MEDICINES CONTROL AGENCY

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GUIDELINE FOR CLINICAL TRIALS IN HUMANS

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TABLE OF CONTENTS

1 INTRODUCTION

1.1 Legal Basis

1.1.1. The regulation of clinical trials of medicines and related products in The Gambia is governed by the provisions and requirements of the Medicines and Related Products Act, 2014 ("Act") as mandated by the Medicines Control Agency (MCA).

1.1.2. Part VII of the Act, *Clinical Trials and Safety Monitoring*, requires that a person shall not conduct a clinical trial of a medicine or related product without the written authorisation of the Agency.

1.1.3. The Medicines and Related Products Regulations, 2020 ("Regulations") details the legal requirements for clinical trial oversight.

1.1.4. The clinical trial of any investigational product (IP) may only be conducted on humans in The Gambia where:

(a) the foreseeable risks and inconveniences are medically justifiable when compared with the benefit on the participant, and the anticipated significance of the investigational product for the advance of medical science; and

(b) unjustifiable harmful effects on the health of a third person and the environment, are not to be expected if the clinical trial consist of genetically modified organism, a combination of genetically modified organisms, contains any other organisms;

(c) the trial subject-

(i) is an adult and has been informed in a language that he or she understands, of the nature, significance and implications of the clinical trial,

(ii) has provided voluntary written informed consent with a signature or a thumb-print on the consent form,

(iii) is a minor or an incapacitated person, and his or her parents or legal guardians have been informed of the nature, significance and implications of the clinical trial and have provided a written voluntary informed consent and assent,

(iv) is informed of his or her right to withdraw from the clinical trial at any time,

(v) is provided with an information sheet with the risks associated to the clinical trials,

(vi) undergoes a counselling session with an investigator or a person designated by the investigator, and

(vii) is informed of the purpose and scope of the collection and use of personal data, especially medical data for the purposes of the trial.

(viii) is unable to read or write English, the informed consent shall be obtained in the presence of at least one impartial witness. The witness, who shall be able to read and write English and understand the local language in which the trial subject is informed, shall not be a member of the investigating team. The consent given by the trial subject shall be documented in

writing, dated and signed by the witness and thumb printed or signed by the trial subject.

(d) a declaration of consent to participate in a clinical trial, may be revoked orally or in writing at any time without prejudice to the trial subject, and the data collected and stored data may continue to be used where necessary;

(e) the trial is conducted in a high-quality facility by a qualified PI in a professional manner who possesses the required educational training and professional experience to be determined by the Agency to conduct a clinical trial;

(f) insurance coverage is provided for the trial subject in the event of an injury or death related to the clinical trial;
Note: The sponsor and PI shall ensure appropriate insurance cover for clinical trial subjects. The insurance policy shall grant specific cover associated with the reimbursement of damages and death caused to subjects by the clinical trial activities throughout the entire study period, thus covering any civil liability of investigators and sponsor of the clinical trial.

(g) advantages are not granted to the trial subject with the exception of adequate compensation;

(h) a medical doctor is responsible for the enrolment and medical care of the trial subject.

1.1.5. A **person** (PI, investigator(s), pharmacist, study nurse or any other study staff) involved in a clinical trial of an investigational product on humans, shall fulfill the requirements of:

(a) Good Clinical Practice provided under the International Council for Harmonisation Guideline for Good Clinical Practice E6 (R2) (“ICH-E6 GCP-Guideline”);

(b) The WHO guidelines for Good Clinical Practice for trials on pharmaceutical products; and

(c) any other requirements to be determined by the Agency.

1.1.6. If a marketing authorisation by MCA for a novel medicine or related product is anticipated, the pivotal clinical trials may be conducted in The Gambia. At least the safety and efficacy of the medicine or related product should have been established in previous clinical trials involving subjects of similar ethnic or environmental background to the intended population in The Gambia.

1.1.7. The Agency charges non-refundable fees for clinical trials, including applications, protocol amendment(s) and IP import permit clearance as specified in the MCA Fee Schedule.

1.1.8. Applicants are required to familiarise themselves with this document and the above stated Act and Regulations before applying for a clinical trial.

1.2 Interpretation and Abbreviations

Interpretations and abbreviations contained in the MCA Glossary can be found on the MCA Website: **www.mca.gm**

The interpretation of terms provided in the Act and Regulations apply, unless further defined in this guideline.

Applicant means sponsor or sponsor 's representative, principal investigator (PI) or sponsor-investigator.

Assent means that the trial subject who is a minor aged between 12 and 17 years agrees to participate in the clinical trial; it is required in addition to the consent of the legal guardian of the trial subject.

Auxiliary medicine or Non-Investigational Medicinal Product (NIMP)
Medicines used in the context of a clinical trial (but not as investigational medicinal products), such as medicines used for background treatment to ensure that adequate medical care is provided for the subjects, challenge agents, rescue/escape medication, or used to assess end-points in a clinical trial.

Concomitant Medication is medication unrelated to the design of the clinical trial, and which is permitted or not permitted before and/or during the trial and their time restrictions.

Food/Dietary or Nutritional Supplement means concentrated sources of nutrients or other substances produced in a pharmaceutical dosage form such as tablets, gelatine capsules (soft or hard), sachets, syrups and powders. Dietary components include herbs, vitamins and minerals (with concentration less than the recommended daily allowance), natural oils, royal jelly, pollen and bee propolis. All these ingredients can be included in dietary supplements on the condition that their sole function is supplementation and improvement of body function.

Food means a substance consisting essentially of protein, carbohydrate, fat, and other nutrients used in the body of an organism to sustain growth and vital processes and to furnish energy

Indemnity means provision of legal and financial coverage for the investigator or the institution against claims arising from the clinical trial, except for claims that arise from malpractice and/or negligence.

Informed Consent means a process by which an adult subject competent to make the decision voluntarily confirms his or her willingness to participate in a particular research study, after having been informed of all aspects of the study that are relevant to the subject's decision to participate

Investigational Product (IP) means any product used in a clinical trial including medicine, herbal medicine, nutritional supplement, homeopathic medicines, food and food/dietary or nutritional supplements, medical device, diagnostics, cosmetics and any other related product.

Investigational Medicinal Product (IMP) means a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved

indication, or when used to gain further information about an approved use.

Legal Guardian means a person who is the guardian of a child (aged <18 years) by virtue of the provision the Children's Act 2005 or a person lawfully appointed to be guardian of the child by Deed or Will or by an order of a court of competent jurisdiction or by operation of law.

Non-interventional study means a study where the medicine is prescribed in the usual manner in accordance with the terms of the marketing authorisation. The assignment of the patient to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within current practice and the prescription of the medicine is clearly separated from the decision to include the patient in the study. No additional diagnostic or monitoring procedures shall be applied to the patients and epidemiological methods shall be used for the analysis of collected data.

CoA	Certificate of Analysis
CRO	Contract Research Organisation
DSMC	Data Safety Monitoring Committee, also Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC)
GCP	Good Clinical Practice
IB	Investigator's Brochure
ICH	International Council for Harmonisation (*previous:* International Conference on Harmonisation)
IMP	Investigational Medicinal Product
IMPD	Investigational Medicinal Product Dossier
IND	Investigational New Drug
IP	Investigational Product
MCA	Medicines Control Agency
MDCG	Medical and Dental Council in The Gambia
MTA	Material Transfer Agreement
PACTR	Pan African Clinical Trials Registry
PI	Principal Investigator
SmPC	Summary of Products Characteristics

1.3 Purpose

1.3.1. In pursuance of the law this document provides guidance to sponsors and investigators on the procedures for applications and conduct of clinical trials in The Gambia including reporting to the MCA.

1.4 Scope

1.4.1. This guideline applies to any investigational product to be used in a clinical trial as defined in this guideline, the Act and Regulations; whether they are unauthorised or marketed products, and to non-investigational products used in the context of a clinical trial (auxiliary medicines), and

to non-interventional/observational clinical studies that involve the use of a medicine or related product.

1.4.2. It does not apply to epidemiological studies.

2 GENERAL CONDITIONS FOR CLINICAL TRIALS

2.1 Classification of Clinical Trials

2.1.1. Clinical trials of medicines in humans are generally classified into Phases I to IV. It is not possible to draw distinct lines between the phases, and diverging opinions about details and methodology do exist. A brief description of the individual phases, based on their purposes as related to clinical development of medicines, is given below:

Phase I

2.1.2. These are the first trials of a new active ingredient or new formulation in humans, often carried out in healthy volunteers (20-100). Their purpose is to establish a preliminary evaluation of the safety, and the pharmacokinetic and, where possible, a pharmacodynamic profile of the active ingredient in humans.

Phase II

2.1.3. These trials are performed in a limited number of subjects (100-300) and are often, at a later stage, of a comparative (e.g. placebo-controlled) design. Their purpose is to demonstrate therapeutic activity and to assess short-term safety of the active ingredient in subjects suffering from a disease or condition (or to prevent the disease or condition in case of vaccines) for which the active ingredient is intended. This phase also aims at the determination of appropriate dose ranges or regimens and (if possible) clarification of dose-response relationships in order to provide an optimal background for the design of extensive therapeutic trials.

Phase III

2.1.4. These are trials in larger (300-3000) and possibly varied subject groups with the purpose of determining the short and long-term safety/efficacy balance of formulation(s) of the active ingredient, and of assessing its overall and relative therapeutic value. The pattern and profile of any frequent adverse reactions must be investigated and special features of the product must be explored (e.g. clinically-relevant drug interactions, factors leading to differences in effect such as age). These trials should preferably be of a randomised double-blind design, but other designs may be acceptable, e.g. long-term safety studies. Generally, the conditions under which these trials are carried out should be as close as possible to normal conditions of use.

Phase IV

2.1.5. These are studies performed after marketing of the medicine. Trials in phase IV are carried out on the basis of the product characteristics for which the marketing authorisation was granted and are normally in the form of post-marketing surveillance, or assessment of therapeutic value or treatment strategies. Although methods may differ, these studies should use the same scientific and ethical standards as applied in

premarketing studies.
Note: After a product has been placed on the market, clinical trials designed to explore new indications, new methods of administration, new combinations, etc. are normally considered as trials for new medicines.

2.2 Application for a Clinical Trial Authorisation

2.2.1. Before commencing a clinical trial in The Gambia, the applicant must obtain a favourable opinion from a nationally established health research Ethics Committee and approval from MCA. An application for a clinical trial can be made to the Ethics Committee and the Agency in either a parallel or sequential submission.

2.2.2. The fee for an application is due at the time of submission of an application.

2.2.3. The application form (MCA-F-501/01), which is available from the MCA website: **www.mca.gm**, must be completed and duly signed and dated by the applicant.

2.2.4. All documentation submitted shall be in English. If documents are written in another language, including e.g. product information for auxiliary medicines, a certified translation is required.

2.2.5. The documents must be submitted electronically in searchable PDF files (email, CD or USB Flash Drive) **and** in hard copy, one (1) of each document.

2.2.6. The hard copies and the CD or USB Flash Drive should be submited by hand delivery or by post to:
Executive Director, Medicines Control Agency, 54 Kairaba Avenue, K.S.M.D, P.O. BOX 3162, The Gambia.

2.2.7. The hard copies should be provided in an organised and structured manner as in file or ring binder(s) clearly indicating the contents of the dossier.

2.2.8. The application will **only be processed after receipt** of the hard copies of the documents.

2.2.9. The applicant shall submit the following documents as part of the clinical trial application dossier:

2.2.9.1. **Cover letter** signed by the applicant; its subject line should contain the invariable sponsor protocol number (clinical trial identification number) with the title of the trial;

2.2.9.2. Completed **Clinical Trial Application Form**, signed by the applicant;

2.2.9.3. **Proof of payment** of the non-refundable application fee;

2.2.9.4. **Clinical Trial Protocol** whose contents and format should follow the requirements as laid down in the International Council for Harmonisation Guideline for Good Clinical Practice. It shall include site specific addendums and be signed and dated by the sponsor or sponsor's representative and PI showing their agreement and committment to the protocol;

2.2.9.5. The protocol should contain a statement that the trial will be

conducted in compliance with the protocol, GCP and the applicable regulatory requirements. If the protocol does not contain such statement or if it contains the statement but is not signed and dated by both parties, a corresponding declaration, signed and dated by both parties shall be provided to the MCA with the application.

2.2.9.6. The name, position and full contact details of the **Sponsor**.

2.2.9.7. The name, position and full contact details of the **PI** who will be responsible for the site(s) where the trial is to be conducted in The Gambia and shall be:

- registered with the relevant statutory health council;
- resident in The Gambia; and
- where the PI is not a medical doctor registered with the Medical and Dental Council in The Gambia (MDCG), he/she must ensure that a MDCG registered medical doctor is responsible for the enrolment of trial subjects and for all trial-related medical decisions including medical care.

If the PI is absent from the site, he/she must delegate his/her duties in writing to an adequately trained and experienced investigator.

The PI should have sufficient education, training and experience in the conduct of clinical trials (e.g. acted as PI or as an investigator in at least one prior clinical trial).

2.2.9.8. **Favourable opinion of the Ethics Committee**. In case of parallel submission, a copy of the application letter to the Ethics Committee and favourable opinion when received including updated versions of documents or information as requested by the Ethics Committee; **Note:** The Agency can reach a decision on the application for a clinical trial only when those documents are provided and the favourable opinion of the Ethics Committee is provided.

2.2.9.9. **Informed consent form, assent form(s) and participant information sheet** as applicable, and its translation into local languages, where applicable (e.g. audio translation, adapted pictorial images for children, etc);

2.2.9.10. **Schematic diagram or flow-chart** of trial design, procedures and stages, if not contained in the protocol;

2.2.9.11. **Certificate of Insurance Cover** as evidence of insurance cover for subjects or proof of indemnity provision for investigators and trial site (see MCA-T-501/04) or equivalent;

2.2.9.12. Signed joint **financial declaration** between the sponsor, funding body, if applicable, and the PI concerning sufficient funds to complete the study (see MCA-F-501/05) or equivalent. Where the clinical trial is sponsored by an **individual**, the applicant shall prove the availability of funds to conduct the trial;

- co-sponsoring by an institution recognised by the Agency where applicable; and
- any other conditions as determined by the Agency.

2.2.9.13. **Investigator's Brochure (IB)** whose contents and format should

follow the requirements as laid down in the International Council for Harmonisation Guideline for Good Clinical Practice. It shall contain a description and brief summary of the relevant chemical, physical and pharmaceutical properties of the IP, and a compilation of the nonclinical and clinical data on the IP relevant to the clinical trial to allow investigators to reach a decision on the safety of its use in the proposed clinical trial. The IB should be reviewed at least annually and submitted to MCA.

2.2.9.14. **Investigational Medicinal Product Dossier (IMPD)** or equivalent, as applicable; it shall give detailed information on the quality of any investigational medicinal product including the manufacture and its controls, and data from non-clinical studies and from previous clinical studies, if any. The non-clinical and clinical information shall include data providing sufficient detail to allow assessors to reach a decision on the potential toxicity of the investigational medicinal product. If the IMP is a placebo, the information requirements shall be limited to quality data.
Note: The IMPD can be submitted directly by the sponsor to the MCA for confidentiality reasons.

2.2.9.15. **Summary of Products Characteristics (SmPC)** or equivalent professional product information for all marketed/registered products used in the trial; if the IMP is used in accordance with the marketing authorisation or registration, an IB or IMPD is not required. If a comparator other than placebo is used that is not a marketed, registered product in The Gambia, a justification is required.

2.2.9.16. Synopsis of previous trials with the investigational product(s), if applicable and not contained in the protocol or IB;

2.2.9.17. Electronic copies of literature that are relevant to the clinical trial, and that provide background for the clinical;

2.2.9.18. Copy/ies of recruitment advertisement(s) and questionnaires, if applicable;

2.2.9.19. **Good Manufacturing Practice (GMP)** certificate(s) for IMPs which must be issued from the National Regulatory Authority of the country where the investigational medicinal products, including comparator and placebo, are manufactured. If the GMP certificate is not available for justifiable reasons, sufficient information must be provided that will satisfy the Agency that the product has a defined quality and is safe, stable and consistent;

2.2.9.20. **Certificates of Analysis** (CoA) for each batch of the IMP(s);

2.2.9.21. Product information and CoA for each batch of rescue medications;

2.2.9.22. Details and, if available, sample of the labelling of the IP, if not provided with the clinical trial protocol;

2.2.9.23. **Signed declaration** by the **Principal Investigator** (see MCA-F-501/02) or equivalent that includes a statement on his/her performance, compliance and on any condition that may influence his/her impartiality and information on his/her current workload.

2.2.9.24. **Signed declaration** by all (**other) investigators** (see MCA-F-

501/11) named in the protocol (e.g. coordinating investigator, clinical trial coordinator, research clinicians, contract research affiliate(s), if applicable, etc), that includes a statement with any condition, that may influence their impartiality; they must have no conflict of interest and no history of GCP serious and/or persistent noncompliance or malpractice;

2.2.9.25. Signed **Curriculum Vitaes** in a format recommended by MCA (MCA-T-501/03) or equivalent and copies of the educational certificates (qualifications) for all key personnel named in the clinical trial protocol participating in the conduct of the clinical trial including contract research affiliate(s), if applicable. The investigators have to show evidence of previous training or experience obtained from work with clinical trials and/or patient care;

2.2.9.26. **Good Clinical Practice (GCP) certificates** (not older than two years at the time of application) and proof of training or experience in other relevant areas in accordance with the delegated tasks and duties for all trial staff;

2.2.9.27. Proof of registration of the PI and key study staff with a professional statutory body, if applicable;

2.2.9.28. Details of the location where the trial is to be conducted including-

- a statement on the suitability of the clinical trial site relating to the nature and use of the investigational product, and
- a description of the suitability of the facilities, equipment, human resources and expertise to be issued by the head of the clinic/hospital or institution or another responsible person of the clinical trial site (medical superintendent or medical officer); the statement can be included in the cover letter, as appropriate;

2.2.9.29. Licence or equivalent of central and local laboratories to be used in the clinical trial, evidence of appropriate laboratory quality management systems or a valid certificates of accreditation and normal ranges to be used for assays of clinical samples;

2.2.9.30. **Material Transfer Agreement (MTA)**, if external laboratories will be used to analyse samples;

2.2.9.31. Proof of registration on the **Pan African Clinical Trials Registry (PACTR)**;

2.2.9.32. **Data Safety Monitoring Committee** (DSMC) charter and composition, where applicable;

2.2.9.33. **Summary** of the clinical trial (100-150 words) to be made publicly available on the MCA website; and

2.2.9.34. Any other documents and information as may be additionally requested by the Agency.

2.2.10. The following should be submitted to the Agency once the trial is authorised and before database lock:

- Data Management Plan;
- Statistical Analysis Plan; and

- Plan for publication.

2.2.11. The MCA may ask the applicant to supply other information as may be required to enable reaching a decision on the application.

2.3 Clinical Trial Protocol

2.3.1. According to Part I (2) of the Regulations, the clinical trial protocol is 'a document that describes the objectives, design, methodology, statistical considerations and organisation of a trial'. Thus, the protocol shall provide the background and rationale for the trial, although these could be provided in other protocol referenced documents.

2.3.2. The protocol shall be identified by the title, the sponsor's protocol number specific for all versions of it (if available), a date and number of version that will be updated when it is amended, and a short title or name assigned to it.

2.3.3. The content and format of the protocol shall follow the requirements as laid down in the International Council for Harmonisation Guideline for Good Clinical Practice and shall thus contain the relevant information for the assessment of the quality, safety, efficacy and the statistical considerations relating to the trial.

2.4 Clinical Trial Amendments

2.4.1. Changes to the approved CT can be made. Depending on the nature of a change, amendments to the trial are regarded as substantial or non-substantial/ minor amendments.

2.4.2. Following cases are not considered as amendments:

- a change to the documentation submitted to the MCA during the ongoing assessment (before approval) of the request for clinical trial authorisation by the MCA, and
- a change to the documentation submitted to the Ethics Committee during the ongoing assessment (before approval) of the request for favourable opinion by the Ethics Committee.

2.4.3. Without prejudice to the points listed below, the Agency reserves the right to direct for an amendment to the clinical trial.

Substantial Amendments

2.4.4. Amendments to a CT are regarded as 'substantial' where they are likely to have a significant impact on the safety or physical or mental integrity of the CT participants, and/or the scientific value of the trial.

2.4.5. Substantial amendments to the conduct of the CT may arise from changes to the protocol, study documentation such as participant information sheets, consent forms, questionnaires, letters of invitation, or from new information relating to the scientific documents in support of the trial.

2.4.6. Progress reports including safety data as well as annual update of the IB is not per se a substantial amendment. However, the PI and sponsor have to verify whether data presented or updates require a change to

the documentation submitted with the request for authorisation of the CT. If this amendment is substantial, the rules for approval of substantial amendments apply to these changes.

2.4.7. Any substantial changes to the clinical trial protocol, the trial arrangements or any supporting documents or the IMP or IP shall be approved by the Ethics Committee and MCA before such amendments are carried out. The PI, sponsor or sponsor's representative should apply for amendment to the Ethics Committee at the same time as to the MCA.

2.4.8. If such amendments are necessary to eliminate an immediate hazard to trial subjects, the urgent amendment may be carried out and the PI, sponsor or sponsor's representative shall inform the MCA and Ethics Committee by writing as soon as possible but not later than 72 hours.

2.4.9. The submission of amendment(s) shall be indicated in a cover letter signed by the applicant identifying the clinical trial, sponsor and applicant, and shall include:

- A summary of the nature and explanation of the amendment(s);
- Possible consequences for subjects already included in the trial; and
- Possible consequences for the evaluation of the results.

2.4.10. The amendment(s) shall be described in a completed Clinical Trial Amendment form (MCA-F-501/08) or equivalent, and the new versions of the documents, identified by an updated version number and date, shall be provided.

2.4.11. Where applicable, supporting information shall be included with the submission.

2.4.12. The favourable opinion of the Ethics Committee is required before MCA can reach a decision on an amendment. MCA shall provide the decision within ten (10) working days of receipt of the favourable opinion.

Non-substantial/minor Amendments

2.4.13. Non-substantial/ minor amendments (except substantial) can be implemented immediately by the sponsor and should always be documented and notified to the MCA and the Ethics Committee.

2.4.14. For example, a change of the contact person or in the contact details of the contact person (e.g. a change of e-mail or postal address) is not considered as a substantial amendment, if the sponsor and legal representative remain identical. However, the sponsor should ensure that the MCA is aware of this change as soon as possible, in order to allow the Authority to exercise its clinical trial oversight function. Documentation of non-substantial amendments should also be available on request for inspection at the trial site or the sponsor premises as appropriate.

2.5 Clinical Trials in Case of Emergency Situations

2.5.1. Under certain circumstances MCA may accept an expedited application and review process for clinical trials. Examples of such situations are epidemics, pandemics or other urgent public health interests that require fast utilisation of new medicines or related products and/or fast gathering of information on products.

2.5.2. The following documents must at least be submitted in such situations together with a cover letter and a completed application form, both signed and dated by the applicant:

- Clinical Trial Protocol;
- Investigator's Brochure or a corresponding product information containing available chemical, physical and pharmaceutical information about the investigational product, non-clinical and clinical data on safety and efficacy, as available;
- Certificate of Analysis (CoA);
- GMP certificate, if available;
- The name, position and full contact details of sponsor;
- A list of the planned clinical trial site(s) and the planned number of subjects at the site(s);
- The name, position and full contact details of the PI who will be responsible for the sites where the trial is to be conducted and shall be-
    - registered with the relevant statutory health council;
    - resident in The Gambia; and
    - where the PI is not a medical doctor registered with the Medical and Dental Council in The Gambia (MDCG), he/she must ensure that a MDCG registered medical doctor is responsible for the enrolment of trial subjects and for all trial-related medical decisions including medical care;
- Proof of current, relevant and appropriate study insurance for all participants or professional indemnity provision for all investigators in the event of an injury or death related to the clinical trial;
- Participant information sheet and informed consent form including assent information, where applicable;
- Recruitment arrangements;
- The favourable opinion of the Ethics Committee and updated version(s) of documents or information as requested by the Ethics Committee, if applicable; and
- Proof of payment of the appropriate application fee.

2.5.3. The MCA may accept CT applications where some of the documents are not available at the time of submission but clearly indicated and justified and that they shall be submitted later as agreed with MCA.

2.5.4. Depending on the phase and nature of the trial, the MCA shall prescribe other relevant information to be provided.

2.5.5. The Agency shall upon initial communication with a prospective applicant, and upon receipt of an application, liaise with relevant stakeholders (including relevant ethics and other oversight bodies) to draw an appropriate plan to facilitate a holistic review of an application in a fast-track manner.

2.5.6. The under listed criteria shall be applied in the emergency clinical trial applications for review:

- Epidemiology of the emergency
- Morbidity / mortality associated with the emergency and/or condition understudy
- Supporting scientific data/information available of the investigational product at the time of submission
- Feasibility of the implementation of the trial design within the context of the emergency
- Risk-Benefit impact of the intervention and/or trial design;

2.5.7. The MCA will review expedited application within 21 working days (excluding clock stops).

2.5.8. As part of the application, the sponsor may request an AVAREF Emergency Joint Review Process of the application.–Such applications shall be considered by the MCA on a case-by-case basis.

2.5.9. Applications for the AVAREF Emergency Joint Review Process shall be submitted at least 14 working days before the proposed date of the joint review.

2.6 Special Pre-Conditions for Clinical Trials

2.6.1. In an emergency where consent cannot be obtained and treatment is required without delay to save the life of the trial subject, restore good health or alleviate suffering, the treatment may be commenced and consent shall be obtained for continued participation.

2.6.2. Where a clinical trial is to be conducted on a minor who suffers or may suffer from a disease, to be treated by the investigational product the-

(a) use of the investigational product shall be indicated according to the findings of medical science to save the life of the person, restore health and alleviate suffering, or prevent disease;

(b) clinical trial shall be of direct benefit to a group of patients suffering from the same disease as the trial subject;

(c) research shall be considered necessary in order to confirm data obtained in clinical trials on other persons or by means of other research methods;

(d) research shall relate to a clinical condition from which the minor concerned is suffering or may suffer; and

(e) research may cause only a minimal risk and minimal burden to the trial subject.

2.6.3. Where a clinical trial is to be conducted on an adult who is incapable of comprehending the nature, significance and implications of the clinical trial and suffers or may suffer from a disease, to be treated by the investigational product the-

(a) use of the investigational product shall be indicated, according to the findings of medical science to save the life of the trial subject, restore health and alleviate suffering;

(b) research shall relate directly to a life-threatening or highly debilitating clinical condition suffered by the trial subject;

(c) degree of burden and the risk threshold shall be defined specifically in the trial protocol and monitored constantly by the investigator;

(d) clinical trial may only be conducted if there is a justified expectation that the benefits of the investigational product for the trial subject outweigh the risks;

(e) consent by the authorised representative may be provided after he or she has been duly informed; and

(f) research shall be absolutely necessary for the confirmation of data obtained from clinical trials conducted on persons capable of granting informed consent or by means of other research methods.

2.7 Application for a Non-interventional Clinical Study Approval

2.7.1. Before the commencement of a non-interventional study in The Gambia, the responsible person must obtain a favourable opinion from a nationally established health research Ethics Committee and approval from MCA. An application for a non-interventional study can be made to the Ethics Committee and the Agency in either a parallel or sequential submission.

2.7.2. The responsible person is a natural or juristic person responsible for the initiation, organisation, planning, conducting, supervising and financing of the non-interventional study.

2.7.3. The fee for an application is due at the time of submission of an application;

2.7.4. The application form (MCA-F-501/12), which is available from the MCA website: **www.mca.gm**, must be completed and duly signed and dated by the responsible person (applicant).

2.7.5. All documentation submitted shall be in English. If documents are written in another language, including e.g. product information for auxiliary medicines, a certified translation is required.

2.7.6. The documents must be submitted electronically in searchable PDF files (email or CD or USB Flash Drive) **and** in hard copy, one (1) of each document.

2.7.7. The hard copy of the application form and documents including the CD or USB Flash Drive should be submited by hand delivery or by post to: **Executive Director, Medicines Control Agency, 54 Kairaba Avenue, K.S.M.D, P.O. BOX 3162, The Gambia.**

2.7.8. The applicant shall submit the following documents:

- Completed Non-interventional Study Application Form, signed by the applicant;
- Proof of payment of the non-refundable application fee;
- Observation plan of the non-interventional study; and
- Case Report Forms (CRF) or Questionnaires;

- In case of parallel submission, a copy of the application letter to the Ethics Committee and favourable opinion when received including updated versions of documents or information as requested by the Ethics Committee; and
- The Summary of the Product Characteristics or other product information of the products under observation.

2.7.9. In case of a substantial amendment the new version of the oberservation plan and other changed documents should be submitted.

2.7.10. The responsible person should submit a Non-interventional Study Report (see MCA-F-501/13) or equivalent after six (6) months of the completion of the data collection and analysis.

2.7.11. If products used in the study are to be imported or exported, the respnsible person should apply for the import or export in accordance with the MCA *Guideline for Import and Export of Medicines and Related Products* (MCA-GL-103).

3 INVESTIGATIONAL PRODUCTS (IPS)

3.1 Manufacturing of IPs

3.1.1. IPs must be manufactured in accordance with the Regulations and internationally recognised current Good Manufacturing Practice requirements, unless it is justified otherwise and approved by MCA.

3.1.2. It is the responsibility of the sponsor to supply the clinical trial site with IPs produced in compliance with GMP, where applicable.

3.2 Labelling

3.2.1. The following information should be included on labels of the primary and/or secondary packaging:

(a) Reference number allowing identification of the trial, site, PI and sponsor;

(b) Medicine(s) to be used by name/identification number, dosage form, route of administration, quantity of dosage units, and in the case of open trials the strength/potency;

(c) Trial subject identification number to whom the medicine is to be administered;

(d) Name, address and telephone number of the investigator who is the main contact for information on the product, clinical trial and emergency unblinding, if not provided to trial subjects elsewhere;

(e) Directions in regard to the manner in which such medicine should be used or reference to where this information is provided;

(f) Date of dispensing, if applicable and use-by or expiry or re-test date, as applicable;

(g) Storage conditions;

(h) Batch number or code number;

(g) Labelled with “For Clinical Trials Only”;

(h) “keep out of reach of children” except when the product is for use in trials where the product is not taken home by subjects; and

(i) Any other information as may be required by the Agency.

3.2.2. If the primary container takes the form of blister packs or small units such as ampoules, the secondary packaging should be provided bearing a label with the required particulars listed above. The primary container should nevertheless bear the following:

- name of the investigator who is the main contact for information on the product, clinical trial and emergency unblinding, if not provided to trial subjects elsewhere;
- route of administration (may be excluded for oral solid dosage forms) and in the case of open trials, the name/identifier of the IP and strength/potency;
- batch and/or code number to identify the contents and packaging operation;
- a trial reference code allowing identification of the trial, site, principal investigator and sponsor if not given elsewhere;
- the trial subject identification number/treatment number and where relevant, the visit number.

3.2.3. If the IP is registered in The Gambia and used in accordance with its registred indications and dosage regimen, MCA may make exemptions from the label requirements as listed in 3.2.1, if justified by the applicant.

3.3 Importation and Exportation/Re-exportation

Importation

3.3.1. If the IP or any auxiliary medicines is to be imported, the clinical trial must be approved by the MCA before the import can be permitted. A parallel submission for approval of the clinical trial and permit for the import is possible. In this case, application for import permit can be included in the clinical trial application package.

3.3.2. IPs or auxiliary medicines may only be imported in a quantity as required by the clinical trial.

3.3.3. Authorised or registered IPs or auxillary medicines may only be imported if they are not locally available or if the need for importation is otherwise justified.

3.3.4. The import application form (MCA-F-501/06), which is available from the MCA website: www.mca.gm, must be completed and duly signed and dated by the PI or sponsor’s representative.

3.3.5. Application for import permit must include at least, the following information:

- The title and identification number of the CT for which the application is made;
- The planned CT sites and the planned number of subjects at the sites;

- Description of the IP(s) by name or code, strength and dosage form, as applicable;
- Unit of issue, total quantity, batch number and expiry dates of the product(s);
- Justification of the quantity of the IP or auxiliary medicines to be imported relative to the timelines as stated in the CT protocol; and
- Letter of authorisation of the CT including the MCA CT number.

3.3.6. The completed application form and required documents can be sent electronically, but a hard copy must be hand delivered or posted to: **Executive Director, Medicines Control Agency, 54 Kairaba Avenue, K.S.M.D, P.O. BOX 3162, The Gambia**.

3.3.7. Approval of an import permit application by the Agency may take up to five (5) working days.

Exportation / re-exportation

3.3.8. If the IP or any auxiliary medicines needs to be exported/re-exported out of The Gambia upon completion of the clinical trial, an approval from MCA is required.

3.3.9. Before exportation or re-exportation, the delivered, used and recovered quantities of IP should be recorded.

3.3.10. Application for export/re-export permit shall be submitted in a letter to the MCA and must include at least, the following information:

- The title, clinical trial identification number and MCA authorisation number of the CT concerned;
- Description of the IP(s) or auxiliary medicine concerned;
- Unit of issue, total quantity, batch number and expiry dates of the products concerned; and
- Justification of the quantity of the IP(s) or auxiliary medicines to be exported/re-exported and reason for export/re-export.

3.4 Repackaging and Re-labelling

3.4.1. Approval for repackaging and/or re-labelling of IPs is required from MCA and the reason for it must be provided.

3.4.2. If it becomes necessary to change the expiry/use-by date, an additional label should be affixed to the IP which should state the new use-by date and repeat the batch number. It may be superimposed on the old date, but for quality control reasons, not on the original batch number.

3.4.3. The operation should be performed at an appropriately authorised manufacturing site, but when justified, may be performed at the investigational site by or under the supervision of preferably the clinical trial site pharmacist, or the PI or by the clinical trial monitor(s) who should be appropriately trained.

3.4.4. Further re-labelling or repackaging of IPs may be carried out in health facilities or other clinical trial sites by pharmacists if the IPs are intended

to be used exclusively in the facilities taking part in the same clinical trial.

3.4.5. Pharmacists must be registered with the Pharmacy Council of The Gambia and must have at least two years' experience in manufacturing or quality management of medicines or related products.

3.4.6. The repackaging or re-labelling operations of IPs should be performed in accordance with Good Manufacturing Practice principles and specific standard operating procedures and should be checked by a second person.

3.4.7. Repackaging or re-labelling should be properly documented. To avoid mistakes the activities should be carried out in an area which is partitioned or separated from other activities. A line clearance at the start and end of activity should be carried out and reconciliation performed. Any discrepancies observed during reconciliation should be investigated and accounted for before release.

3.5 Disposal of Investigational Products

3.5.1. Before disposal, the delivered, used and recovered quantities of IP should be recorded and an IP(s) accountability report sent to MCA, reconciled and verified by or on behalf of the sponsor for each trial site and each trial period in The Gambia.

3.5.2. The PI must apply to MCA for approval before destruction, indicating the procedure of disposal and the name, dosage form/strength, batch number, expiry date and amount of the IP to be destroyed and reason for destruction.

3.5.3. Destruction of unused investigational products should be carried out for a given trial site or a given trial period only after any discrepancies have been investigated and satisfactorily explained and the reconciliation has been accepted by the sponsor.

3.5.4. The disposal of investigational products at investigational site(s) in The Gambia shall be recorded and conducted in a professional manner by the PI or sponsor's representative like the clinical trial monitor.

3.5.5. Recording of destruction operations should be carried out in such a manner that all operations may be accounted for. The record of disposal shall clearly identify the batch for disposal, the subject numbers and the quantities to be destroyed.

3.5.6. The disposal exercise must be witnessed by MCA. When destruction of investigational products takes place, the MCA shall issue a dated certificate of, or receipt for destruction, to the sponsor. These documents should clearly identify, or allow traceability to, the batches and/or subject numbers involved and the actual quantities destroyed.

4 TIMELINES FOR CLINICAL TRIAL APPLICATIONS

4.1. All clinical trial applications and applications for substantial clinical trial amendments shall be screened by the MCA for completeness.

4.2. MCA shall inform the applicant in writing about the receipt of a valid or

complete clinical trial application or amendment within 10 working days from the receipt of the complete application. However, if deficiencies are identified at screening, these would be addressed by a Request for Clarification or a Screening Rejection Letter specifying the formal grounds for non-acceptance, also within 10 working days from the receipt of the application. The applicant shall address formal grounds for non-acceptance within 10 working days.

4.3. The MCA shall inform the applicant in writing about the outcome of the assessment of the clinical trial within a maximum of sixty (60) calendar days after validation of a formally complete clinical trial application, or 120 calendar days if the IP contains a genetically modified organisms.

4.4. During evaluation, additional documents or changes may be requested through a query letter. Once a query has been raised and issued to the applicant, the process stops until when MCA receives a written response to the query. If the applicant fails to modify the application correspondingly within a maximum of 30 calendar days, following the reasoned objections, the application shall be deemed to be rejected.

4.5. In general, CT applications should be processed as per the prescribed timelines presented in the flowchart in the appendix.

4.6. Applications on substantial amendments to the clinical trial should be processed by MCA within thirty (30) calendar days after submission of all required information and documents.

4.7. The MCA shall inform the responsible person of a non-interventional study in writing about the outcome of the assessment of the study within a maximum of thirty (30) calendar days after receiving a complete application.

5 OPINION FROM THE ETHICS COMMITTEE

5.1. An application for a favourable opinion shall be made by the PI to the Ethics Committee in the prescribed form.

5.2. The principal investigator shall submit any other information as determined by the Ethics Committee to assess the application.

5.3. The Ethics Committee-

(a) may rely on its personal scientific findings, consult experts or request for an expert opinion to assess any application;

(b) shall provide its opinion on an application for a clinical trial based on its written standard operating procedures;

(c) may refuse to grant a favourable opinion where the-

(i) documents submitted are incomplete and the PI fails to submit the appropriate documents within the time frame provided by the Ethics Committee,

(ii) documents submitted, including the trial protocol, the investigator's brochure, the modalities for selection of trial subjects and the informed consent documents, do not correspond with the scientific knowledge available and the

clinical trial is considered unsuitable to provide proof of the safety and efficacy of an investigational product;

(iii) requirements specified under Section 73 of the Regulations are not fulfilled.

5.4. The Agency shall provide the Ethics Committee with any information of significance, if required for the assessment of any application for a favourable opinion.

5.5. The Agency shall provide information to Ethics Committee, when required, on aborted or prematurely discontinued investigations.

6 DECISION ON CLINICAL TRIAL APPLICATIONS

6.1. All clinical trial applications shall be evaluated with the same set of criteria based on the up-to-date scientific knowledge and ethics standards, regardless of the applicant.

6.2. During the CT assessment process, relevant CT decisions, reports or information from other national regulatory authorities or regional and international bodies can be recognised or used by the MCA.

6.3. MCA shall establish advisory or ad-hoc committees for the review of a clinical trial application, if special expertise is required.

6.4. Persuant to the Act, a clinical trial authorisation letter (certificate) shall be issued to the applicant by MCA upon approval indicating the MCA CT number. The clinical trial authorisation letter may contain conditions required by MCA with the respect to the conduct or reporting of the clinical trial.

6.5. If the clinical trial application was rejected, the applicant can appeal which shall be made in writing to the Executive Director within sixty (60) calendar days of receipt of the rejection notice.

6.6. No information given in an application shall be disclosed by the MCA to a third party except:

- with the written consent of the applicant; or
- in accordance with the directive of the Governing Board of MCA; or
- for the purpose of a legal process under the Medicines and Related Products Act, 2014.

6.7. MCA shall register all clinical trial applications in a database.

6.8. An authorisation may be rejected in accordance with section 40 of the Act where the-

(a) documents submitted are incomplete and the PI or sponsor fails to submit the appropriate documents within the time frame provided by the Agency;

(b) documents submitted, including data on the investigational products, the trial protocol, investigator's brochure and the investigational medicinal product dossier, do not correspond with the scientific knowledge available and the clinical trial is considered unsuitable to provide proof of the safety and efficacy of an investigational product;

(c) the requirements stipulated under provision 73 of the Regulations are not fulfilled; and

(d) the Agency is in possession of findings which indicate that the clinical trial facility is not a conducive environment for the trial to be conducted.

6.9. The Agency may use relevant clinical trial decisions, reports or information from other regulatory authorities as the Agency may consider necessary to assess any application.

6.10. It is mandatory that all clinical trials shall be registered by the sponsor or PI in the Pan African Clinical Trials Registry (PACTR).

7 INSPECTION OF CLINICAL TRIALS

7.1. Any site involved in a clinical trial may be subject to inspection by the MCA as stipulated under Section 79 of the Regulations.

7.2. The MCA may thus inspect clinical trial sites and/or the sponsor's premises and/or the manufacturer and/or any laboratory used for clinical trial analyses to ensure adequate protection of the trial subjects is provided and that the trial is conducted in accordance with ICH GCP E6 R2 or amended versions and regulatory requirements.

7.3. GCP inspections by MCA would involve verification of conformity to applicable GCP guidelines to secure the compliance before, during or after the conduct of a clinical trial.

7.4. Contract research organisations/facilities acting under arrangements with a sponsor or investigator to perform some or all of the functions of the sponsor or investigator, may also be subject to GCP inspection.

7.5. Inspections may be conducted on a routine basis or may arise as a result of a specific trigger.

7.6. Before the inspection MCA shall notify the PI and/or sponsor and/or manufacturer in writing two (2) to four (4) weeks prior to the proposed inspection date. However, if MCA has reasonable cause to believe that the approved protocol is being violated an unannounced inspection may be conducted.

7.7. Following inspections, an inspection report shall be prepared by MCA and findings be made available to the inspected party and sponsor while safeguarding confidential aspects. It may be made available to the Ethics Committee and other regulatory authorities at their written request.

8 REPORTING OF ADVERSE EVENTS

8.1. For purposes of safety monitoring, procedures for the collection, management and reporting of suspected adverse reactions/adverse events should be put in place and summarised in the clinical trial protocol.

8.2. The sponsor or PI of an ongoing clinical trial shall report to the Agency serious adverse events suspected to be related to the IMP within seven (7) calendar days by using a Serious Adverse Event Report form provided

by MCA (MCA-F-501/09), which is available from the MCA website: www.mca.gm, or an equivalent.

ADDENDUM

The reporting of serious adverse events suspected to be related to the IMP (SARs) within seven (7) calendar days is recommended in this guideline for your implementation for reasons of harmonisation even though it is mandatory in part XI, section 80 (a) of the Regulations to report SARs within fifteen (15) calendar days to the Agency.

8.3. Any serious adverse event to the investigational product shall receive immediate medical attention before reporting same to the MCA.

8.4. Fatal serious adverse events shall be reported within seven (7) calendar days to MCA whether suspected to be related to the IP or not. They shall be followed by a formal or verbal autopsy report. Verbal autopsy shall be conducted in line with the World Health Organization guideline for verbal autopsy. The cause of death shall be classified according to current ICD guideline.

ADDENDUM

The Regulations stipulate in part XI, section 80 (b) to report fatal events within 72 hours which can be an informal notification, while a detailed report must be submitted within seven (7) calendar days.

8.5. Any adverse events that are relevant with respect to nature or frequency shall be reported to MCA within specified timelines with progress reports.

8.6. The sponsor or PI is required to submit follow-up information as soon as it becomes available. Additional information may include copies of diagnostic test results, laboratory reports, or medical record progress notes. All additional information should be clearly marked as update information and should include the Protocol Number and Participant Number.

8.7. MCA shall ensure to record and evaluate all reports on suspected serious adverse reactions to an IP which are brought to its attention.

9 NOTIFICATIONS AND CLINICAL TRIAL REPORTS

9.1. A notification of arrival and receipt confirmation of imported products stating the name(s) of product(s), batch numbers or code numbers and quantities received should be sent immediately by scanned email and then delivered in hard copy to MCA within (5) five working days.

9.2. The sponsor or PI shall notify the MCA of the start of the trial within 15 working days; the start of the trial is the date when the first act of recruitment of a potential subject was performed (e.g. date of the first contact with potential trial subjects).

9.3. If the trial does not start within six (6) months of issuance of the authorisation letter or at the date as stipulated by the applicant, the sponsor or PI shall inform MCA of the planned date of commencement.

9.4. The sponsor or PI shall inform the MCA of early termination or suspension of a clinical trial within 15 working days by using the Final Clinical Trial Report Form (MCA-F-501/10) and the reasons clearly explained.

9.5. The sponsor or PI shall provide progress reports on the clinical trial including safety data at least annually or as stipulated in the clinical trial authorisation letter to MCA starting from the date of issuance of the clinical trial authorisation letter by using the Clinical Trial Progress Report form (MCA-F-501/07). The report form is available from the MCA website: www.mca.gm.

9.6. The sponsor or PI shall notify MCA within 15 working days of the end of a clinical trial; the end of the clinical trial shall be defined in the clinical trial protocol (e.g. last subject last visit or database lock).

9.7. The sponsor or PI shall submit a final clinical trial report to MCA within six (6) months of the end of the clinical trial by using the Final Clinical Trial Report form or (MCA-F-501/10) or equivalent.

10 CLINICAL TRIAL FILES AND ARCHIVING

10.1. The PI shall keep an Investigator Site File (ISF) and the sponsor a Trial Master File (TMF) containing the essential documents relating to the clinical trial as indicated in the ICH E6 GCP guideline, which allow verification of the conduct of the clinical trial and the quality of the data generated, taking into account all characteristics of the clinical trial.

10.2. The files shall be readily available, and directly accessible upon request, to the MCA.

10.3. The sponsor and the PI shall archive the contents of the TMF and ISF, respectively, for at least 10 years for marketed products and 25 years for unauthorised IPs after the end of the clinical trial.

11 FINAL PROVISIONS

11.1. This guideline is the second version published by the MCA and will become effective on 15 February 2021.

11.2. This guideline will be reviewed within 3 years of becoming effective.

12 DOCUMENTS NEEDED FOR THIS GUIDELINE

Document No	**Title** (as referenced on the document)
MCA-F-501/01	Clinical Trial Application Form
MCA-F-501/02	Declaration and Workload of Principal Investigator
MCA-T-501/03	Curriculum Vitae for Key Personnel Conducting Clinical Trials
MCA-F-501/04	Indemnity Statement
MCA-F-501/05	Declaration of Sufficient Funds
MCA-T-501/06	Import Application Form
MCA-F-501/07	Clinical Trial Progress Report
MCA-F-501/08	Clinical Trial Amendment Form
MCA-T-501/09	Serious Adverse Event Report Form

MCA-F-501/10	Final Clinical Trial Report
MCA-F-501/11	Declaration of Investigators
MCA-F-501/12	Non-interventional Study Application Form
MCA-F-501/13	Non-interventional Study Report

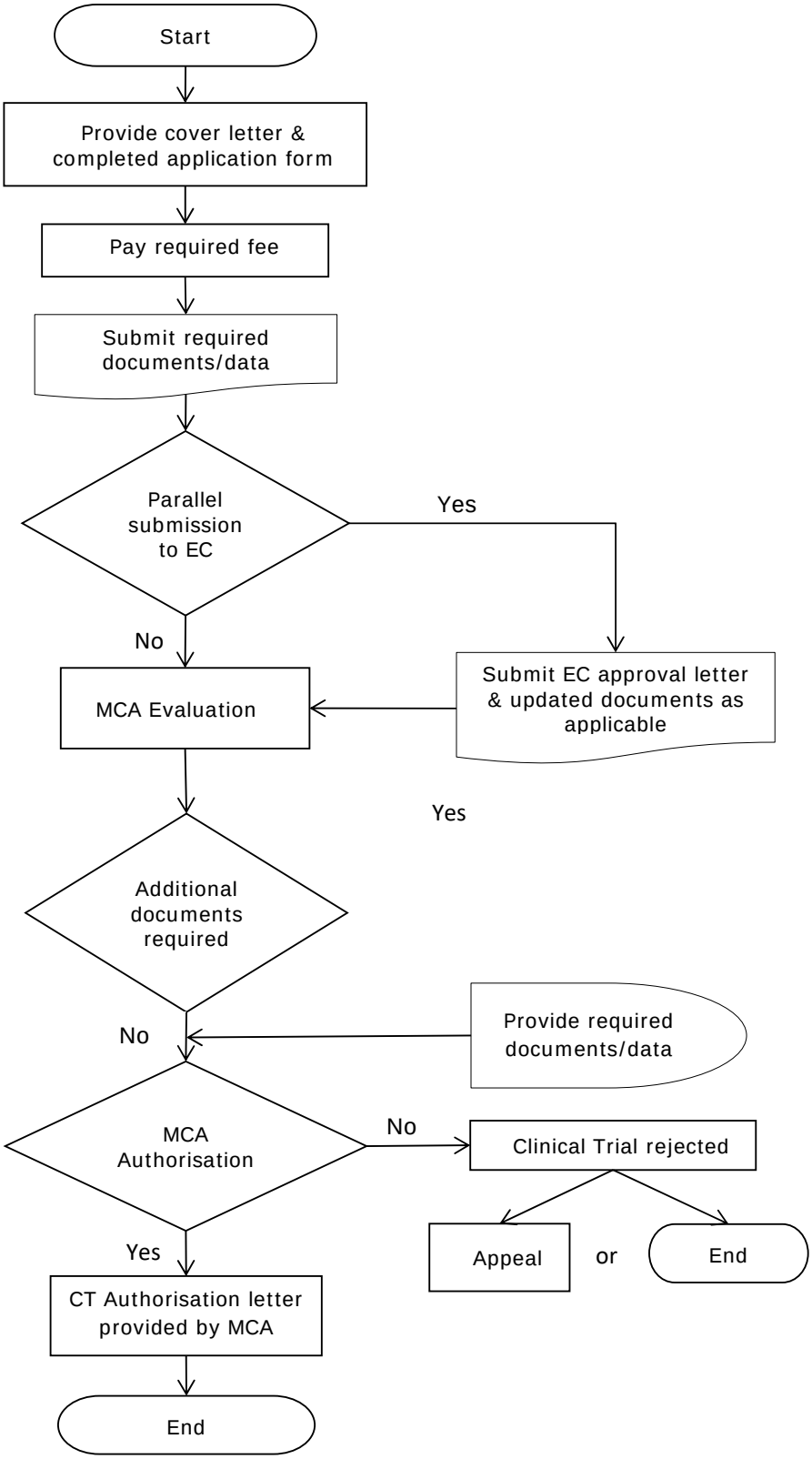
13 REFERENCES

- Medicines and Related Products Act, 2014
- Medicines and Related Products Regulations, 2020
- MCA Fee Schedule
- International Council for Harmonisation (ICH), Integrated Addendum to ICH E6 (R1), Guideline for Good Clinical Practice E6 (R2), 2016
- World Health Organization, Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, WHO Technical Report Series, No. 850, Annex 3, 1995
- African Vaccine Regulatory Forum (AVAREF), Clinical Trial Application Form, October 2019
- African Vaccine Regulatory Forum (AVAREF), guideline for joint and assisted reviews of clinical trial applications, Draft, October 2019
- Communication from the Commission (2010/C 82/01), Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1), 30 March 2010
- Regulation (EU) No 536/2014 of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, 16 April 2014

14 DOCUMENT HISTORY

Version #	**Implementation Date**	**Reasons for Change:**
1	06 November 2020	New document
2	15 February 2021	Inclusion of Addendum for clarification

15 FLOW CHART: APPLICATION FOR A CLINICAL TRIAL



16 FLOW CHART: TIMELINES FOR CLINICAL TRIAL APPLICATIONS