STATUTORY INSTRUMENT NO. OF 2022

The National Health Research Act, 2013
(Act No. 2 of 2013)

The National Health Research (Conduct of Clinical Trials on Animal Subjects and Human Participants) Regulations, 2022

IN EXERCISE of the powers contained in section 54 of the National Health Research Act, 2013, the following Regulations are made:

PART I
PRELIMINARY PROVISIONS

Title

1. These Regulations may be cited as the National Health Research (Conduct of Clinical Trials on Animal Subjects and Human Participants) Regulations, 2022.

Interpretation

2. In these Regulations unless the context otherwise requires-

"adult" means a person who has attained the age of eighteen years;

"Adverse Drug Event (ADE)" means any untoward medical occurrence in a patient or clinical investigation participant administered with a pharmaceutical product which does not necessarily have a causal relationship with the treatment. An Adverse Drug Event (ADE) include any unfavourable and unintended sign which is an abnormal laboratory finding, symptom, or disease temporarily associated with the use of a medicinal investigational

product, whether or not related to the medicinal investigational product;

"Adverse Drug Reactions (ADRs)" means a response to a medicine which is noxious or harmful and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for modification of physiological function;

"animal subject" has the meaning assigned to the words in the Act;

"Board" means the National Health Research Ethics Board constituted under the Act;

"blinded clinical trial" means a trial involving one or more parties in which both the research team and participants are no aware of the treatment that has been assigned to a participant;

"clinical trial monitor" means the person responsible for ensuring that the study is performed at the agreed progression and that the study is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practices (GCP), and the applicable regulatory requirement;

"comparator or product" means an investigational or marketed product whch is active control, or placebo which is inactive control, used as a

reference in a clinical trial;

"compliance in relation to trials" means adherence to trial-related requirements, Good Clinical Practices (GCP) requirements, and the applicable regulatory requirements;

"Contract Research Organisation (CRO)" means a person or organisation, commercial, academic or other institution contracted by the sponsor to perform one or more of the sponsor's trial related duties and functions;

"documentation" means records, in any form, including, but not limited to, written, electronic, magnetic, optical records, scans, x-rays, and electrocardiograms that describe or record the methods, conduct and, or results of a trial, the factors affecting a trial and the actions taken;

"ethical approval" has the meaning assigned to the words in the Act;

"Good Clinical Practices (GCP)" means standards for the design, conduct, performance, monitoring, auditing, recording, analysing, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the safety, rights, integrity, and confidentiality of human participants and animal subjects are protected;

"Health research ethics committee" has the meaning assigned to the words in the Act;

"human participant" has the meaning assigned tothe words in the Act;

“Independent Data-Monitoring Committee (IDMC) means an Independent Data-Monitoring Committee that may be established by the sponsor, to assess at intervals, the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and recommend to the sponsor whether to continue, modify, or stop a trial and includes Data and Safety Monitoring Board, Monitoring Committee and Data Monitoring Committee;

“informed consent” means a decision, which is written, dated and signed b a person who intends to take part in a clinical trial, after being duly informed of its nature, significance, implications and risks and appropriately documented, by a person capable of giving consent or, where the person is not capable of giving consent based on age or otherwise, by that person’s legal representative, where that person concerned is unable to write, oral consent may be given in exceptional cases in the presence of at least one witness , and the thumb print of the person giving the said consent may be used in lieu of a signature;

“inspection” means the act by a regulatory authority of conducting an official review of documents, facilities, records, and any other resources that are deemed by the regulatory authority to be related to the clinical trial and that may be located at the site of the trial, at the sponsor’s

or Contract Research Organisation's (CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority;

"investigator" means ...;

"investigator's brochure" means a document containing a summary of the clinical and non-clinical data on the investigational product which is relevant to the study of the investigational medicinal product in human participants;

"monitoring report" means written report from the monitor to the sponsor after each site visit and, or other trial-related communication according to the sponsor's standard operating procedures;

"principal investigator" means a person responsible for the conduct of the clinical trial at a trial site;

"protocol" means a document that describes the background, rationale, objective, design, methodology, statistical considerations, and organisation of a trial;

"research institution" means an organisation, whether public or private, including a university, which undertakes health research;

"Research Ethics Committee (REC)" means a committee registered and accredited by the Board under section 18 of the Act;

"Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (SADR)" means an untoward medical occurrence which at any dose results -

(a) in death;

(b) is life-threatening;

(c) requires inpatient hospitalization;

(d) is prolongation of existing hospitalization;

(e) results in persistent or significant disability;

(f) results incapacity; or

(g) is a congenital anomaly or birth defect;

"source data" means information in original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial and source data shall be construed accordingly;

"source documents" means original documents, data, and records which may include hospital records, clinical and office charts, laboratory notes, memoranda, participants' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial. This also includes electronic data sets, electronic patient files;

"sponsor" means an individual, company, institution, or organisation, which takes responsibility for the initiation, management, and, or financing of

a clinical trial, where two or more persons take responsibility for the matters in relation to a clinical trial, those persons may-

(a) take joint responsibility for carrying out the functions of the sponsor of that trial under these Regulations; or

(b) delegate responsibility for carrying out the functions of the sponsor of that trial;

"sub-investigator" means an individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and,make important trial-related decisions on associates, residents or research fellows; and

"trial site" means the location approved by the Board where trial-related activities are conducted and may include a hospital, health centre, surgery or other establishment or facility at or from which a clinical trial, or any part of a trial, may be conducted.

PART II
CLINICAL TRIAL APPLICATION

Application for ethical approval to conduct a clinical trial

3. (1) A principal investigator who intends to conduct a clinical trial on a human participant or animal subject shall apply for a conditional ethical approval to an accredited health research ethics committee in accordance with the procedures determined by the health research ethics committee.

(2) A clinical trial that has been approved by the health research ethics committee under sub-regulation (1) shall be recommended to the Board for authorisation to conduct a clinical trial.

(3) Where a health research ethics committee fails to make a decision on an application refered to under subregulation (1), the application shall be referred to the Board for review, on payment of a fee set out in the First Schedule.

(4) A principal researcher, health research or health institution may directly apply for ethical approval to conduct a clinical trial on human participants or animal subjects to the Board on payment of a fee set out in the First Schedule.

Application for authority to conduct a clinical trial

4. (1) A principal researcher, health research or health institution that has obtained a conditional ethical approval from an accredited health research ethics committee shall apply for authorisation to conduct a clinical trial to the Board in Form I, set out in the First Schedule on payment of a fee set out in the Second Schedule.

(2) The Board shall within sixty days of receipt of the application under subregulation (1), grant or reject the application.

(3) The Board shall, where the Board grants an application under subregulation (2), notify the applicant within seven days of the decision in Form III set out in the First Schedule.

(4) The Board shall, where the Board rejects an application under subregulation (2), notify the applicant within seven days of the decision in Form V set out in the

First Schedule.

(5) The Board may request for further particulars or information from the applicant in Form II set out in the First Schedule.

Rejection of an application to conduct clinical trial

5. Subject to the other provisions of these Regulations, the Board may reject an application for authority to conduct a clinical trial if -

(a) the principal researcher or health research institution fails to comply with the Act, these Regulations or any other writen law;

(b) the principal researcher or health research institution cnducted a clinical trial by fraud, misrepresentation or concealment of a material fact;

(c) if a principal researcher or health institution obtained a conduct of a clinical trial by deliberately or negligently submitting false information or making a false statement;

(d) contravenes the terms and conditions of a clinical trial;

(e) has ceased to fulfil the elegibility requirement under these Regulations;

(f) the Board determines that some critical issues in the protocol were inadequately addressed; and

(g) the Board determines that the safety and wellbeing of the trial participants and

animal subjects is not well covered.

Terms and conditions for authority to conduct a clinical trial

6. The Board may issue an authority to conduct a clinical trial on such terms and conditions as the Authority may determine.

Validity of approval of conduct clinical trial

7. (1) The validity period of an approval to conduct a clinical trial shall be one year and subject to renewal.

Renewal of approval to conduct clinical trial

8. (1) A principal researcher or health research institution may, ninety days before expiration of approval to conduct a clinical trial apply to the Board for a renewal of approval to conduct a clinical trial in Form IV set out in the First Schedule on payment of a fee set out in the Second Schedule.

(2) The Board shall, within thirty days of receipt of an application under subregulation (1) approve or reject the application.

(3) The Board shall, where the Board approves an application under subregulation (2), notify the applicant within seven days of the decision in Form III set out in the First Schedule.

(4) The Board shall, where the Board rejects an application under subregulation (2), notify the applicant within seven days of the decision in Form V set out in the First Schedule.

Suspension or revocation of Authority to conduct a clinical trial

9. (1) Subject to the other provisions of these Regulations, the Board may suspend or revoke the authority to conduct a clinical trial where the principal researcher or health research institution -

(a) fails to comply with the Act, these Regulations or any other written law;

(b) obtained the clinical trial by fraud, misrepresentation or concealment of fact;

(c) if a principal researcher or health institution obtained a conduct of a clinical trial by deliberately or negligently submitting false information or making a false statement;

(d) contravenes the terms and conditions of a clinical trial;

(e) has ceased to fulfil the elegibility requirement under these Regulations;

(f) the Board determines that some critical issues in the protocol were inadequately addressed; and

(g) the Board determines that the safety and wellbeing of the trial participants and animal subjects is not well covered.

(2) The Board shall, within thirty days before suspending or revoking the approval to conduct a clinical trial, give notice of its intention to suspend or revoke, in writing, to the principal researcher or health research institution giving reasons for the suspension or revocation.

(3) The Board shall, before suspending or revoking the clinical trial in accordance with subregulation (2), notify

the principal researcher or health research institution of the Board's intention to suspend or revoke the clinical trial and requiring the principal researcher or health research institution to -

(a) to show cause, within a period specified in the notice why the clinical trial should not be suspended or revoked; and

(b) take remedial measures, within a period specified in the notice, to the satisfaction of the Board to prevent the suspension or revocation of the clinical trial.

(4) The Board shall, before suspending or revoking the clinical trial in accordance with subregulation (2), notify the principal researcher or health research institution of the Board's intention to suspend or revoke the clinical trial and requiring the principal researcher or health research institution to -

(a) to show cause, within a period specified in the notice why the clinical trial should not be suspended or revoked; and

(b) take remedial measures, within a period specified in the notice, to the satisfaction of the Board to prevent the suspension or revocation of the clinical trial.

(5) The Board may, after giving the principal researcher or health research institution an opportunity to be heard in persn or in writing, suspend o revoke the approval to cnduct a clinical trial, if the principal researcher or health research institution -

(a) fails to give reasons to the satisfaction of the Board, why the approval to conduct a clinical trial should not be suspended or revoked; or

(b) does not take remedial measures to the satisfaction of the Board, within the period specified under subregulation (2).

(5) The Board shall not suspend or revoke the approval to conduct a clinical trial if remedial measures are taken to the satisfaction of the Board, that ensure compliance with the Act, these Regulations or other relevant written law within the period specified under subregulation (2).

(6) The principal researcher or health research institution shall, where the Board suspends or revokes approval to conduct a clinical trial, as soon as is practicable, inform the trial participants, assure continuation of appropriate therapy and follow-up for the human participants or animal subjects.

(7) The Board may determine the fate of the clinical trial under subregulation (6) including the welfare of trial participants, collected specimens and information, on a case by case basis, on revocation of approval to conduct a clinical trial.

Appeal against rejection, suspension, and revocation

10. (1) A principal researcher or health research institution who is aggrieved with the decision of the Board may within thirty days of receipt of the decision appeal to the Council.

(2) The Council shall, within ninety days of receipt of the appeal make a decision on the appeal.

(3) A principal researcher or health research institution aggrieved with a decision of the Council may appeal to the High Court.

Transfer of clinical trial

11. A principal researcher or health research institution shall not transfer a clinical trial to a third party.

Amendment to clinical trial

12. (1) A principal researcher or health research institution in a clinical trial shall, where a principal researcher or health research institution intends to change the scope of the activity applicable to the clinical trial or the time stipulated in a clinical trial apply to the Board for an amendment to a clinical trial in Form VI set out in the First Schedule and on payment of a fee set out in the Second Schedule.

(2) The Board shall, within thirty days of receipt of an application under subregulation (1), approve or reject the application.

(3) The Board shall, within seven days of the approval of an application under subregulation (1), issue the applicant with the notice of approval in Form VII set out in the First Schedule.

(3) The Board shall, where the Board rejects an application under subregulation (1), notify the applicant in Form VIII set out in the First Schedule stating the reasons for the rejection.

(4) Despite the provisions in subregulation (1), a principal researcher or health research institution may

implement an amendment in subregulation (1) where the principal researcher or health research institution intends to eliminate an immediate hazard to trial human participants or animal subjects, or when the change involves logistical or administrative aspects of the trial.

Register of clinical trials

13. (1) The Authority shall maintain a register of clinical trials in Form IX set out in the First Schedule.

(2) The register referred to in subregulation (1) shall be kept at the offices of the Authority and shall be open for inspection to the public at the Authority during normal working hours and on such conditions as the Authority may determine.

PART III
CONDUCT OF CLINICAL TRIAL

Conduct of trial

14. (1) The conduct of a clinical trial shall include the following:

(a) Phase 0 clinical trial which involves experimental treatment on a small group of at least ten to twenty healthy human participants or animal subjects to evaluate a safe dosage range and identify side effects;

(b) Phase I clinical trial which involves experimental treatment on a small group of at least twenty to eighty healthy human participants or animal subjects to evaluate a safe dosage range and identify side effects;

(c) Phase II which involves the use of more human participants or animal subjects of at least hundred to three hundred aimed at obtaining preliminary data on the efficacy in human participants and animal subjects who have a certain condition or disease;

(d) Phase III clinical trials which gathers more information about safety and effectiveness, different populations and different dosages and the use of the investigational product in combination with other drugs and the number of human participants and animal subjects ranges from several hundreds to at least three thousand subjects; and

(e) Phase IV clinical trials on investigational product or devices that take place after approval for their use.

(2) The conduct of clinical trials shall have the following main stakeholders:

(a) sponsor;

(b) clinical monitor;

(c) principal researcher; and

(d) trial participant.

Responsibilities of sponsor

15. (1) A sponsor shall -

(a) implement and maintain quality assurance and quality control systems with written standard operating

procedures;

(b) be responsible for the delivery and maintenance of records for the investigational product;

(c) retain essential documents where the product is approved or where the sponsor intends to apply for approval;

(d) provide insurance and indemnify the investigator or the health research institution against claims arising from the trial except claims arising from malpractice or negligence;

(e) ensure that the trial subjects are insured and indemnified;

(f) ensure that financial aspects of the trial are documented in an agreement between the sponsor and the investigator or health research institution;

(g) ensure that the Investigator's Brochure is updated regularly;

(h) utilise appropriately qualified individuals to supervise the overall conduct of the trial to handle the data, to verify the data, to conduct statistical analysis and to prepare trial reports;

(i) consider establishing an Independent Data Monitoring Committee to assess the progress of the clinical trial including the safety data, and the critical efficacy points at intervals, and to recommend to

the sponsor whether to continue, modify, or stop a trial.

(j) investigate and report adverse drug reactions that are both serious and unexpected to the regulatory authority and health research ethics committees;

(k) submit safety updates and periodic reports to the regulatory authority and health research ethics committees;

(l) devise the method of ensuring clinical trials are monitored in a systematic manner prioritising a risk-based approach.

(2) Despite subregulation (1), the sponsor may delegate any of the sponsor's functions to a Contract Research Organisation.

(3) The sponsor shall appoint individuals who are independent of the clinical trials or systems, to conduct audits.

Responsibility of clinical trial monitor

16. (1) A clinical trial monitor shall act as the main line of communication between the sponsor and the health researcher and ensure that a health researcher has the adequate qualification and resource during the clinical trial period.

(2) The clinical trial monitor shall in relation to the investigational product ensure that the investigational product -

(a) is stored in acceptable conditions during the clinical trial;

(b) is adequately supplied during the clinical trial;

(c) is supplied to human participants and animal subjects who are eligible to receive the investigational product and at the protocol specified dose;

(d) is properly used, handled, stored and returned with necessary instructions to human participants and persons responsible for animal subjects;

(e) is controlled and documented adequately in relation to receipt, use, and return at the clinical trial site;

(f) that is unused at the clinical trial site and the disposition conform to the applicable requirements;

(g) verify that the principal researcher follows the approved protocol and approved amendment;

(h) verify that written informed consent was obtained before each human participant and animal subject ‘s participation in the trial;

(i) verify that the principal researcher and the trial staff are adequately informed about the trial;

(j) verify that the principal researcher and the trial staff are performing the specified trial functions, in accordance with the protocol, standard operation procedures

and any other written agreement between the sponsor and the investigator or health research institution, and have not delegated these functions to unauthorised individuals.

Non-compliance during the conduct of a trial

17. (1) The sponsor shall, where a principal researcher, health research institution or member of the sponsor's staff fails to comply with the protocol, standard operating procedures, good clinical practice or any other applicable regulatory requirement, take action to secure compliance.

(2) The sponsor shall, where noncompliance that significantly affects or has the potential to significantly affect human participants or animal subjects or the reliability of clinical trial results is discovered, perform a root cause analysis and implement appropriate corrective and preventive actions.

(3) The sponsor shall, where, the sponsor identifies serious or persistent non-compliance of a principal researcher or health research institution, through the monitoring or auditing procedure, terminate the principal researcher or health research institution's participation in the clinical trial and notify the authority.

(4) Despite subregulations (1), (2) and (3), the Authority may determine any corrective measures that maybe undertaken in the event of non-compliance.

Responsibilities of the principal researcher

18. (1) A principal researcher shall -

(a) provide oversight of all clinical activities;

and

(b) ensure that adequate medical care is provided to a human participant or animal subject for any adverse event.

(2) In addition to responsibilities set out under subregulation (1), the principal researcher may assign duties for investigational product accountability at the clinical trial site to a pharmacist.

(3) The principal researcher shall explain the correct use of investigational product to each human participant or person responsible for animal subjects to ensure that instructions for taking the investigational products are being followed correctly.

Informed consent of human participants and animal subjects

19. (1) The principal researcher shall be responsible for obtaining informed consent of human participants and a person responsible for animal subjects.

(2) A principal researcher shall inform the human participant or person responsible for animal subjects of appropriate aspects of the clinical trial, including the written information and the approval by the health research ethics committees.

(2) The principal researcher shall, where the human participant or person responsible for animal subject is unable to provide informed consent, acquire informed consent from a legally acceptable representative.

(3) Where consent of the human participant or animal subject's legally acceptable representative is not available, enrolment of the human participant or animal subject shall require measures described in the research

protocol with documented approval by the health research ethics committee.

Source documents, records and trial site reports

20. (1) The principal researcher shall maintain adequate and accurate source documents and trial site records that include appropriate observations on each of the clinical trial site's subjects.

(2) The principal researcher shall take measures to prevent accidental or premature destruction of these documents.

Progress reports

21. (1) The principal researcher shall submit written progress reports of the clinical trial status to the Authority or health research ethics committees bi-annually, or a shorter period as the Authority or health research ethics committee may determine.

(2) The principal researcher shall promptly provide written reports to the sponsor, the Authority or health research ethics committees and the health research institution were necessary, on any changes significantly affecting the conduct of the clinical trial or increasing the risk to the subjects.

Safety Reporting

22. (1) Serious Adverse Events shall be reported to the sponsor except Serious Adverse Events that the research protocol or other document identifies as not requiring immediate reporting.

(2) The principal researcher shall comply with the applicable regulatory requirements related to the reporting of unexpected Serious Adverse Drug reactions to the

regulatory authority and the health research ethics committees .

(3) The principal researcher shall, where a death is reported, supply the sponsor and the health research ethics committees any additional information requested.

Health research ethics committee

23. (1) The health research ethics committee shall safeguard the rights, safety, and well-being of clinical trial human participants and animal subjects.

(2) Subject to subregulation (1), special attention shall be paid to clinical trials that may include vulnerable clinical trial human participants and animal subjects and clinical trial for vulnerable clinical trial human participant and animal subjects shall be subject to continuing review of each ongoing clinical trial at intervals appropriate to the degree of risk to human participants and animal subjects.

Conclusion or termination of a clinical trial

24. (1) A sponsor or principal researcher shall, within thirty days of the conclusion or termination of a clinical trial notify the Board, in writing, of the conclusion or termination of a clinical trial.

(2) The sponsor or principal researcher shall, within twelve months of the conclusion or the termination of the clinical trial, submit a summary of the final research report to the Board .