI to lead the study, the capacity of the team to undertake the study, soundness of the methodological approach as well as safeguards to the study participants and the general public. Examples include but are not limited to lack of CV of the PI; investigating team that in totality is lacking expertise in one or more critical components of the proposed research; commitment letter(s) is/are from individual(s) who is/are not affiliated to an institution or from an institution that is not credible or permitted to undertake human research; lack of alignment of the title, problem statement, study questions, objectives and rationale; study design that is not appropriate for the objectives; sample size that is not statistically justified or is incorrectly estimated (for quantitative studies); study population, sampling population and sampling methods that are not appropriate for the objectives; inclusion and exclusion criteria that are unclear or ambiguous; entire sections missing (such as abstract, introduction, rationale, budget, ethical procedures etc.); missing data collection tools in appendices; data collection tools gathering information that is inadequate for the study objectives or outside scope of study; data analysis plan that addresses the study objectives inadequately or incorrectly; lack of consent forms or plans for MTA, DSTA or where warranted; unnecessary involvement of the vulnerable population or lack of adequate protection if their involvement is justified, and references that do not support the claims to which they are cited.

d. **Not recommended for approval** - generally involving major concerns such as unacceptable risk (for example, unjustified separation of new-born babies from their mothers for prolonged periods), unethical practices (for example, studies observing long-term effects of untreated conditions to which treatment options exist), studies that have no relevance to the Tanzanian population or in case the study investigates an area to which adequate scientific knowledge already exists.

Section C: Review of New Protocols (Clinical Trials)

Procedures are as in B above (Review of new protocols, non-clinical trials). A clinical trial may have an investigational medicinal product (IMP) or it may not.

1. The additional items for attention relevant to clinical trials listed below depend on the type of clinical trial:
    a. Submitted documents should include the Investigator's Brochure of the study drug or investigational product, document describing the drug/product and study procedures to participants, a recruitment plan, a randomisation plan and adverse events forms.
    b. The study site should be appropriate in terms of premises and other facilities, expertise, and patient/study populations intended/targeted to be involved in the trial.
    c. Literature should provide sufficient information on the disease or medical condition that the clinical trial addresses, as well as investigational product/process, preclinical and early clinical findings, etc. The applicant(s) should demonstrate the value/benefit of the study to society and its social acceptability.
    d. There should be a review of known risks of the investigational product/process. The risks(s) of the drug/device, if any, should be acceptable for the expected benefit.
    e. For protocols involving IMP, the protocol should describe benefits sharing to include if and how the drug(s)/device(s) will be made available in Tanzania after the trial or if the product is registered.
    f. If applicable, there should be an explanation of the rationale for choosing the comparator/placebo. The use of a control group should be well justified. If the control group comprises patients with a disease or condition, critically review if the control group will receive, at minimum, the standard treatment they would have received had they not been part of the study.
    g. For randomised, double-blind trials, the protocol should describe who will be blinded after assignment to interventions (for example, trial participants, care providers, outcome assessors, and data analysts).
    h. Protocol should describe the method of generating the allocation sequence for randomisation, such as computer-generated random numbers and a list of any

factors for stratification. To reduce the predictability of a random sequence, details of any planned restriction, for example, blocking, should be provided and clarified on how this will be avoided, especially to those who enrol participants or assign interventions.

i. The randomised controlled trial protocol should describe measures to minimise bias, such as randomisation, blinding, maintenance of randomisation codes, and procedures for breaking codes.
j. If applicable, the protocol should also explain situations under which unblinding is permissible and the procedure for revealing a participant's allocated intervention during the trial.
k. The consent form should clearly describe alternative treatments/prevention or procedures. Study participants must be informed of all options for receiving care, including those available outside the trial setting, before consenting to participate. For a trial intervention that offers no direct benefits to participants, the participant information sheet should clearly state.
l. Protocol should describe the commitment to register the trial in a public registry and TMDA clinical trial registry before the recruitment begins. Public registries include clinicaltrials.gov, Pan-African Clinical Trials Registry or the World Health Organization's International Clinical Trials Registry Platform (http://www.who.int/ictrp/en/). Intervention trials that do not have a drug or device as an intervention, e.g., ones studying the effectiveness of an education intervention, do not have to be processed or registered at TMDA but can be registered in public registries as a requirement for dissemination in international platforms such as scientific journals.
m. The protocol should give the rationale, description and justification for the Route of administration, dosage, treatment periods, and Device/process specifications.
n. The protocol should have clear procedures for interim analysis and appropriate criteria for suspending or terminating the study on the safety and/or efficacy.
o. The protocol should describe a clear plan for collecting, assessing, reporting, and managing solicited and unsolicited Adverse Events and other unintended effects of trial interventions or trial conduct.
p. The protocol should describe the composition of the Data and Safety Monitoring Board (DSMB) or a Body with similar functions. At a minimum, this should

include a summary of its role and reporting structure, a statement of whether it is independent of the sponsor and competing interests; and a reference to where further details about its charter can be found, if not in the protocol. If DSMB is not needed, the protocol should explain why this is the case. At least one member of DSMB must be a Tanzanian.

q. In the event of interim analysis and stopping rules, the protocol must explain who will have access to the interim results and who will decide to terminate the trial.
r. The protocol should explain the frequency and procedures for monitoring and auditing trial conduct, if any, and whether the process will be independent of investigators and the sponsor.
s. The submission should be accompanied by a local insurer's clinical trial insurance (or intent). Additionally, medical insurance for study participants and professional indemnity insurance for investigators are highly encouraged.

2. The reviewer will summarise in REIMS recommendations for one of the following:
   a. **Recommended for approval as presented** - for adequately presented submissions with no need for changes or clarifications in any component.
   b. **Recommended for approval after minor revisions** – in case minor clarifications or documentation are needed and generally involve minor concerns that do not affect the understanding, appropriateness and alignment of the problem statement, study questions, objectives, rationale and methodology, including ethical procedures. Examples are as in Section A above on review of new protocols (non-clinical trials). Nevertheless, additional comments are allowed where appropriate, and these may include; if observed, inadequate description of the recruitment, randomisation process, blinding and how errors will be minimised, missing appropriate attachments, and lack of description of how the investigated drug or product will be made available in Tanzania after being approved for human use.
   c. **Recommended for approval after major revisions** - in case any number of clarifications or documentation are needed in areas which are critical for evaluating the ability of the PI to lead the study, the capacity of the team to undertake the study, soundness of the methodological approach as well as safeguards to the study participants and the general public (*see Section B:*

review of new protocols for non-clinical trials). Consider also possible errors such as the following:

► lack of or inadequate preliminary data or insufficient literature review of the drug or product being studied.

► the applicant may have mentioned one or more of the proposed sites(s) which is/are inappropriate for the study.

► inappropriate choice of the control/comparator group(s),

► inadequate description of plans for interim analysis and DSMB processes where warranted,

► lack of a clear description (in text and consent form) of study benefits and risks as well as options for medical care for participants in case of study-related illness or injury,

► lack of clinical trial insurance,

► lack of attachment of investigator's brochure, a document describing product and study procedures to participants, and

► lack of adverse events form.

d. **Not recommended for approval** - generally refers to the following major concerns:

► unacceptable risk, e.g., unjustified increase in drug dosage above what is recommended,

► unethical practices, e.g., a phase 3 clinical trial that is not guided by safety and dosage data from a proper phase 1/2 trial(s),

► studies that have no relevance to the Tanzanian population or, in the case of the study, investigate an area in which adequate scientific knowledge already exists.

Section D: Review of Protocol Amendments

The reviewer should evaluate requests for amendments by taking into consideration the following:

1. Completeness of submitted materials.

    a. Cover Letter – should be signed by the PI and provide a brief submission of the proposed change(s) and the reason(s) for the change(s).
    b. A detailed summary specifying each amendment either on the cover letter or a separate summary in table format.
    c. An amended protocol with highlighted and tracked changes.
    d. Additional Letters – if the amendment proposes to change the study PI, the outgoing PI must submit a letter to indicate consent or an agreement with the decision reached for change of position and reason(s) for stepping down, unless this is not possible as in case of demise. Similarly, if the proposed amendments originate from the study Sponsor, a letter from the Sponsor should also be provided and evaluated.
    e. Protocols – copies of both existing approved protocol and amended protocol should be evaluated.
    f. Appendices – other documents to be evaluated as appropriate include but are not limited to current ethical clearance certificate, and curriculum vitae of any new investigators added to the study.
2. In reviewing the documents above, the reviewer will pay particular attention to whether the name of PI is the same as on initial certificate or has changed and if there are changes to other members of the research team (whose CV's must be attached), changes in title, rationale, objectives, study design, recruitment, study site, confidentiality, source of funding, whether study funder/sponsor is informed of the amendments and number of previous amendments approved. Further, the reviewer will need to evaluate whether the amendment increases what participants are asked to do and whether the amendments will require changes in consent form. Based on these, the reviewer will determine whether the risk-benefit ratio has changed substantially.
3. Main focus for the reviewer is to check to his/her satisfaction that the changes proposed are acceptable as amendments (to be recommended as presented or

following minor/major revisions) or not acceptable as amendments and warrant submission as a new protocol. The reviewer shall bear the following in mind:

a. Amendments are acceptable where the overall aim and approach of research remain intact. This includes minor changes that do not involve study questions, objectives, rationale or critical components of methodology such as study design and population. Examples include but are not limited to editorial clarifications, minor changes to the consent form and recruitment procedures, reimbursement, reduction in number or volume of samples collected, the addition of a new study site, removal of invasive procedures, changes in inclusion and exclusion criteria or change of PI that overall do not adversely impact the risk-benefit ratio of the study. Depending on the thoroughness of the presentation, the requested amendments may be accepted as presented or following minor or major revisions.
b. Amendments are not acceptable, and requests should be submitted as new protocols if there are major changes/additions that modify the focus of the study/protocol or the research questions, which will consequently affect the objectives, rationale and critical components of the methodology, e.g., study design, study population and sampling approach even if this builds on the knowledge learned from the existing study. A change of research questions or objectives is likely to change the risk-benefit balance. Hence a new submission may be necessary to enable a fair/just evaluation of the new balance of risks against the benefits.
c. Additionally, the reviewer must examine the study procedures to determine if there is a significant change from what was initially submitted, usually a result of multiple previous approvals of amendments. Likewise, suppose the changes make study procedures more complex (multiple add-ons), challenging to implement or create a risk for non-compliance and potential negative impact on the risk and data quality. In that case, a new protocol needs to be recommended.
d. New submission should also be recommended for the protocols that have been active for an extended period; the same applies to protocols in which, at the time of submission for amendment, some of the proposed sections/issues have been overtaken by time or event. And this may be due to the sense that some

objectives have been answered by other investigators and or is no longer in the knowledge gap.

4. The reviewer will summarise on REIMS recommendation for one of the following:
    a. **Recommended for approval as presented** - for adequately presented changes that generally involve minor changes, and the study has not been amended four (4) or more times previously for non-clinical trials.
    b. **Recommended for approval after minor revisions** – if a few additional clarifications or documentation are needed and generally involve minor changes and the study has not been amended four (4) or more times previously for non-clinical trials.
    c. **Recommended for approval after major revisions** - in case several clarifications or documentation are needed and generally involve minor changes. The study has not been amended four (4) or more times previously for non-clinical trials.
    d. **Not recommended for amendment, and changes should be submitted as new protocol** - generally involving major changes or if the study has been amended four (4) or more times previously for non-clinical trials.

References

1. TFDA, Guidelines for Conducting Good Clinical Practise (GCP) And Good Clinical Laboratory Practices (GCLP) Inspection, First edition. June 2017.
2. The Guidelines on the Practice of Ethics Committees in Medical Research Involving Human Subjects was described by the London Royal College of Physicians in 1991.
3. The National Health Research Ethics Committee (NatHREC) Standard Operational Procedures (2014).
4. NACOSTI, Guidelines for Accreditation of Institutional Ethics Review Committees in Kenya, Nairobi October 2017.
5. WHO, Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants, 2011.