MEDICINES AND RELATED SUBSTANCES ACT, 2025

(Act No. 29 of 2025)

CLINICAL TRIALS REGULATIONS, 2026

(Published on _____, 2026)

ARRANGEMENT OF REGULATIONS

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IN EXERCISE of the powers conferred on the Minister of Health by section 123 of the Medicines and Related Substances Act, 2025, the following Regulations are hereby made—

PART I – PRELIMINARY

Citation and commencement

1. (1) These Regulations may be cited as the Clinical Trials Regulations, 2025.

(2) These Regulations shall come into operation on such date as the Minister may, by notice published in the *Gazette*, appoint.

Interpretation

2. In these Regulations, unless the context otherwise requires—

"Act" means the Medicines and Related Substances Act, 2025;

"adverse event" or "AE" means any untoward medical occurrence in a trial participant or untoward clinical observation in a trial animal administered an investigational product, which does not necessarily have a causal relationship with the treatment;

"adverse reaction" means any untoward and unintended response to an investigational product related to any dose administered;

"animal owner" means any person who has legal ownership, custody or control of an animal enrolled or proposed to be enrolled in a clinical trial;

"audit" means a systematic and independent examination of trial-related activities and documents to determine whether the evaluated activities were conducted, and data recorded, analysed and accurately reported according to the protocol, applicable regulatory requirements and guidelines;

"Authority" means the Botswana Medicines Regulatory Authority;

"bioavailability study" means a study to assess the rate and extent of absorption of an active substance from a pharmaceutical form;

"bioequivalence study" means a study to demonstrate that bioavailability of two pharmaceutical forms is similar to such a degree that their effects can be expected to be essentially the same;

"blinding" means a procedure in which one or more parties to the trial are kept unaware of the treatment assignment;

"case report form" or "CRF" means a document designed to record all protocol-required information on each trial participant or trial animal;

"clinical trial" has the meaning assigned to it under section 2 of the Act;

"clinical trial authorisation" or "CTA" means authorisation granted by the Authority to conduct a clinical trial;

"contract research organisation" or "CRO" means a person or organisation contracted by the sponsor to perform one or more trial-related duties and functions;

"Department of Veterinary Services" or "DVS" means the Department of Veterinary Services in the Ministry responsible for agriculture;

"Development Safety Update Report" or "DSUR" means a periodic report providing comprehensive annual review and evaluation of safety information;

"essential documents" means documents which individually and collectively permit evaluation of the conduct of a trial and the quality of data produced;

"ethics committee" means an independent body responsible for ensuring the protection of the rights, safety and well-being of human trial participants;

"Good Clinical Practice" or "GCP" means an international ethical and scientific quality standard for designing, conducting, recording and reporting trials involving human participants, as set out in ICH E6 guidelines and WHO guidance;

"informed consent" means a process by which a participant voluntarily confirms willingness to participate in a trial, after being informed of all aspects relevant to the decision;

"inspection" means the act by the Authority of conducting an official review of documents, facilities, records and any other resources related to a clinical trial;

"Institutional Review Board" or "IRB" has the same meaning as ethics committee;

"investigational product" means a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, whether for human medicines, medical devices or veterinary use;

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

"investigator's brochure" means a compilation of clinical and non-clinical data relevant to the study of the investigational product in human participants or animals;

"monitor" means a person appointed by the sponsor to oversee progress of the trial and ensure it is conducted in accordance with the protocol and applicable requirements;

"monitoring" means the act of overseeing the progress of a clinical trial and ensuring it is conducted, recorded and reported in accordance with the protocol and applicable requirements;

Mutual recognition-means the acceptance by the Authority of a certification of standards and procedures for medical products regulation by another medical products regulatory Authority.

"principal investigator" means the investigator with overall responsibility for the conduct of the trial at a particular site;

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

"serious adverse event" or "SAE" means any adverse event that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in

persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is a medically important event;

"source data" means all information in original records and certified copies of original records of clinical findings, observations or other activities necessary for the reconstruction and evaluation of the trial;

"source documents" means original documents, data and records;

"sponsor" means an individual, company, institution or organisation that takes responsibility for the initiation, management and financing of a clinical trial;

"sub-investigator" means any member of the clinical trial team designated and supervised by the investigator to perform critical trial-related procedures;

"suspected unexpected serious adverse reaction" or "SUSAR" means a serious adverse reaction that is not consistent with applicable product information;

"Three Rs Principle" means the principles of Replacement, Reduction and Refinement applied to the use of animals in clinical trials, whereby Replacement refers to the use of alternative methods to avoid or replace the use of animals, Reduction refers to the use of methods that minimise the number of animals used per experiment, and Refinement refers to modifications of procedures that minimise pain, suffering, distress and lasting harm to animals;

"trial animal" means an animal enrolled in a clinical trial, either as a recipient of the investigational product or as a control;

"trial participant" means a human individual who participates in a clinical trial, either as a recipient of the investigational product or as a control;

"trial site" means the location where trial-related activities are conducted;

"veterinary trial" means a clinical trial conducted in animals to discover or verify the clinical, pharmacological or pharmacodynamic effects of an investigational veterinary medicinal product, identify adverse reactions, or study absorption, distribution, metabolism and excretion, with the objective of ascertaining its safety or efficacy;

"vulnerable population" means individuals whose willingness to participate may be unduly influenced by the expectation of benefits or fear of retaliation, or who may have diminished capacity to provide informed consent.

Application and scope

3. (1) These Regulations apply to all clinical trials conducted in Botswana involving—

(a) investigational medicinal products for human use;

(b) Investigational medicinal products for use in animals ;

(c) medical devices under clinical investigation;

(d) biologicals and vaccines for human or veterinary use;

(e) advanced therapy medicinal products;

(f) diagnostic agents; and

(g) such other products as may be specified.

(2) These Regulations apply regardless of whether the trial is—

(a) sponsored by a local or international entity;

(b) single-site or multi-site;

(c) single-country or multi-country;

(d) interventional or observational where investigational products are involved;

(e) conducted in humans or in animals; or

(f) commercially or non-commercially sponsored.

(3) These Regulations do not apply to—

(a) studies using only marketed products in accordance with approved labelling;

(b) retrospective studies using existing data only;

(c) studies involving human biological samples only, without administration of investigational products; and

(d) studies excluded by guidelines issued by the Authority.

(4) For device clinical trials, these Regulations shall be read together with the Medical Devices Regulations.

Guiding principles

4. (1) All clinical trials shall be conducted in accordance with—

(a) the principles of the Declaration of Helsinki,;

(b) Good Clinical Practice as set out in ICH E6 and WHO guidance, in respect of trials involving human participants;

(c) the VICH guidelines on Good Clinical Practice for veterinary medicinal products, in respect of veterinary clinical trials;

(d) the Three Rs Principle, in respect of trials involving animals;

(e) applicable laws of Botswana; and

(f) guidelines issued by the Authority.

(2) The rights, safety and well-being of trial participants shall take precedence over the interests of science and society.

(3) In respect of veterinary clinical trials, the welfare of trial animals shall be safeguarded at all times, and unnecessary pain, suffering, distress and lasting harm shall be avoided.

(4) Clinical trials shall be scientifically justified and described in a clear, detailed protocol.

(5) Trials shall only be conducted if the anticipated benefits justify the foreseeable risks.

(6) The Authority shall recognise and, where appropriate, accept or rely on—

(a) clinical trial authorisations from recognised regulatory authorities;

(b) inspection reports from regulatory authorities with comparable standards;

(c) ethics committee approvals meeting international standards; and

(d) GCP certifications from accredited bodies.

(7) Detailed requirements and procedures shall be set out in guidelines issued by the Authority, which may be amended without amendment to these Regulations.

PART II – CLINICAL TRIAL AUTHORISATION

Requirement for authorisation

5. (1) In accordance with section 46 of the Act, no person shall conduct a clinical trial unless—

(a) authorisation has been granted by the Authority; and

(b) ethics committee approval has been obtained, in respect of trials involving human participants; or

(c) approval from the Director of Veterinary services has been obtained, in respect of veterinary clinical trials.

(2) A clinical trial authorisation shall be specific to—

(a) the investigational product;

(b) the protocol;

(c) the trial sites; and

(d) the investigators.

(3) Conducting a trial without authorisation is an offence under section 57 of the Act.

Application for authorisation

6. (1) An application for clinical trial authorisation shall be made in Form CT-01 set out in Schedule 1.

(2) Applications shall be submitted by—

(a) the sponsor; or

(b) the sponsor's authorised representative in Botswana.

(3) Where the sponsor is not established in Botswana, a local sponsor representative shall be appointed in accordance with regulation 28.

(4) Applications shall be accompanied by—

(a) the prescribed fee as set out in the Fees Regulations;

(b) documentation as specified in regulation 7 and Schedule 2;

(c) proof of ethics committee submission or approval, in respect of trials involving human participants;

(d) proof of submission to or approval by the Director of Veterinary services , in respect of veterinary clinical trials; and

(e) such other information as the Authority may require.

(5) The Authority shall publish guidelines specifying application procedures, which may provide for—

(a) electronic submission;

(b) phased submission;

(c) parallel ethics and regulatory review; and

(d) pre-submission consultation.

Documentation requirements

7. (1) Applications shall include the following documentation as applicable—

(a) Administrative documentation—

(i) completed application form;

(ii) cover letter;

(iii) sponsor information;

(iv) investigator information;

(v) site information;

(vi) ethics committee approval or submission confirmation, or Director of Veterinary services approval or submission confirmation, as appropriate;

(vii) insurance certificate; and

(viii) fee payment proof.

(b) Protocol documentation—

(i) clinical trial protocol with all amendments;

(ii) protocol synopsis;

(iii) case report forms;

(iv) informed consent documents, in respect of trials involving human participants;

(v) animal owner consent documents, in respect of veterinary clinical trials;

(vi) participant information sheet or animal owner information sheet, as applicable;

(vii) participant recruitment materials; and

(viii) participant diary or questionnaires.

(c) Investigational product documentation—

(i) investigator's brochure or summary of product characteristics;

(ii) product dossier including quality, non-clinical and clinical data;

(iii) GMP certificate for manufacturing site;

(iv) certificate of analysis;

(v) labelling information; and

(vi) import documentation where applicable.

(d) Investigator documentation—

(i) curriculum vitae;

(ii) professional registration certificate;

(iii) GCP training certificate;

(iv) financial disclosure; and

(v) delegation log.

(e) Site documentation—

(i) site suitability assessment;

(ii) facilities description;

(iii) laboratory accreditation where applicable; and

(iv) emergency procedures.

(2) Documentation requirements by trial phase are set out in Schedule 2.

(3) The Authority may, by guideline, specify—

(a) additional documentation requirements;

(b) reduced requirements for certain trial types;

(c) accepted formats and standards; and

(d) reference to documentation held by other regulatory authorities.

Assessment of applications

8. (1) The Authority shall assess applications having regard to—

(a) scientific validity of the trial design;

(b) adequacy of preclinical and clinical data supporting safety;

(c) risk-benefit balance for participants or trial animals, as applicable;

(d) quality and safety of the investigational product;

(e) adequacy of participant or animal protection measures;

(f) suitability of investigators and sites;

(g) appropriateness of informed consent procedures or animal owner consent, as applicable;

(h) adequacy of safety monitoring and reporting; and

(i) in respect of veterinary clinical trials, compliance with the Three Rs Principle.

(2) The Authority may—

(a) request additional information or clarification;

(b) consult with external experts;

(c) consult the Director of Veterinary services , in respect of veterinary clinical trials;

(d) conduct pre-approval inspection; and

(e) seek information from other regulatory authorities.

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(4) The Authority shall issue guidelines specifying assessment procedures and timelines for different trial categories.

Authorisation decision

9. (1) Upon completion of assessment, the Authority shall—

(a) grant authorisation;

(b) grant authorisation with conditions;

(c) request modifications to the protocol; or

(d) refuse authorisation with written reasons.

(2) Where authorisation is granted, the Authority shall issue a Clinical Trial Authorisation Certificate specifying—

(a) authorisation number;

(b) protocol title and version;

(c) investigational product;

(d) approved sites and investigators;

(e) any conditions;

(f) validity period; and

(g) reporting requirements.

(3) Conditions may relate to—

(a) participant selection criteria or animal selection criteria, as applicable;

(b) safety monitoring requirements;

(c) reporting frequency;

(d) Data Safety Monitoring Board requirements;

(e) stopping rules; and

(f) any other matter relevant to participant safety or animal welfare.

(4) Authorisation shall not be unreasonably refused or delayed.

Conditions of authorisation

10. (1) Every authorisation shall be subject to the following standard conditions—

(a) compliance with the approved protocol;

(b) maintenance of valid ethics committee approval, in respect of trials involving human participants, or maintenance of valid /Director of Veterinary services approval, in respect of veterinary clinical trials;

(c) compliance with applicable GCP requirements,

(d) timely safety reporting;

(e) notification of amendments;

(f) maintenance of essential documents;

(g) facilitation of Authority inspections;

(h) notification of trial completion or termination; and

(i) submission of clinical trial reports.

(2) The Authority may impose additional conditions based on risk assessment.

(3) Failure to comply with conditions may result in—

(a) warning;

(b) requirement for corrective action;

(c) suspension of authorisation; or

(d) revocation of authorisation.

Validity and renewal

11. (1) A clinical trial authorisation shall be valid for—

(a) the duration specified in the protocol; or

(b) five years from the date of issue,

whichever is shorter.

(2) For trials exceeding five years, renewal shall be applied for at least six months before expiry.

(3) Renewal applications shall include—

(a) updated safety information;

(b) progress report;

(c) renewed ethics approval or Director of Veterinary services approval, as applicable; and

(d) justification for continuation.

Expedited authorisation pathways

~~**12.** (1) The Authority may operate expedited authorisation pathways for—~~

~~(a) trials addressing serious or life-threatening conditions;~~

~~(b) trials for diseases with high burden in Botswana;~~

~~(c) trials already authorised by stringent regulatory authorities;~~

~~(d) bioequivalence studies;~~

~~(e) veterinary clinical trials addressing urgent animal health needs; and~~

~~(f) trials during public health emergencies.~~

~~(2) Expedited pathways may include—~~

~~(a) reduced assessment timelines;~~

~~(b) rolling review of documentation;~~

~~(c) parallel processing with ethics review or Department of Veterinary Services review;~~

~~(d) reliance on prior authorisations; and~~

~~(e) conditional authorisation with post-authorisation requirements.~~

~~(3) Eligibility criteria and procedures for expedited pathways shall be set out in guidelines.~~

12A. (1) In exercising its functions under these Regulations, the Authority may, where appropriate, rely upon or recognise regulatory decisions, scientific assessments or inspection outcomes issued by recognised regulatory authorities or international organisations.

(2) For purposes of these Regulations, a recognised regulatory authority means a national or regional regulatory authority, or an international organisation, that the Authority has determined to operate in accordance with internationally accepted regulatory standards and principles.

(3) The Authority may rely upon one or more of the following:

(a) clinical trial authorisations issued by recognised regulatory authorities;

(b) scientific assessment reports relating to clinical trial applications;

(c) Good Clinical Practice inspection reports;

(d) Good Manufacturing Practice inspection reports relating to investigational products;

(e) ethics committee opinions issued by ethics committees recognised by the Authority;

(f) product quality assessments relating to investigational products;

(g) regulatory decisions relating to protocol amendments, safety measures, suspension or termination of clinical trials;

(h) decisions arising from regional or international collaborative review mechanisms, including the African Vaccine Regulatory Forum (AVAREF), the African Medicines Agency (AMA), the World Health Organization Collaborative Registration Procedures, or such other mechanisms recognised by the Authority.

(4) Before relying on a regulatory decision, the Authority shall consider-

(a) whether the decision was made using internationally accepted scientific and regulatory standards;

(b) the relevance of the decision to the Botswana context;

(c) differences in disease epidemiology, medical practice or participant populations;

(d) whether additional information is required; and

(e) any other matter relevant to the protection of trial participants, public health or animal welfare.

(5) Reliance shall not prevent the Authority from-

(a) conducting its own scientific assessment;

(b) requesting additional information;

(c) imposing additional conditions;

(d) conducting inspections;

(e) refusing, suspending or revoking a clinical trial authorisation where justified.

(6) The Authority shall maintain written records of every reliance decision, including-

(a) the authority or organisation relied upon;

(b) the scope of reliance;

(c) the scientific justification;

(d) any limitations placed on the reliance decision; and

(e) the final decision of the Authority.

(7) The Authority remains solely responsible for every regulatory decision made under these Regulations, notwithstanding any reliance placed on another authority or organisation.

(8) The Authority may issue guidelines specifying:

(a) recognised authorities;

(b) eligibility criteria for reliance;

(c) reliance procedures;

(d) documentation requirements;

(e) confidentiality arrangements;

(f) joint reviews; and

(g) work-sharing arrangements.

PART III – ETHICS REVIEW AND ANIMAL WELFARE OVERSIGHT

Ethics committee approval required

13. (1) In accordance with section 46 of the Act, no clinical trial involving human participants shall commence without approval from an ethics committee.

(2) Ethics approval shall be obtained before—

(a) recruitment of participants;

(b) administration of investigational products; and

(c) collection of trial-specific data.

(3) Ethics approval shall be maintained throughout the trial duration.

(4) Loss of ethics approval shall result in suspension of the trial.

Recognised ethics committees

14. (1) Ethics review for trials involving human participants shall be conducted by—

(a) the National Health Research Ethics Committee established under section 101 of the Act;

(b) institutional ethics committees registered with the Authority; or

(c) ethics committees recognised by the Authority.

(2) The Authority shall maintain a register of recognised ethics committees.

(3) Recognition criteria shall include—

(a) compliance with WHO and CIOMS guidelines;

(b) adequate membership and expertise;

(c) documented procedures;

(d) independence from sponsors;

(e) regular meeting frequency; and

(f) record-keeping capacity.

(4) The Authority may accept ethics approvals from—

(a) WHO-listed ethics committees; and

(b) ethics committees in countries with comparable standards,

subject to local ethics notification or review as specified in guidelines.

(5) Approval by a foreign or internationally recognised ethics committee shall not, of itself, authorise the conduct of a clinical trial in Botswana and shall not replace the requirement for local ethical oversight unless expressly recognised by the Authority under an approved ethics reliance framework developed in consultation with the National Health Research Ethics Committee.

(6) Where reliance on a foreign ethics committee is approved, the Authority may require-

(a) local acknowledgement by the National Health Research Ethics Committee;

(b) review of Botswana-specific ethical, legal, cultural or public health considerations;

(c) compliance with any conditions imposed by the Authority or the National Health Research Ethics Committee; and

(d) submission of any additional information considered necessary.

(7) The Authority and the National Health Research Ethics Committee shall remain jointly responsible for ensuring that every clinical trial conducted in Botswana complies with the ethical principles of the Act, these Regulations and applicable national and international ethical standards.

Informed consent requirements for human participants

15. (1) In accordance with section 53 of the Act, informed consent shall be obtained from every human trial participant or their legally authorised representative.

(2) Informed consent shall be—

(a) voluntary and free from coercion;

(b) based on adequate information;

(c) documented in writing;

(d) obtained before any trial-specific procedures; and

(e) ongoing throughout the trial.

(3) Information provided shall include—

(a) that the study involves research;

(b) the purpose of the trial;

(c) trial procedures and duration;

(d) reasonably foreseeable risks and discomforts;

(e) potential benefits;

(f) available alternatives;

(g) compensation and treatment for injury;

(h) confidentiality protections;

(i) voluntary nature and right to withdraw; and

(j) contact information.

(4) Consent documents shall be in a language understood by the participant.

(5) Special consent procedures may apply as specified in guidelines for—

(a) emergency research;

(b) cluster trials;

(c) research in unconscious patients; and

(d) waiver of documentation.

Vulnerable populations

16. (1) Additional protections shall apply for trials involving—

(a) children and minors;

(b) pregnant or lactating women;

(c) prisoners or detainees;

(d) persons with diminished mental capacity;

(e) students or employees of the investigator;

(f) economically or educationally disadvantaged persons; and

(g) other vulnerable groups as defined in guidelines.

(2) Trials in vulnerable populations shall only be conducted where—

(a) the research question cannot be adequately addressed in non-vulnerable populations;

(b) there is potential for direct benefit or minimal risk;

(c) additional consent requirements are met; and

(d) enhanced monitoring is in place.

(3) Specific requirements for vulnerable populations shall be set out in guidelines.

Ongoing ethics oversight

17. (1) Investigators shall provide ongoing reports to the ethics committee, in respect of trials involving human participants, or to the Director of Veterinary services , in respect of veterinary clinical trials, including—

(a) progress reports;

(b) safety reports;

(c) protocol amendments;

(d) changes to informed consent or animal owner consent;

(e) new safety information; and

(f) final reports.

(2) The ethics committee or the Director of Veterinary services , as the case may be, shall conduct continuing review at intervals determined by risk.

(3) The ethics committee or the Director of Veterinary Services may—

(a) request modifications;

(b) suspend approval; or

(c) terminate approval.

PART IV – CLINICAL TRIALS INVOLVING VETERINARY MEDICINES

Application of this Part

18. (1) This Part applies to all clinical trials conducted in Botswana in which an investigational veterinary medicinal product is tested or investigated in animals.

(2) The provisions of this Part are in addition to and shall be read together with the other provisions of these Regulations, and where any conflict arises between the provisions of this Part and the other provisions of these Regulations, the provisions of this Part shall prevail to the extent of the inconsistency in respect of veterinary clinical trials.

Role of the Director of Veterinary Services

19. (1) The Director of Veterinary services shall, in respect of veterinary clinical trials, perform the role equivalent to that performed by the ethics committee in respect of clinical trials involving human participants.

(2) The Director of Veterinary services shall—

(a) review and approve or reject applications for veterinary clinical trials;

(b) ensure the welfare of animals enrolled in clinical trials;

(c) monitor compliance with the Three Rs Principle;

(d) require and review progress reports, safety reports and final reports;

(e) suspend or terminate approval where animal welfare is compromised or where the trial no longer meets prescribed requirements; and

(f) advise the Authority on matters concerning veterinary clinical trials.

(3) The Authority shall consult the Director of Veterinary services before granting, varying, suspending or revoking a clinical trial authorisation in respect of a veterinary clinical trial.

Approval by the Director of Veterinary services

20. (1) No veterinary clinical trial shall commence without prior written approval from the Director of Veterinary services .

(2) An application for approval shall be submitted in Form CT-09 set out in Schedule 1 and shall be accompanied by—

(a) the clinical trial protocol;

(b) a statement demonstrating compliance with the Three Rs Principle;

(c) a description of animal welfare measures to be implemented;

(d) the proposed informed consent documents for animal owners;

(e) a description of the investigational veterinary product;

(f) details of the qualifications and experience of the principal investigator and trial personnel;

(g) a description of the trial site and its facilities for animal housing and care;

(h) the proposed arrangements for the monitoring of animal welfare during the trial; and

(i) such other information as the Director of Veterinary services may require.

(3) The Director of Veterinary services shall assess the application and may—

(a) approve the application;

(b) approve the application subject to conditions;

(c) request additional information; or

(d) refuse the application with written reasons.

(4) The Director of Veterinary Services shall communicate its decision to the applicant and to the Authority in writing.

he Three Rs Principle

Consent of animal owner

22. (1) In accordance with section 53(3) of the Act, where a clinical trial involves an animal, voluntary written consent of the owner shall be obtained before the enrolment of any animal in the trial.

(2) Consent shall be obtained using Form CT-10 set out in Schedule 1 and shall be—

(a) voluntary and free from coercion or undue influence;

(b) based on adequate information provided in a language understood by the owner;

(c) documented in writing and signed by the owner; and

(d) obtained before any trial-related procedure is performed on the animal.

(3) The information provided to the animal owner shall include—

(a) a description of the nature and purpose of the trial;

(b) the procedures to be performed on the animal;

(c) the expected duration of the animal's participation;

(d) the reasonably foreseeable risks and potential discomforts to the animal;

(e) the potential benefits to the animal;

(f) available alternative treatments;

(g) the arrangements for compensation in the event of trial-related injury, illness or death of the animal;

(h) the right of the owner to withdraw the animal from the trial at any time without penalty or loss of benefits;

(i) the identity and contact details of the investigator; and

(j) any restrictions on the use of the animal or its products, including any applicable withdrawal periods, during and after the trial.

(4) A study participant or owner of an animal may withdraw consent to a clinical trial at any time without any penalty or loss of benefits, in accordance with section 53(4) of the Act.

Compensation to animal owner

23. (1) The sponsor shall make provision for compensation to the owner of an animal that suffers injury, illness, disability or death as a direct result of its participation in a veterinary clinical trial.

(2) The compensation arrangements shall—

(a) be described in the animal owner consent document;

(b) not require the owner to prove fault on the part of the sponsor, investigator or any other person;

(c) cover veterinary treatment costs for trial-related injury or illness;

(d) provide for fair compensation in respect of the death or permanent disability of the animal, having regard to the market value or replacement value of the animal; and

(e) not require the owner to waive any legal rights.

(3) Disputes regarding compensation may be referred to the Authority for determination.

(4) The sponsor shall maintain adequate insurance or indemnity arrangements to meet its obligations under this regulation.

Welfare of animals in trials

24. (1) The investigator shall ensure that the welfare of every animal enrolled in a veterinary clinical trial is safeguarded at all times.

(2) The investigator shall ensure that—

(a) animals receive proper veterinary care throughout the trial;

(b) appropriate housing, nutrition, water and environmental conditions are maintained;

(c) pain, suffering and distress are minimised;

(d) humane endpoints are observed and implemented;

(e) animals are monitored regularly for signs of adverse reactions, illness or distress;

(f) an animal is withdrawn from the trial where continued participation would cause unacceptable suffering; and

(g) appropriate arrangements are made for the care of animals after the conclusion of the trial.

(3) The investigator shall maintain records of all welfare assessments and interventions made during the trial.

Additional requirements for trials in food-producing animals

25. (1) Where a veterinary clinical trial involves food-producing animals, the investigator shall ensure that—

(a) appropriate withdrawal periods are established and communicated to the animal owner;

(b) the animal owner is informed of any restrictions on the sale or use of the animal or its products during and after the trial;

(c) residue depletion data are collected where necessary;

(d) compliance with applicable maximum residue limits is ensured; and

(e) the protocol addresses the potential impact on food safety

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(2) The animal shall not enter the food chain unless maximum residue limits (MRLs) and/or appropriate withdrawal periods have been

Reporting of adverse events in animal trials

26. (1) The investigator shall report to the sponsor all adverse events observed in trial animals, including—

(a) unexpected death;

(b) serious adverse reactions;

(c) lack of expected efficacy;

(d) adverse reactions in humans handling or exposed to the investigational product; and

(e) environmental incidents associated with the investigational product.

(2) The sponsor shall report to the Authority and to the Director of Veterinary Services all serious adverse events in trial animals—

(a) immediately, and in writing within twenty-four hours, in respect of unexpected death or life-threatening adverse reactions; and

(b) within seven calendar days, in respect of other serious adverse events.

(3) Follow-up reports shall be submitted until the adverse event has been resolved or stabilised.

PART IV – CLINICAL TRIALS INVOLVING MEDICAL DEVICES

Clinical investigation authorisation

53. (1) In accordance with section 46 of the Act, clinical investigations of medical devices shall require authorisation from the Authority and ethics committee approval.

(2) Applications shall be submitted in accordance with the Clinical Trials Regulations and shall be accompanied by the prescribed fee as set out in the Fees Regulations.

(3) Specific requirements for medical device clinical investigations shall be specified in guidelines.

1) Clinical investigations of medical devices shall be authorized by the Authority before commencement.

(2) An application for clinical investigation authorization shall be made on Form MD-12 and shall include—

(a) the clinical investigation plan;

(b) the investigator's brochure or device description;

(c) evidence of ethics committee approval;

(d) investigator qualifications and site information;

(e) informed consent forms and patient information leaflets;

(f) risk analysis and risk management plan; and

(g) insurance or indemnity arrangements.

(3) The Authority shall process clinical investigation applications within sixty days of receipt of a complete application.

(4) For device investigations involving minimal risk, the Authority may waive certain requirements.

(5) Conducting a clinical trial without authorization is an offence under section 57 of the Act.

Good clinical practice for medical devices

54. Medical device clinical investigations shall comply with ISO 14155 or equivalent standards and the Clinical Trials Regulations, with specific considerations for investigator training, device accountability procedures, malfunction reporting and device-specific adverse event assessment.

Medical device clinical investigations shall comply with applicable standards or an equivalent standard on good clinical practice for clinical investigations of medical devices in human subjects.

Ethical requirements

55. Ethics committee approval shall be obtained before commencing a clinical investigation, with informed consent requirements as specified in the Clinical Trials Regulations, and special considerations for investigations involving implantable medical devices, companion diagnostics, high-risk medical devices and vulnerable populations.

57. (1) Ethics committee approval shall be obtained
before commencing a clinical investigation.

(2) A valid informed consent process in accordance with national bioethics legislation shall be in place for all investigation subjects.

(3) The rights, safety and wellbeing of subjects shall take precedence over the interests of science and society.

Clinical investigation conduct

56. Investigations shall be conducted according to the approved protocol, deviations shall be documented and reported, and the Authority may inspect investigation sites.

58. Investigations shall be conducted according to the approved protocol; deviations shall be documented and reported; and the investigator shall permit Authority inspection
of clinical investigation records, facilities and data at any time.

Safety reporting for clinical investigations by sponsors

57. (1) All serious adverse events affecting the patient, user, third-party, including serious health threats, regardless of cause, and medical device deficiencies that might have led to serious adverse events if suitable action had not been taken, intervention had not been made; or if circumstances had been less fortunate shall be reported within the timelines prescribed in the Clinical Trials Regulations and guidelines.

(2) Periodic safety reports shall be submitted as required for adverse events that:

a. led to a death;

b. led to a serious deterioration in the health of the subject that either:

I) resulted in a life threatening illness of injury, or

II) resulted in a permanent impairment of a body structure or a body function, or

III) required in-patient hopsitalization or prolongation of existing hospitailzation, or

IV) resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function;

c. led to fetal distress, fetal death or congenital abnormality or birth defect

(3) A planned hospitalization for pre-existing condition, or a procedure required by the clinical investigation plan, without a serious deterioration in health is not considered to be a serious adverse event.

Clinical investigation reports

58. A clinical investigation report following ISO 14155 or equivalent standards shall be submitted upon completion, regardless of outcome.

PART V – INVESTIGATORS AND SPONSORS

Sponsor obligations

27. (1) The sponsor shall be responsible for—

(a) implementing and maintaining quality assurance and quality control systems;

(b) ensuring the trial is conducted in accordance with applicable standards for clinical investigations.

(c) selecting qualified investigators;

(d) providing adequate resources;

(e) providing investigational products meeting GMP requirements;

(f) ensuring appropriate insurance coverage;

(g) reporting safety information to the Authority;

(h) maintaining essential documents;

(i) ensuring data quality and integrity;

(j) notifying the Authority of serious breaches;

(k) ensuring compensation for trial-related injuries to human participants or trial-related injuries to animals, as applicable; and

(l) in respect of veterinary clinical trials, ensuring compliance with the Three Rs Principle.

(2) The sponsor may delegate functions to a contract research organisation but retains ultimate responsibility.

(3) Transfer of sponsorship requires Authority notification and approval.

Principal investigator qualifications

29. (1) A principal investigator for a clinical trial involving human participants shall—

(a)(b) have qualifications and experience appropriate to the trial;

(c) have completed training in GCP

(d) be familiar with the investigational product;

(e) have adequate time to conduct the trial; and

(f) have access to adequate facilities and staff.

(2) A principal investigator for a veterinary clinical trial shall—

(a) be a veterinary surgeon registered under the Veterinary Surgeons Act;

(b) have qualifications and experience appropriate to the trial and the animal species involved;

(c) have completed training inGCP or equivalent ;

(d) be familiar with the investigational veterinary product; and

(e) have access to adequate facilities and staff for the care of trial animals.

(3) The Authority may specify additional qualification requirements in guidelines for specific trial types.

Investigator responsibilities

30. (1) The investigator shall be responsible for—

(a) ensuring participant welfare and safety, or animal welfare, as applicable;

(b) conducting the trial in accordance with the protocol;

(c) compliance with applicable standards.

as applicable;

(d) obtaining informed consent or animal owner consent, as applicable;

(e) providing medical care to participants or veterinary care to trial animals, as applicable;

(f) timely reporting of adverse events;

(g) accurate data recording;

(h) maintaining confidentiality;

(i) accountability for investigational products;

(j) allowing monitoring and audit; and

(k) maintaining essential documents.

(2) The investigator shall not implement any deviation from the protocol without sponsor and ethics committee or Director of Veterinary Services approval, except to eliminate immediate hazards.

Investigator's brochure

31. (1) The sponsor shall provide an investigator's brochure containing all relevant information about the investigational product.

(2) The investigator's brochure shall be updated as new information becomes available.

(3) Requirements for investigator's brochure content shall be as specified in guidelines.

Delegation of responsibilities

32. (1) The investigator may delegate trial-related duties to qualified members of the trial team.

(2) Delegation shall be—

(a) documented in a delegation log;

(b) based on qualifications and training;

(c) subject to adequate supervision; and

(d) maintained current.

(3) The investigator retains overall responsibility for delegated tasks.

PART VI – TRIAL SITES

Site suitability requirements

33. (1) Trial sites shall have—

(a) adequate facilities for the proposed trial activities;

(b) qualified and trained personnel;

(c) access to appropriate medical or veterinary care, as applicable;

(d) capacity for emergency treatment;

(e) adequate record-keeping systems;

(f) pharmacy or investigational product management capability;

(g) laboratory services as required;

(h) equipment appropriate to the trial; and

(i) in respect of veterinary clinical trials, adequate housing, husbandry and care facilities for the species concerned.

(2) Specific site requirements shall be set out in guidelines.

Site qualification assessment

34. (1) Sponsors shall conduct site qualification assessments before site selection.

(2) The Authority may require site approval for—

-(b) first-in-human trials;

-(d) high-risk trials as determined by the Authority.

(3) Site assessment criteria shall be specified in guidelines.

Facilities and equipment

35. (1) Trial sites shall maintain—

(a) appropriate clinical or veterinary facilities;

(b) secure storage for investigational products;

(c) temperature monitoring where required;

(d) sample processing and storage capability;

(e) emergency equipment; and

(f) communication systems.

(2) Equipment shall be maintained, calibrated and qualified as appropriate.

Site personnel

36. (1) Site personnel shall—

(a) be qualified for their delegated responsibilities;

(b) receive training on the protocol and investigational product;

(c) receive GCP training, as applicable;

(d) have documented training records; and

(e) be listed on the delegation log.

Site master file

37. (1) Each trial site shall maintain a site master file containing essential documents.

(2) The site master file shall be available for monitoring, audit and inspection.

(3) Essential documents as per the guidelines.

PART VII – INVESTIGATIONAL PRODUCTS

Manufacture of investigational products

38. (1) Investigational products shall be manufactured in accordance with—

(a) Good Manufacturing Practice for investigational products;

(b) the product specification file; and

(c) any additional requirements specified in guidelines.

(d) Good laboratory practice for Investigational Products manufactured in the Laboratory

(2) Manufacturing sites shall hold appropriate GMP certification.

(3) The Authority may accept GMP certifications from recognised regulatory authorities.

Importation of investigational products

39. (1) In accordance with section 55 of the Act, importation of investigational products requires—

(a) valid clinical trial authorisation; and

(b) import permit from the Authority.

(2) Applications for import permits shall be made in Form CT-03 set out in Schedule 1.

(3) Import permits shall specify—

(a) product details;

(b) quantities;

(c) consignment details;

(d) storage requirements; and

(e) any conditions.

(4) Expedited import procedures may apply for urgent clinical needs.

Labelling requirements

40. (1) Investigational products shall be labelled with—

(a) the words "For Clinical Trial Use Only" or "For Veterinary Clinical Trial Use Only", as applicable;

(b) trial identification;

(c) product identification;

(d) batch number;

(e) expiry date;

(f) storage conditions;

(g) sponsor name and contact; and

(h) directions for use where appropriate.

(2) Blinding requirements shall be maintained in labelling.

(3) Labelling shall be in English, with local language as appropriate.

(4) Detailed labelling requirements shall be specified in guidelines.

Storage and handling

41. (1) Investigational products shall be stored—

(a) in accordance with product requirements;

(b) in secure, access-controlled areas;

(c) with temperature monitoring where required;

(d) separately from commercial stock; and

(e) with documentation of receipt and storage conditions.

(2) Cold chain requirements shall be maintained and documented.

Accountability and reconciliation

42. (1) Complete accountability shall be maintained for investigational products including—

(a) quantities received;

(b) quantities dispensed or administered;

(c) quantities returned;

(d) quantities destroyed; and

(e) reconciliation.

(2) Accountability records shall be maintained at sponsor and site level.

Destruction and disposal

43. (1) Unused investigational products shall be destroyed or returned to the sponsor.

(2) Destruction shall be—

(a) documented;

(b) conducted by authorised methods;

(c) witnessed where required; and

(d) reported to the sponsor.

(3) Disposal shall comply with environmental requirements.

PART VIII – TRIAL CONDUCT

Protocol compliance

44. (1) The trial shall be conducted in strict accordance with the approved protocol.

Randomisation and blinding

45. (1) Randomisation procedures shall be described in the protocol, implemented as specified, documented and verifiable.

Source documentation

46. (1) All trial data shall be supported by source documents which shall be original, accurate, complete, legible, timely and available for verification.

Case report forms

47. (1) Case report forms shall capture all protocol-required data and be consistent with source documents.

Data management

48. (1) Data management shall ensure data quality and integrity through validated data entry, query management, audit trails, security controls and backup and recovery.

Biological sample handling

49. (1) Collection, processing, storage and transport of biological samples shall comply with protocol requirements, laboratory standards, biosafety requirements and ethics committee or Department of Veterinary Services approvals for sample use.

PART IX – PROTOCOL AMENDMENTS AND VARIATIONS

Classification of amendments

50. (1) Protocol amendments shall be classified as—

(a) substantial amendments requiring prior Authority approval; or

(b) non-substantial amendments requiring notification only.

(2) Classification criteria shall be specified in guidelines.

Substantial amendments

51. (1) Substantial amendments include changes that may significantly affect—

(a) participant safety or animal welfare;

(b) scientific validity;

(c) conduct or management of the trial;

(d) quality of data; or

(e) interpretation of results.

(2) Applications for substantial amendments shall be made in Form CT-04 set out in Schedule 1.

(3) Substantial amendments shall not be implemented until approved by the Authority and the ethics committee or Director of Veterinary Services, as applicable.

Non-substantial amendments

52. (1) Non-substantial amendments are administrative or logistical changes that do not significantly affect the matters in regulation 51(1).

(2) Non-substantial amendments shall be notified to the Authority within the timeframe specified in guidelines.

(3) The Authority may reclassify a non-substantial amendment as substantial.

Urgent safety measures

53. (1) In accordance with section 50 of the Act, urgent safety measures may be implemented immediately to protect participant safety or animal welfare.

(2) The Authority and the ethics committee or the Director of Veterinary Services, as applicable, shall be notified within twenty-four hours of implementing urgent safety measures.

Authority notification requirements

54. (1) The sponsor shall notify the Authority of—

(a) all amendments;

(b) urgent safety measures;

(c) temporary halt or early termination;

(d) serious breaches;

(e) suspected unexpected serious adverse reactions;

(f) regulatory actions in other countries; and

(g) completion of the trial.

PART X – SAFETY REPORTING

Definitions for safety reporting

55. For the purposes of this Part—

"expected" means an adverse reaction that is consistent with applicable product information;

"life-threatening" means an event in which the participant or trial animal was at immediate risk of death;

"serious" means an adverse event meeting the criteria in the definition of serious adverse event;

"unexpected" means an adverse reaction that is not consistent with applicable product information.

Investigator safety reporting

56. (1) Investigators shall report to the sponsor—

(a) all serious adverse events immediately, and in writing within twenty-four hours;

(b) non-serious adverse events as specified in the protocol;

(c) pregnancies occurring during the trial, in respect of human trials; and

(d) adverse events of special interest as defined in the protocol.

Sponsor safety reporting to Authority

57. (1) The sponsor shall report to the Authority—

(a) suspected unexpected serious adverse reactions;

(b) safety issues that may affect participant safety or animal welfare;

(c) new information affecting benefit-risk assessment;

(d) regulatory actions in other countries; and

(e) safety information specified in guidelines.

(2) SUSAR reports shall be submitted using Form CT-05 set out in Schedule 1 or through electronic systems specified by the Authority.

Development Safety Update Reports

58. (1) The sponsor shall submit Development Safety Update Reports annually.

(2) DSURs shall be submitted within sixty days of the data lock point.

(3) DSUR format and content shall follow ICH E2F guidelines or VICH equivalent, as applicable.

Safety reporting timelines

59. (1) Reporting timelines are set out in Schedule 3.

(2) Timelines run from the date the sponsor first becomes aware of the reportable information.

Expedited safety reports

60. (1) Fatal or life-threatening SUSARs shall be reported within seven calendar days of first awareness.

(2) Other SUSARs shall be reported within fifteen calendar days of first awareness.

(3) Follow-up reports shall be submitted within eight calendar days of receipt of new information.

Annual safety reports

61. (1) Annual safety reports shall be submitted for each investigational product throughout its clinical development.

(2) The Authority may specify additional periodic reporting requirements in guidelines or conditions of authorisation.

PART XI – MONITORING AND QUALITY ASSURANCE

Monitoring requirements

62. (1) The sponsor shall ensure appropriate monitoring of the trial, the extent and nature of which shall be determined by trial complexity, risk assessment, trial phase, site experience and regulatory requirements.

Risk-based monitoring

63. (1) Sponsors may implement risk-based monitoring approaches, which shall be documented in the monitoring plan.

Auditing

64. (1) The sponsor may conduct audits of trial sites, facilities and processes, and audit findings shall be documented and addressed through corrective actions.

Quality management system

65. (1) Sponsors shall implement a quality management system covering protocol development, trial conduct, data management, safety reporting, document management and corrective and preventive actions.

Corrective and preventive actions

66. (1) Non-conformances identified through monitoring, audit or inspection shall be addressed through corrective and preventive actions including root cause analysis, corrective action, preventive action and verification of effectiveness.

PART XII – INSPECTION

Authority inspection powers

67. (1) In accordance with section 54 of the Act, the Authority may inspect trial sites, sponsor facilities, laboratories, manufacturing sites, contract research organisations and any other location where trial-related activities occur.

96. (1) In accordance with section 77 of the Act, the Chief Executive Officer shall appoint qualified inspectors to carry out inspections of persons and premises regulated under these Regulations.

(2) (2) Inspectors shall hold appropriate qualifications, receive training in inspection procedures, be furnished with certificates specifying their scope of authority, carry official identification, and be bound by a code of conduct.

(3) (3) Inspectors shall declare any conflicts of interest and shall not inspect entities with which they have personal or financial connections.

Powers of inspectors

types of inspections

68. (1) The Authority may conduct routine inspections, pre-approval inspections, , end of trial inspections, which may be announced or unannounced.

Inspection procedures

69. (1) Inspections shall be conducted in accordance with documented procedures.

Inspection findings classification

70. (1) Inspection findings shall be classified according to Schedule 5 as critical, major, minor or observations.

Response to inspection findings

71. (1) Responses to inspection findings shall be submitted within the timeframes specified—

(a) critical findings: immediate action required, response within five working days;

(b) major findings: response within fifteen working days; and

(c) minor findings: response within thirty working days.

International inspection cooperation

72. (1) The Authority may participate in joint inspections with other regulatory authorities, accept or rely on inspection reports from recognised authorities, share inspection findings and participate in international inspection programmes.

PART XIII – SUSPENSION AND TERMINATION

Grounds for suspension

73. (1) In accordance with section 50 of the Act, the Authority may suspend a clinical trial authorisation where—

(a) participant safety or animal welfare is at risk;

(b) serious or repeated GCP violations occur;

(c) data integrity is compromised;

(d) conditions of authorisation are not met;

(e) the sponsor fails to respond to safety concerns;

(f) ethics approval or Director of Veterinary Services approval is withdrawn; or

(g) continued conduct would be contrary to the public interest.

Suspension procedures

74. (1) Before suspension, except for immediate safety concerns, the Authority shall notify the sponsor of the concerns, provide opportunity for response and consider the response.

(2) For immediate safety concerns, the Authority may suspend without prior notice.

Termination by sponsor

75. (1) The sponsor may terminate a trial for any reason and shall notify the Authority within fifteen days of the decision to terminate.

Termination by Authority

76. (1) In accordance with section 51 of the Act, the Authority may terminate authorisation where suspension grounds persist, the trial can no longer achieve its objectives, the benefit-risk balance is unfavourable or fraud or serious misconduct is established.

Post-termination obligations

77. (1) Following termination or completion, the sponsor shall ensure appropriate care for participants or animals, preserve all trial data and documents, account for investigational products, submit required reports, archive essential documents and notify the Authority of completion of wind-down activities.

PART XIV – RECORDS AND REPORTING

Essential documents

78. (1) Essential documents as listed in Schedule 4 shall be maintained throughout the trial and be available for monitoring, audit and inspection.

Record retention

79. (1) In accordance with section 102 of the Act, trial records shall be retained for—

(a) fifteen years from trial completion; or

(b) such longer period as required by applicable laws or guidelines.

Clinical trial reports

80. (1) The sponsor shall submit a clinical trial report to the Authority within one year of trial completion or such other timeframe as specified in the guidelines.

(2) The Authority may require clarification or additional information regarding any Annual Progress Report.

(3) Failure to submit an Annual Progress Report within the prescribed period constitutes non-compliance with these Regulations and may result in-

(a) issuance of a warning;

(b) request for corrective and preventive action;

(c) suspension of recruitment;

(d) suspension of the clinical trial authorisation; or

(e) such other regulatory action as the Authority considers appropriate.

(4) The Authority may issue guidelines specifying the format, content and electronic submission requirements for Annual Progress Reports.

Publication and disclosure

81. (1) In accordance with section 56 of the Act, trial results shall be made publicly available through publication and clinical trial registries. The applicant shall notify the authority about publications in writing.

Clinical trial registry

82. (1) In accordance with section 47(8) of the Act, all trials shall be registered in a WHO-recognised clinical trial registry before enrolment of the first participant or first animal.

(2) The Authority shall establish, maintain or publish a national register of clinical trials authorised under these Regulations.

(3) The register may contain, subject to applicable confidentiality requirements—

(a) clinical trial authorisation number;

(b) protocol title;

(c) sponsor;

(d) principal investigator;

(e) investigational product;

(f) therapeutic area;

(g) trial phase;

(h) approved trial sites;

(i) date of authorisation;

(j) current regulatory status; and

(k) such other information as the Authority may determine.

(4) The Authority shall update the register as necessary to reflect—

(a) new authorisations;

(b) amendments affecting trial status;

(c) temporary halts;

(d) suspensions;

(e) revocations;

(f) early terminations;

(g) completed clinical trials; and

(h) final study reports where appropriate.

(5) The Authority may publish summaries of regulatory decisions relating to clinical trials in accordance with its transparency policy, provided that confidential commercial information and personal data are protected.

(6) Nothing in this regulation authorises disclosure of confidential commercial information, trade secrets or personal information contrary to the Act or any other applicable law.

PART XV – SPECIAL CATEGORIES OF TRIALS

First-in-human trials

83. (1) First-in-human trials are subject to enhanced requirements including comprehensive preclinical data, detailed dose escalation plans, stopping rules, enhanced monitoring, immediate access to emergency care, independent safety review and pre-approval inspection where required.

Paediatric trials

84. (1) Trials in children and minors shall comply with the requirements of regulation 16 and additional requirements specified in guidelines, including age-appropriate consent processes and formulations.

Trials in pregnant and lactating women

85. (1) Trials in pregnant women shall only be conducted where the research addresses health needs of pregnant women or their offspring, and appropriate preclinical reproductive toxicology data are available.

Cluster and public health trials

87. (1) Cluster trials and public health trials may utilise community consent mechanisms, opt-out procedures and modified monitoring approaches, subject to specific ethics committee approval.

Adaptive and platform trials

88. (1) Adaptive trials and platform trials shall have pre-specified adaptation rules, maintain study integrity and meet regulatory requirements for each adaptation.

Bioequivalence and bioavailability studies

89. (1) Bioequivalence and bioavailability studies are subject to simplified documentation requirements and expedited assessment timelines as specified in guidelines.

PART XVI – TRIALS DURING PUBLIC HEALTH EMERGENCIES

Emergency trial authorisation

90. (1) During declared public health or animal health emergencies, the Authority may expedite clinical trial authorisation, accept rolling submissions, provide rapid review, grant conditional authorisation and rely on emergency authorisations from other authorities.

Modified requirements

91. (1) During public health emergencies, the Authority may modify documentation requirements, assessment timelines, fee requirements, inspection requirements and reporting requirements, provided that modifications are proportionate to the emergency and do not compromise participant safety or animal welfare.

Expedited ethics review

92. (1) Ethics committees and the Director of Veterinary Services shall establish expedited review procedures for emergency trials.

Real-world evidence integration

93. (1) Trials during emergencies may incorporate real-world evidence and pragmatic designs as specified in guidelines.

PART XVII – COMPENSATION AND INSURANCE

Insurance requirements

94. (1) In accordance with section 53(5) of the Act, the Principal Investigator, where applicable, shall ensure clinical trial participant or subjects has an adequate and valid insurance cover to

protect trial participants or subjects against any clinical trial related injuries or harm.

(2) Insurance shall cover medical treatment or veterinary treatment for trial-related injuries, compensation for disability or death, and legal liability.

(3) Insurance shall remain valid throughout the trial and for such period thereafter as specified in guidelines.

Compensation for trial-related injury

95. (1) Participants or subjects who suffer trial-related injury shall receive treatmetment treatment and compensation as appropriate, without requiring proof of fault.

(2) Compensation arrangements for animal owners are as provided in regulation 23.

Post-trial access

96. (1) Sponsors shall describe in the protocol arrangements for post-trial access to beneficial investigational medical products and continued care.

PART XVIII – OFFENCES AND PENALTIES

Offences

97. A person commits an offence who—

(a) conducts a clinical trial without authorisation;

(b) conducts a clinical trial without ethics approval or Director of Veterinary Services approval, as applicable;

(c) administers investigational products without informed consent or animal owner consent, as applicable;

(d) provides false or misleading information to the Authority;

(e) fails to report serious adverse events as required;

(f) fails to report SUSARs as required;

(g) fails to implement urgent safety measures when required;

(h) obstructs an inspection;

(i) fails to maintain essential documents;

(j) breaches participant confidentiality or animal owner confidentiality;

(k) continues a trial after suspension;

(l) imports investigational products without authorisation;

(m) conducts a veterinary clinical trial in contravention of the Three Rs Principle; or

(n) contravenes any other provision of these Regulations.

Penalties

98. (1) A person who commits an offence under regulation 97 is liable to the penalties specified in section 57 of the Act.

(2) The maximum penalties are—

(a) a fine not exceeding P5 000 000;

(b) imprisonment not exceeding seven years; or

(c) both.

(3) The court may additionally order—

(a) termination of the trial;

(b) forfeiture of investigational products;

(c) compensation to affected participants or animal owners;

(d) publication of the conviction; and

(e) disqualification from conducting trials.

Compounding of offences

99. (1) The Authority may compound offences in accordance with section 121 of the Act.

(2) Compounding is not available for offences involving—

(a) participant harm or animal harm;

(b) fraud or deliberate misconduct;

(c) repeat violations; or

(d) obstruction of investigation.

PART XIX – TRANSITIONAL AND FINAL PROVISIONS

Guidelines

100. (1) The Authority shall issue guidelines on all matters requiring detailed specification under these Regulations.

(2) Guidelines may be issued, amended or revoked without amendment to these Regulations.

(3) Guidelines shall be—

(a) developed with stakeholder consultation where appropriate;

(b) aligned with international standards;

(c) published on the Authority's website; and

(d) regularly reviewed and updated.

Transitional provisions

101. (1) Clinical trials authorised before commencement of these Regulations shall continue under previous authorisation terms until—

(a) completion of the trial;

(b) renewal of authorisation; or

(c) such date as the Authority may specify.

(2) Applications submitted before commencement shall be processed under regulations in force at submission.

Repeal

102. Any regulations relating to clinical trials under the repealed Medicines and Related Substances Act (Cap. 63:04) are hereby repealed

SCHEDULES

SCHEDULE 1 – FORMS

Form	Title	Regulation
CT-01	Application for Clinical Trial Authorisation	6
	Clinical Trial Authorisation Certificate	
CT-03	Import Permit Application	39
CT-04	Application for Amendment	51
CT-05	SAE Report Form	57
CT-06	Annual Progress Report	61
CT-07	End of Trial Report	54
CT-08		54
CT-09	Application for Director of Veterinary Services Approval	20
CT-10	Animal Owner Consent Form	22
CT-11	Veterinary Clinical Trial Adverse Event Report	26

[Detailed forms to be prescribed by the Authority]

Made this _____ day of _____, 2025

_____

MINISTER OF HEALTH

MEDICINES AND RELATED SUBSTANCES ACT, 2025

CLINICAL TRIALS REGULATIONS, 2025

SCHEDULE 1 – FORMS

APPLICATION FOR USE OF MEDICINES FOR CLINICAL TRIALS
APPLICATION TO CONDUCT A CLINICAL TRIAL

SECTION 1 – CHECKLIST OF REQUIRED DOCUMENTATION

To be completed by Applicants for all Clinical Trials

FOR OFFICIAL USE

ACKNOWLEDGEMENT OF RECEIPT OF APPLICATION (Contact details to be completed by the applicant). Whole cover sheet to be faxed/emailed to applicant once details in block above are completed.

Contact Details: Name: **Fax No:**
Receipt of new application is hereby acknowledged. **E-mail:**
Signature (of recipient): **Date:**
Name:

APPLICATION TO CONDUCT A CLINICAL TRIAL
COVER SHEET
Study Title: _____
Protocol No: _____
Version No: _____ **Date of Protocol:** _____
Study Medicine: _____
Ref number (if applicable): _____
Ref number(s) of comparator medicine(s) (if applicable): _____
Ref number(s) of concomitant medicine(s) (if applicable): _____
Date(s) Regulatory approval of previous protocol(s): _____
Sponsor: _____
Applicant: _____
Contact Person: _____
Address: _____
Telephone Number: _____ **Fax Number:** _____
Cell Number: _____
E-mail address:

CHECKLIST

No.	Mark (x)	Item

1.	☐	Cover letter including list of documents submitted and their version number and date
2.	☐	Completed clinical trial application form including cover page
3.	☐	Clinical trial protocol including site specific addendums
4.	☐	Informed consent form(s)
5.	☐	Product information if the investigational medical product is registered: summary of product characteristics, patient information leaflet/package insert, and labelling
6.	☐	Investigator's brochure
7.	☐	If applicable, synopsis of previous trials with the investigational medical product(s)
8.	☐	If applicable, electronic copies of key peer reviewed publications to support the application.
9.	☐	Copy/ies of patient recruitment advertisement(s) (if applicable) and questionnaires
10.	☐	Investigational medical product dossier (If applicable)
11.	☐	Product information and certificate of analysis for the concomitant and rescue medications
12.	☐	GMP certificate for the site(s) producing the IMP(s)2
13.	☐	Certificate(s) of analysis of the IMP(s)
14.	☐	Certificate(s) of accreditation for the central laboratories
15.	☐	Signed declaration by the national principal investigator
16.	☐	Workload forms for investigators
17.	☐	Signed curriculum vitae for all key staff participating in the conduct of the clinical trial, eg national principal investigator, principal and/or co-investigators, study coordinator, regional and local monitor, contract research affiliate, etc
18.	☐	Signed declaration(s) by each investigator(s)
19.	☐	Signed joint financial declaration between the sponsor and the national principal investigator

20.	☐	Signed declaration by the sub-investigators and key staff participating in the clinical trial
21.	☐	Signed declaration by the regional monitor(s)
22.	☐	Proof of registration on PACTR or other WHO primary accessible registry
23.	☐	Active clinical trials insurance (Phase I, II, III)
24.	☐	Proof of sponsor indemnification for investigators and trial site
25.	☐	GCP certificates for the investigators
26.	☐	Proof of registration of the key investigators with a professional statutory body (if applicable)
27.	☐	Proof of professional indemnity (malpractice insurance)
28.	☐	Study budget
29.	☐	Evidence of submission to the national ethics committee
30.	☐	Data Safety Monitoring Board charter and composition
31.	☐	Proof of Payment from BoMRA

Electronic versions of the application form (Sections 1-30, the protocol, the investigator's brochure and/or other relevant documents:

☐ **LABELLED CD-ROM (MS WORD OR RICH TEXT FORMAT)**

List of files submitted on CD-ROM:

NB: INCOMPLETE APPLICATIONS WILL NOT BE PROCESSED

Declaration by applicant:

We, the undersigned have submitted all requested and required documentation, and have dis-closed all information which may influence the approval of this application.

We, the undersigned, hereby declare that all information contained in, or referenced by, this application is complete and accurate and is not false or misleading.

We, the undersigned, agree to ensure that if the above-said clinical trial is approved, it will be conducted according to the submitted protocol and all applicable legal, ethical and regulatory requirements.

_____

_____

Applicant (local contact) *Date*

_____

_____

National Principal Investigator/ Date
National Co-coordinator/
Other (state designation)

SECTION 2 – ADMINISTRATIVE AND SUPPLEMENTARY DETAILS

Title:
Protocol Number/identification:
Date of final protocol:

Part 1: CONTRACT DETAILS (NAME/ADDRESS/TEL/CELL/FAX/E-MAIL)

1.1 Applicant: (as in Section 1)
1.2 Sponsor: (as in Section 1)
1.3 If no sponsor, person, or organization initiating, managing, and or funding the clinical trial:
1.4 Local Contact Person for correspondence:
1.5 National Principal Investigator/Coordinator: (or equivalent person)
1.6 International Principal Investigator: (if applicable)
1.7 Regional Monitor:
1.8 Study Coordinator:

PART 2: DETAILS OF INVESTIGATIONAL PRODUCT(S)

2.1 Name(s) and details of investigational product(s) to be used in trail:
[*A summary of the chemistry and manufacturing data, formulation, composition, excipients and strength should be provided. Complete chemistry and manufacturing data should be included in the investigator's brochure. Product(s) registration number(s) and date(s) of registration, if application, should be included]*

2.2 Name(s) and details (as above) of comparator product(s) and product registration number(s)
and date(s) of registration if applicable:
[*As in 2.1, where applicable. Package inserts for registered comparator products should be included*]

2.3 Name(s) and details (as above) of concomitant medication(s) including rescue medications which are required in the protocol, and product registration number(s) if applicable:
[*As in 2.1, where applicable. Package inserts for registered products should be included*]

2.4 Estimated Quantity of Trial Material (each medicine detailed separately) for which exemption will be required:

2.5 If any of the above medicines are marketed locally, explain whether locally sourced products will be used in the trial:

2.6 Details of receipt of medicines from supplier, packaging, storage, and shelf-life and dispensing:

2.7 Date (or envisaged date) of application for registration of trial medication:
[*Provide an explanation if registration is not envisaged*]

2.8 Registration status of trail medication, for the indication to be tested in this trial, in other countries:
[*i.e., Country: date registered/date applied for/date registration refused/date registration withdrawn by applicant/date registration cancelled by regulatory authority. Attach as an appendix if necessary*]

PART 3: DETAILS OF TRIALIST(S) AND TRIAL SITE(S)

3.1 Details of Investigator(s):
[*Designation and title of principal investigators/investigators/ Include Name/ Address/ Tel/ Cell/ Fax/ E-Mail*]

3.2 Current workload of Investigator(s):
[*Number of studies currently undertaken by trialist(s) as principal and or co- or sub-investigator, and the total number of patients represented by these studies. Time commitments of researcher(s) in relation to clinical trial work and non-trial work*]

Recommended format for Investigator workload:

<table>
<tr><td>Investigator (Name and designation):</td><td colspan="3"></td></tr>
<tr><td>Total number of current studies (all stages) on specified date</td><td>Number</td><td colspan="2">Date</td></tr>
<tr><td>Total number of patients / participants for which responsible on specified date</td><td>Number</td><td colspan="2">Date</td></tr>
<tr><td colspan="2">ESTIMATED TIME PER WEEK [168 hours denominator]</td><td>Hours</td><td>%</td></tr>
<tr><td rowspan="2">Clinical trials</td><td>Clinical work (patient contact)</td><td rowspan="2"></td><td rowspan="2"></td></tr>
<tr><td>Administrative work</td></tr>
<tr><td rowspan="2">Organization (Practice/ university / employer)</td><td>Clinical work</td><td rowspan="2"></td><td rowspan="2"></td></tr>
<tr><td>Administrative work</td></tr>
<tr><td rowspan="2">Teaching</td><td>Preparation / evaluation</td><td rowspan="2"></td><td rowspan="2"></td></tr>
<tr><td>Lectures / tutorials</td></tr>
<tr><td>Writing up work for publication / presentation</td><td></td><td></td><td></td></tr>
</table>

Reading/sourcing information (e.g., internet searches)			
Others (specify)			

3.3 Details of Trial Site(s):
[*Name of site, physical address, contact details, contact person, etc*]

3.4 Capacity of Trial Site(s):
[*Number of staff, names, qualifications, experience – including study coordinators, site facilities, emergency facilities, other relevant infrastructure*]

PART 4: PARTICIPANTS (TRIAL SUBJECTS)

4.1 Number of local participants:
4.2 Total number of participants worldwide:
4.3 Total enrolment in each local site/Centre:
[*If competitive enrolment, state minimum and maximum number per site.*]
4.4 Volunteer base from which local participants will be drawn:
4.5 Retrospective data indicating potential of each site to recruit required number of participants within envisaged duration of trial:

PART 5: OTHER DETAILS

5.1 Provide an explanation if the trial is to be conducted locally only and not in the host country of the applicant / sponsor:
5.2 Estimated duration of trial:
5.3 Details of other Regulatory Authorities to which applications to conduct this trial have been submitted, but approval has not yet been granted. Include date(s) of application:
5.4 Details of other Regulatory Authorities which have approved this trial. Include date(s) of approval and number of sites per country:
5.5 Details of other Regulatory Authorities or Research Ethics Committees which have rejected this trial, if applicable, and provide reasons for the rejection:
5.6 Details of and reasons for this trial having been suspended at any stage by other Regulatory Authorities, if applicable:
5.7 Details if this trial is being undertaken in other SADC countries, any other country in Africa, or any country where there is no regulatory control of clinical trials:
5.8 Previous studies using this agent which have been approved by the Regulatory Authority:

Approval number:
Study title:

Protocol number:

Date of approval:

Principal Investigator:

Date(s) of progress report(s):

Date of final report:

5.9 If any sub-studies are proposed as part of this protocol, indicate whether these will also be conducted locally. If not, please explain:

PART 6: ETHICS

6.1 Research Ethics Committee responsible for each site, date of approval or date of application:
[*Attach copy of response(s) made by, and/or conditions required by Research Ethics Committee(s) if available*]

6.2 State which Good Clinical Practice (GCP) guidelines are being followed:

6.3 Details of capacity building component of the trial, if any.

6.4 Details of GCP training of investigators, monitors, study co-coordinators in terms of conducting this trial:

6.5 Details safety and monitoring plan for each site:
[*Attach as an appendix if necessary*]

6.6 Details of trail insurance:
[*e.g., insurer, policy holder, policy number, insurance cover, period of validity*]

6.7 Details of possible conflict of interest of any person(s)/organization(s) who/which will be involve in the trial:

6.8 Remuneration to be received by investigators, trial participants or others:
[*Indicate breakdown of costs to be covered, if applicable. Indicate compensation to be received by participants for travel and incidental expenses.*]

SECTION 3 – APPLICANT'S REPORT / PRESENTATION

[*Please use Black 12-point Arial Font, using MS Word for the electronic version*]
[*The following section should be fully completed*]

1. Title:

2. Protocol Number/Identification:

3. Summary of the Rationale for study:
   [*Provide a brief description of the rationale and relevance of the study, e.g. why should this trial be undertaken at all?*]

4. Summary of the Background Information:

[*Provide a brief statement on each of the following:*]
Disease/problem
Local relevance (e.g. local epidemiology)
Properties of trial medicine (e.g. pharmacological/chemical/pharmaceutical)
Pre-clinical findings: (e.g. laboratory/animal/ toxicity/mutagenicity, etc)
Clinical findings (e.g. pharmacokinetics, safety, tolerability, efficacy)

5. Objectives of study:

6. Study design:

[*These should be clearly described, and each component justified. Include study phase, use of placebo, dosages, randomization, blinding, duration of treatment, etc.]*

7. Trial Participants:

[*Number of participants; ability to enroll required number within stated time, etc*]

8. Criteria for selection, eligibility, and enrolment:

[*Inclusion and exclusion criteria listed and justified*]

9. Treatment modalities and regimens, medicine accountability:

[*These should be clearly explained and justified for all participant groups/arms, e.g. route of administration, dose, etc. Clearly describe medicine accountability*]

10. Outcome measurements/variables:

[*These should be clearly stated and justified*]

11. Adverse events:

[*Measures to monitor, assess and report all adverse events should be clearly stated and justified*]

12. Statistical measures:

[*Provide a clear and justified description of the following:*]

Determination of sample size
Statistical method(s) and analysis of quantitative measures
Statistical method(s) and analysis of qualitative measures
Data processing (*e.g., how, where, when, who)*
Interim analysis and stopping rules if applicable

13. Ethical Issues:

[*The following additional information, in respect of the proposed trial, is required:*]

- Comment on which GCP Guidelines are being followed
- Comment on choice of investigators
- Comment on need for appropriateness of, and relevance of GCP training/updating/for staff involved in this trial
- Comment on capacity building element of trial
- Comment on resources of sites and sponsor
- Comment on monitors and monitoring plan
- Indicate how additional staff (monitors, pharmacists, nursing staff, etc.) will maintain patient confidentiality, follow the protocol, and abide by ethical and regulatory requirements
- Comment on insurance and indemnity measures
- Comment on availability and completeness of separate Patient Information leaflets and Informed Consent forms for any proposed archiving of biological specimens for later research or for genetics research.
- Comment on ethics of the publication policy
- Comment on treatment and/or management of participants and their disease condition(s) after completion of trial
- Comment on ethics committee capacity to monitor sites and conduct of trial
- Provide an explanation if minimum recommended compensation for participants is not being provided.

14. Other relevant information not included above:
    - Are references adequate and dates of references current?
    - Are there discrepancies between the protocol and investigator's brochure or package inserts?
    - Are there specific explanation(s) for these discrepancies?
    - Other comments on this trial.

For Office use:

Reviewer's questions and concerns to be considered and/ or forwarded to applicant:

Reviewer's recommendation:

Declaration of conflict of interests by reviewer (if applicable):

Signature of reviewer: *Date:*

CHECKLIST FOR APPLICATION TO CONDUCT A CLINICAL TRIAL

The following are the requirements when submitting an application to conduct a clinical trial:

i. Cover letter including list of documents submitted and their version number and date
ii. Completed clinical trial application form including cover page
iii. Clinical trial protocol including site specific addendums
iv. Informed consent form(s)
v. Product information if the investigational medical product is registered: summary of product characteristics, patient information leaflet/package insert, and labelling
vi. Investigator's brochure
vii. If applicable, synopsis of previous trials with the investigational medical product(s)
viii. If applicable, electronic copies of key peer reviewed publications to support the application.
ix. Copy/ies of patient recruitment advertisement(s) (if applicable) and questionnaires
x. Investigational medical product dossier (If applicable)
xi. Product information and certificate of analysis for the concomitant and rescue medications
xii. GMP certificate for the site(s) producing the IMP(s)2
xiii. Certificate(s) of analysis of the IMP(s)
xiv. Certificate(s) of accreditation for the central laboratories
xv. Signed declaration by the national principal investigator
xvi. Workload forms for investigators
xvii. Signed curriculum vitae for all key staff participating in the conduct of the clinical trial, e.g., national principal investigator, principal and/or co-investigators, study coordinator, regional and local monitor, contract research affiliate, etc.
xviii. Signed declaration(s) by each investigator(s)
xix. Signed joint financial declaration between the sponsor and the national principal investigator
xx. Signed declaration by the sub-investigators and key staff participating in the clinical trial
xxi. Signed declaration by the regional monitor(s)
xxii. Proof of registration on PACTR or other WHO primary accessible registry
xxiii. Active clinical trials insurance (Phase I, II, III)
xxiv. Proof of sponsor indemnification for investigators and trial site
xxv. GCP certificates for the investigators
xxvi. Proof of registration of the key investigators with a professional statutory body (if applicable)
xxvii. Proof of professional indemnity (malpractice insurance)
xxviii. Study budget
xxix. Evidence of submission to the national ethics committee
xxx. Data Safety Monitoring Board charter and composition
xxxi. Proof of Payment from BoMRA

FORM 10

(An application in terms of Section 62, 66, and 55 of the Medicines and Related Substances Act, 2025)

APPLICATION FOR IMPORT PERMIT

Application to be sent to:

Botswana Medicines Regulatory Authority
Private Bag 2,
GABORONE
Tel: +2673731720/43/44

Attention: Director, Licensing and Enforcement
Proforma invoice, proof of payment and this application form in editable format to be emailed ahead to impex@bomra.co.bw prior to submission of hard copies

1. Full name and address of importing company:

   _____

   _____

2. License number: _____ Authorised Person: _____
3. Tel: _____fax: _____email: _____

Type of business: _____
(Specify Wholesale/Pharmaceutical Manufacturer /Other)

hereby apply for permit to import pharmaceutical products into Botswana.

4. Full name and address of supplier in exporting country

   _____

   _____

   Tel: _____ Fax: _____ email: _____

5. Purpose for which the medicines are required:
   (Tick whichever is applicable)

[ ] Registration samples
[ ] Patient exemption
[ ] Bulk exemption
[ ] Clinical trials
[ ] Wholesaling and distribution
[ ] Veterinary use only
[ ] General medical use;

Other_____ (Specify)

6. Attached herewith the Proforma Invoice/Purchase Order No _____ Date_____

7. Method of transportation: road [ ]/rail [ ]/ airfreight [ ]

8. Port of entry _____ Expected date _____

9. Details of medicines to be imported as quoted in the PO:

Item No.	Trade Name of Medicine	International Non-Proprietary Name (INN) of medicine	Strength	Total Quantity	Name and Address of Manufacturer	Product Registration Number	Schedule No.

Declaration:
I certify that the information provided in the application form and proforma invoice is true and correct.

Date of application_____ Signature of Applicant_____

FOR OFFICIAL USE ONLY:

Received by: _____Signature: _____

APPLICATION APPROVED [ ]/REJECTED [ ] If rejected issue Rejection Form

RECOMMENDED_____

___

APPROVED_____

___

PERMIT No. _____ ISSUED

ON_____

____(DATE)

SIGNED _____

For/CHIEF EXCECUTIVE OFFICER
BOTSWANA MEDICINES REGULATORY AUTHORITY

Stamp

FORM CT-04

(reg. 51)

APPLICATION FOR SUBSTANTIAL AMENDMENT

REFERENCE/TRACKING NUMBER FOR THIS CORRESPONDENCE: Click or tap here to enter text.

APPLICATION FOR APPROVAL OF:

☐ **PROTOCOL AMENDMENT**
☐ **INCREASE IN NUMBER OF PATIENTS PARTICIPATING**
☐ **CHANGES IN DOSE / REGIMENT OF STUDY DRUG**

STUDY TITLE: Click or tap here to enter text.

PROTOCOL NUMBER: Click or tap here to enter text.
DATE: Click or tap here to enter text.

1. APPLICANT

Name: Click or tap here to enter text.
Address: Click or tap here to enter text.
Telephone: Click or tap here to enter text.
Fax Number: Click or tap here to enter text.

1.1 Local Sponsor Company details (if applicable):

Name: Click or tap here to enter text.
Address: Click or tap here to enter text.
Telephone: Click or tap here to enter text.
Fax Number: Click or tap here to enter text.

1.2 Name, designation, and qualifications of person representing the Applicant:

Name: Click or tap here to enter text.
Designation: Click or tap here to enter text.
Qualification: Click or tap here to enter text.

1.3 National Coordinator

Name: Click or tap here to enter text.
Address: Click or tap here to enter text.
Telephone: Click or tap here to enter text.
Fax Number: Click or tap here to enter text.

1.4 International Principal Investigator

Name: Click or tap here to enter text.
Address: Click or tap here to enter text.
Telephone: Click or tap here to enter text.
Fax Number: Click or tap here to enter text.

1.5 Name of sponsor:

Name: Click or tap here to enter text.
Address: Click or tap here to enter text.
Telephone: Click or tap here to enter text.

Fax Number: Click or tap here to enter text.

2. TRIAL PARTICULARS (original application)

2.1 **Trial Approval Number:**
Click or tap here to enter text.

2.2 **Date of Approval of original protocol:**
Click or tap here to enter text.

2.3 **Number of local Investigators approved for this trial:**
Click or tap here to enter text.

2.4 **Number of local sites approved for this trial:**
Click or tap here to enter text.

2.5 **Number of participants approved for this trial:**
Click or tap here to enter text.

3 AMENDMENT PARTICULARS

Does the applicant wish to increase the number of local subjects participating in this trial?

Yes ☐
No ☐

Does the applicant wish to change the dose / regimen of the study drug?

Yes ☐
No ☐

Does this amendment request require a new consent form to be signed by the participant?

Yes ☐
No ☐

If **"Yes"** please submit new PIL together with this application.

3.1 Protocol Amendment Number:
Click or tap here to enter text.

3.2 Version Number and Date of Protocol Amendment (for each document submitted):
Click or tap here to enter text.

3.3 General motivation for the proposed Amendment:
Click or tap here to enter text.

3.4 Details of the proposed Protocol Amendment:
Click or tap here to enter text.

3.5 Will this Amendment apply to all approved investigators/sites:

YES ☐

NO☐

If NO: Specify the investigator(s) / site(s) for which the Amendment will apply:

Click or tap here to enter text.

4. ETHICS COMMITTEE APPROVAL

4.1 Have the Research Ethics Committee(s) responsible for each centre to which this amendment applies been notified?

Click or tap here to enter text.

4.2 Research Ethics Committee(s) responsible:

Click or tap here to enter text.

4.3 Date of application to Ethics Committee:

Click or tap here to enter text.

4.4 Date of approval by Ethics Committee:

Click or tap here to enter text.

I ……, the undersigned, agree to conduct / manage the above-mentioned trial under the conditions as stated in this application. (The person(s) undertaking legal responsibility to sign this form).

_____ _____

Applicant (local contact) Date

CTA Reference No:	
Protocol No:	
Protocol Title:	
Sponsor:	
Amendment No:	
Date of Amendment:	
Type of Amendment:	

DESCRIPTION OF AMENDMENT

Provide a detailed description of the amendment(s) and the reasons therefor:

ASSESSMENT OF IMPACT

Does the amendment affect:	Yes	No
Participant safety or animal welfare?		
Scientific validity of the trial?		
Conduct or management of the trial?		
Quality or interpretation of data?		
Informed consent or animal owner consent?		

DOCUMENTS SUBMITTED

□ Amended protocol (tracked changes and clean version)

□ Amended informed consent / animal owner consent form(s)

□ Amended investigator's brochure

□ Updated safety data

□ Ethics Committee / DVS approval for amendment

□ Other (specify): _____

DECLARATION

I, the undersigned, hereby declare that this amendment has been classified as substantial and that the information provided is complete and accurate.

_____

Sponsor / Applicant

_____ _____

Signature Date

FOR OFFICIAL USE ONLY	
Date application received:	

Tracking/Reference No:	
Application fee paid:	
Received by (Name):	
Signature:	

FORM CT-05

(reg. 57)

Instructions: Complete entire form. Do not leave any blank spaces

Reporting period: Fatal or life-threatening SAEs should be reported to BoMRA within 24 hours by e-mail followed by a complete report within 72 hours.

Please use a separate adverse event reporting form for separate reportable adverse events

HRDC Protocol #:		***Institution***	
BoMRA Protocol #			
Principal Investigator:		***Phone:***	
		Email:	
Report prepared by:	***Designation in the study:***	***Date Form completed***	

Study Title:	
Study Sponsor:	

Date of Adverse Event:	**Participant ID:**	**Sex:**	**Type of Report:**
			Initial *Follow-up* *Resolution*
Date of Site Awareness:	**Date of Birth:**		
		1. Male 2.Female	*Study week:-*
			Visit number:-

1a. What type of SAE, is it:

1. Fatal
2. Life-threatening (an actual risk of death at the time of the event).
3. Caused or prolonged hospitalization (non-elective).
4. Resulted in persistent or significant disability or incapacity.
5. Congenital anomaly/birth defect
6. Any other important medical event.

1b. Toxicity Grade: Grade 1 Grade 2 Grade 3. Grade 4 Grade 5

2a. Any previous Adverse Event's report on this participant?: Yes No	**If yes, how many?**	
2b. Total Number of SAEs to date for the whole study:		

3. Location of the current Adverse Event:

1. Home 2. Clinic/Hospital 3. Work 4. Study site 5. Other, specify:

4. Research involves a: **1.** Drug 2. Device 3. Procedure 4. Vaccine 5. Other	**5. Name of Drug, Device or Procedure:**

6. Is the drug/device investigational: Yes No

7. List all study / intervention drugs being taken at the time of onset of the SAE, or within 30 days prior to onset, and describe their relationship to the SAE:

Drug/ Device/Vaccine	Dose	Route	Schedule	Date commenced	Taking drug at onset of SAE	Relationship of SAE to drug					
						Definitely related	Probably related	Possibly related	Probably not related	Not related	Pending
					Yes No						
					Yes No						
					Yes No						

8. Was the patient taking any other drug at the time of onset of the AE? …… Yes No

9. If yes, then list all concomitant medication being taken at least one month before the onset of the SAE and describe the relationship to the SAE:

Concomitant medication	Date commenced	Relationship of SAE to medication					
		Definitely related	Probably related	Possibly related	Probably not related	Not related	Pending
					.		

10. Has the Adverse Event been reported to:	(a) BoMRA	(b) HRDC	(c) Sponsor	(d) IRB
	Yes No	Yes No	Yes No	Yes No
If YES, Date of reports:				

11. Describe the SAE with diagnosis, immediate cause or precipitating events, symptoms, any investigations, management, results and outcome (with dates where possible). Include relevant medical history. Additional narrative, photocopies of results of abnormal investigations and a hospital discharge letter may be attached:

Summary of relevant past medical history of participant	
(a) Diagnosis :	
(b) Immediate Cause:	
(c) Symptoms:	

(d) Investigations-Laboratory and any other significant investigations conducted:	

Lab test	Abnormal Result	Site Normal Range	Collection date	Lab value previous or subsequent to this event	Collection date

(e) Results:	
(f) Management (Include management of study treatment, continued, temporarily held, reduced dose, permanent discontinuation, off Product):	
(g) Outcome:	

NB If the outcome is death, please complete & attach the death form.

12.D

D1. Was this Adverse Event originally addressed in the protocol and consent form? Yes No N/A

D2. Was this Adverse Event originally addressed in Investigators Brochure? Yes No N/A

D3. Are changes required to the protocol as a result of this SAE? Yes No N/A

D4. Are changes required to the consent form as a result of this SAE? Yes No N/A

If changes are **required** on the protocol/consent Yes/No

If changes are **not required**, please explain as to why changes to the protocol /consent form are not necessary based on the event.

From the data obtained or from currently available information, do you see any need to reassess the risks and benefits to the subjects in this research. Yes No

_____ P.I. Signature

_____ Date

SUSPECTED UNEXPECTED SERIOUS ADVERSE REACTION (SUSAR) REPORT

CTA Reference No:	
Protocol No:	
Protocol Title:	
Sponsor:	
Report type (Initial/Follow-up):	
SUSAR Reference No:	
Date of this report:	
Date sponsor became aware:	

PARTICIPANT / ANIMAL DETAILS

Subject identification No:	
Type of trial (Human/Veterinary):	
Age / Species and breed (if animal):	
Sex:	
Weight:	
Trial site:	
Investigator:	

ADVERSE REACTION DETAILS

Description of reaction:	
Date of onset:	
Seriousness criteria:	
Outcome (recovered / not recovered / fatal / unknown):	

Date of outcome:	

SERIOUSNESS CRITERIA (tick all that apply)

□ Results in death

□ Life-threatening

□ Requires hospitalisation or prolongation of hospitalisation

□ Results in persistent or significant disability or incapacity

□ Congenital anomaly or birth defect

□ Other medically important event

INVESTIGATIONAL PRODUCT DETAILS

Product name and dose:	
Route of administration:	
Date of first dose:	
Date of last dose:	
Batch number:	
Action taken with product:	
Causality assessment:	

NARRATIVE

Provide a detailed narrative of the event, including relevant medical/veterinary history, concomitant medications, and clinical course:

_____

Reporter (Name, Designation)

_____ _____

Signature Date

FORM CT-06

(reg. 61)

ANNUAL PROGRESS REPORT

Title of the Protocol	
Protocol Number	
Date of BoMRA approval	
Date of Ethics Committee approval	
Name of Principal Investigator	
Name of Co-Investigator	
Date of Study initiation:	
Date of enrollment of first patient:	
Total number of patients screened:	
Total number of patients enrolled till date:	
Number of Patients withdrawn from the study. Reasons? (a. By the investigator; b. Voluntary; c. Due to SAE; d. Loss to follow-up; e. Other)	
Number of patients lost to follow up:	
Total number of patients completed the study:	
Date of last visit of the last patient:	
Number of Protocol Deviations reported:	

Serious Adverse Event reported from the site (if any) with details of Casualty assessment of PI & sponsor, Subject ID, Date of SAE:	
Adverse Event reported from the site (if any) with details of Subject ID, Date of AE:	
IMP Balance	

CTA Reference No:	
Protocol No:	
Protocol Title:	
Sponsor:	
Principal Investigator:	
Reporting period:	
Date of report:	
Current status of trial:	

TRIAL PROGRESS

	Planned	**Actual**
Number of participants/animals enrolled:		
Number of participants/animals completed:		
Number of participants/animals withdrawn:		
Number of SAEs reported:		
Number of SUSARs reported:		
Number of protocol deviations:		

SAFETY SUMMARY

Provide a summary of the safety profile of the investigational product during the reporting period, including any changes to the benefit-risk assessment:

PROTOCOL AMENDMENTS

List all amendments approved during the reporting period:

PROBLEMS AND DEVIATIONS

Describe any significant problems or deviations encountered:

_____

Sponsor / Applicant

_____ _____

Signature Date

_____

Principal Investigator

_____ _____

Signature Date

FORM CT-07

(reg. 54)

END OF TRIAL NOTIFICATION

End of Clinical Trial Study Report

STRUCTURE, CONTENTS AND FORMAT FOR CLINICAL STUDY REPORTS

1. Title Page:

This page should contain the following information

- Title of the study
- the protocol code
- name of the investigational product tested
- development Phase, indication studied
- a brief description of the trial design
- the start and end date of patient accrual
- the names of the Sponsor and the participating Institutes (Investigators)

2. Study Synopsis (1 to 2 pages):

A brief overview of the study from the protocol development to the trial closure should be given here. This section will only summarize the important conclusions derived from the study.

3. Statement of compliance with the 'Botswana Clinical Trial Guidelines on Human Participants'

4. List of Abbreviations and Definitions

5. Table of contents

- should include a list and the locations within the study report of appendices.

6. Ethics Committee:

This section should document that the study was conducted in accordance with the ethical principles of Declaration of Helsinki. A description of the Ethics Committee constitution and date(s) of approvals of trial documents for each of the participating sites should be provided. A declaration should state that EC notifications as per Good Clinical Practice Guidelines issued have been followed and the study was performed in compliance with ICH Good Clinical Practice (GCP) including the archiving of essential documents.

7. Study Team:

Briefly describe the administrative structure of the study (Investigators, site staff, Sponsor/ designates, Central laboratory etc.).

8. Introduction:

A brief description of the product development rationale should be given here.

9. Study Objective:

A statement describing the overall purpose of the study and the primary and secondary objectives to be achieved should be mentioned here.

10. Investigational Plan:

This section should describe the overall trial design, the Subject selection criteria, the treatment procedures, blinding / randomization techniques if any, allowed, disallowed concomitant treatment, the efficacy and safety criteria assessed, the data quality assurance procedures and the statistical methods planned for the analysis of the data obtained.

11. Trial Subjects:

A clear accounting of all trial Subjects who entered the study shall be given here. Mention should also be made of all cases that were dropouts or protocol deviations. Enumerate the patients screened, randomised, and prematurely discontinued. State reasons for premature discontinuation of therapy in each applicable case.

12. Efficacy evaluation

The results of evaluation of all the efficacy variables will be described in this section with appropriate tabular and graphical representation. A brief description of the demographic characteristics of the trial patients should also be provided along with a listing of patients and observations excluded from efficacy analysis.

13. Safety Evaluation:

This section should include the complete list of

- All serious adverse events, whether expected or unexpected and
- Unexpected adverse events whether serious or not

The comparison of adverse events across study groups may be presented in a tabular or graphical form, this section should also give a brief narrative of all important events considered related to the investigational product.

14. Discussion and overall Conclusion:

Discussion of the important conclusions derived from the trial and scope for further development shall be mentioned

15. List of References:

16. Appendices:

List of Appendices to the Clinical Trial Report

(a) Protocol and amendments

(b) Specimen of Case Record Form

(c) Investigators' name(s) with contact addresses, phone, e-mail etc.

(e) List of trial participants treated with investigational product

(f) Discontinued participants

(g) Protocol deviations

(h) CRFs of cases involving death and life threatening adverse event cases

(i) Publications from the trial

(j) Important publications referenced in the study

(k) Audit certificate, if available

(l) Investigator's certificate that he/she has read the report and that the report accurately describes the conduct and the results of the study.

CTA Reference No:	
Protocol No:	
Protocol Title:	
Sponsor:	
Principal Investigator:	
Date of first enrolment:	
Date of last participant/animal's last visit:	
Date of trial completion/termination:	
Reason for termination (if early):	

SUMMARY

Total number of participants/animals enrolled:	
Total number completed:	
Total number withdrawn:	
Total number of SAEs:	
Total number of deaths:	

POST-TRIAL ARRANGEMENTS

□ Participants/animals are receiving appropriate follow-up care

□ All investigational products have been accounted for

□ Data management activities are complete / in progress

□ Clinical trial report will be submitted by: _____

□ Results will be posted to clinical trial registry by: _____

□ Essential documents have been archived / will be archived by: _____

DECLARATION

I, the undersigned, hereby confirm that the above information is complete and accurate and that all obligations regarding the end of the trial will be fulfilled in accordance with the Clinical Trials Regulations, 2025.

_____

Sponsor / Applicant

_____ _____

Signature Date

FORM CT-09

(reg. 20)

APPLICATION FOR DIRECTOR OF VETERINARY SERVICES APPROVAL FOR VETERINARY CLINICAL TRIAL

In accordance with regulation 20 of the Clinical Trials Regulations, 2025, application is hereby made for approval to conduct a veterinary clinical trial.

SECTION 1: TRIAL DETAILS

Protocol title:	
Protocol number and version:	
Sponsor:	
Principal Investigator:	
Professional registration No (Veterinary Council):	
Trial site(s):	
Estimated duration:	
CTA Reference No (if issued):	

SECTION 2: ANIMAL DETAILS

Species:	
Breed:	
Age range:	
Number of animals:	
Source of animals:	
Food-producing animals (Yes/No):	
Ownership of animals:	

SECTION 3: THREE Rs PRINCIPLE STATEMENT

Replacement:

Explain why the use of live animals is necessary and whether alternative methods were considered:

Reduction:

Justify the number of animals to be used, including the statistical basis for the sample size:

Refinement:

Describe measures to minimise pain, suffering, distress and lasting harm, including anaesthesia, analgesia, humane endpoints and post-trial care arrangements:

SECTION 4: ANIMAL WELFARE MEASURES

Describe the housing, husbandry, nutrition and veterinary care to be provided to trial animals:

Describe the monitoring and assessment procedures for animal welfare during the trial:

Describe the humane endpoints and criteria for withdrawal of individual animals from the trial:

Describe arrangements for animals after completion of the trial:

SECTION 5: FOOD SAFETY (if applicable)

Where the trial involves food-producing animals, provide details of:

(a) Proposed withdrawal periods:

(b) Restrictions on the use of animal products during and after the trial:

(c) Arrangements for monitoring residue levels:

SECTION 6: DOCUMENTS SUBMITTED

□ Clinical trial protocol

□ Investigator's brochure

□ Three Rs Principle statement

□ Animal owner consent form

□ Animal welfare monitoring plan

□ Investigator's CV and professional registration

□ Site description and facilities

□ Insurance / indemnity arrangements

□ Proof of CTA application or CTA approval

DECLARATION

I, the undersigned, hereby declare that the information provided in this application is complete and accurate, and that the veterinary clinical trial will be conducted in compliance with the Three Rs Principle and all applicable animal welfare requirements.

_____

Principal Investigator

_____ _____

Signature Date

FOR DEPARTMENT OF VETERINARY SERVICES USE ONLY

Date received:	
Reference No:	
Decision (Approved / Approved with conditions / Refused):	
Conditions (if any):	
Reasons for refusal (if applicable):	
Authorised officer:	
Signature:	**Date:**

FORM CT-10

(reg. 22)

ANIMAL OWNER CONSENT FORM FOR VETERINARY CLINICAL TRIAL

SECTION 1: TRIAL INFORMATION

Protocol title:	
Protocol number:	
Investigator:	
Contact details of Investigator:	
Sponsor:	

SECTION 2: ANIMAL DETAILS

Species and breed:	
Age:	
Sex:	
Identification (tag, microchip, etc.):	
Name or description of animal:	
Number of animals enrolled:	

SECTION 3: OWNER DETAILS

Full name of owner:	
Omang/Passport No:	
Physical address:	
Postal address:	
Telephone / Cell:	
E-mail:	

SECTION 4: CONSENT

I, the undersigned, hereby confirm that:

1. I have been informed of the nature, purpose and expected duration of the clinical trial.

2. I have been informed of the procedures to be performed on my animal(s).

3. I have been informed of the reasonably foreseeable risks and potential discomforts to my animal(s).

4. I have been informed of the potential benefits to my animal(s).

5. I have been informed of available alternative treatments.

6. I have been informed of the arrangements for compensation in the event of trial-related injury, illness or death of my animal(s).

7. I understand that I may withdraw my animal(s) from the trial at any time without penalty or loss of benefits to which my animal(s) would otherwise be entitled.

8. I have been informed of any restrictions on the use of my animal(s) or their products during and after the trial, including any applicable withdrawal periods.

9. I have had the opportunity to ask questions and have received satisfactory answers.

10. I voluntarily consent to the enrolment of my animal(s) in this clinical trial.

_____ _____

Full Name of Owner Date

_____

Signature of Owner

_____ _____

Name of Witness Date

_____

Signature of Witness

_____ _____

Name of Investigator Date

_____

Signature of Investigator

FORM CT-11

(reg. 26)

VETERINARY CLINICAL TRIAL ADVERSE EVENT REPORT

CTA Reference No:	
Protocol No:	
Protocol Title:	
Sponsor:	
Investigator:	
Trial site:	
Report type (Initial / Follow-up):	
Report reference No:	
Date of this report:	

ANIMAL DETAILS

Animal identification No:	
Species and breed:	
Age:	
Sex:	
Weight:	
Owner name:	
Food-producing animal (Yes/No):	

ADVERSE EVENT DETAILS

Description of event:	
Date of onset:	
Severity (mild / moderate / severe):	
Seriousness (serious / non-serious):	

If serious, criteria met:	
Outcome (recovered / not recovered / euthanised / died / unknown):	
Date of outcome:	
Treatment given for event:	

TYPE OF EVENT (tick all that apply)

□ Unexpected death

□ Serious adverse reaction

□ Lack of expected efficacy

□ Adverse reaction in human handler

□ Environmental incident

□ Other (specify): _____

INVESTIGATIONAL PRODUCT DETAILS

Product name and dose:	
Route of administration:	
Date of first dose:	
Date of last dose:	
Batch number:	
Action taken with product:	
Causality assessment (related / possibly related / unrelated / unknown):	

NARRATIVE

Provide a detailed narrative of the event, including relevant animal history, concomitant treatments and clinical course:

_____

Investigator

_____ _____

Signature Date

Copy to: (1) Sponsor; (2) Botswana Medicines Regulatory Authority; (3) Department of Veterinary Services