FOOD AND DRUGS AUTHORITY

GUIDELINES FOR CONDUCTING CLINICAL TRIALS OF MEDICINES, FOOD SUPPLEMENTS, VACCINES AND MEDICAL DEVICES IN GHANA

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1.0. INTRODUCTION

In pursuance of the Public Health Act, 2012, Act 851, Part 8, 150-166, these Guidelines are hereby made by the Food and Drugs Authority, hereafter referred to as **The Authority**, to define the general norms and scientific principles and to set applicable standards for the conduct, performance and control of clinical trials in human beings in Ghana. They do not cover veterinary trials.

These Guidelines are addressed to investigators, pharmaceutical manufacturers and other sponsors of clinical trials whether for academic purposes or for generation of data intended for inclusion in the regulatory submissions for medicinal products. They are intended to be applied during all stages of drug development both prior to and subsequent to product registration and marketing.

Clinical trials shall be categorized as follows;

1. Trials initiated by The Authority.
2. Trials initiated by pharmaceutical companies or agencies.
3. Trials initiated by pharmaceutical companies on advice of The Authority, to be carried out locally for pharmacogenetic or other reasons peculiar to the population in Ghana.
4. Trials initiated by academic and research institutions either locally or as part of an international multi-centre study.

In all the categories above the primary end-point of the trial shall be clearly specified.

2.0. GLOSSARY

The definitions below apply specifically to the terms used in this guide:

"Adult" A person who is eighteen (18) years of age or over that age.

"Adverse Drug Reaction (ADR)" All noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase responses to a medicinal product means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.
Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

"Adverse Event (AE)" Any undesirable experience occurring to a subject during a clinical trial, whether or not considered related to the investigational product(s). An unexpected AE is an experience not reported in the current Investigators Brochure or elsewhere.

"Amendment" A written description of a change(s) to or formal clarification of a protocol.

"Applicable Regulatory Requirement(s)" Any law(s) and regulation(s) addressing the conduct of clinical trials of investigational products.

"Approval(s)" The affirmative decision of the appropriate institutions (FDA, IRB/IEC and GHS-EC) that the clinical trial has been reviewed and may be conducted at the institution site within the constraints set forth by the appropriate institutions, Good Clinical Practice (GCP), and the applicable regulatory requirements.

"Audit Certificate" A declaration of confirmation by the auditor that an audit has taken place.

"Audit Report" A written evaluation by the sponsor's auditor of the results of the audit.

"Audit Trail" Documentation that allows reconstruction of the course of events.

"*Audit"* A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analyzed and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

"Blinding/Masking" A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double-blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

"Case Report Form" A printed, optical or electronic document designed to record all of the protocol required information. There should be assurance of accurate input and presentation and it should allow verification.

"Certificate of Analysis (COA)" An authenticated document issued by an appropriate authority that certifies the quality and purity of pharmaceuticals, and animal and plant products.

"Child/Minor" A person who is below eighteen (18) years of age or the definition of child as defined in the current Children's Act of Ghana.

"Clinical Trial Site" The location(s) where trial-related activities are actually conducted.

"Clinical Trial" means an investigation consisting of a particular description by, or under the direction of a medical practitioner, dentist or veterinary surgeon to the patient or animal where there is evidence that a medicine, medical device or procedure or herbal medicinal product of that description has effects which may be beneficial to and safe to the patient or animal, and the medicine, medical device or procedure or herbal medicine is for the purpose of ascertaining beneficial or harmful effects.

"Clinical Trials Technical Advisory Committee (CT-TAC)" As established by Section 150 of the Public Health Act 2012, Act 851.

"Contract Research Organization (CRO)" A scientific body (commercial or academic) contracted by a Sponsor to perform some of the Sponsors trial related duties and function

"Data Safety Monitoring Board (DSMB)" An independent data-monitoring committee that may be established by the Sponsor to assess at intervals the progress of a clinical, the safety data, and the critical efficacy endpoints, and to recommend to the Sponsor whether to continue, modify, or stop a trial.

"Date of Commencement" For the purpose of the Clinical Trial Certificate and Quarterly Progress Report Form, this is defined as the date when the clinical trial site shall start to enroll participants in the clinical trial.

"Drug/Medicine" Includes

1 A substance referred to in a publication mentioned in the Fourth Schedule,
2 A substance or mixture of substances prepared, sold or represented for use in
   i. Restoring, correcting or modifying organic functions in man or animal, and
   ii. The diagnosis, treatment, mitigation or prevention of disease, disorder of abnormal, physical state or the symptoms of it, in man or animal, or
3 Nutritional supplements

"FDA" means Food and Drugs Authority

"Good Clinical Practice (GCP) Inspection" The act by the FDA of conducting an official review of documents, facilities, records and any other resources that are deemed to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organization's (CRO's) facilities, or at other establishments deemed appropriate by the FDA.

"Good Manufacturing Practice (GMP)" The part of pharmaceutical quality assurance which ensures that products are consistently produced and controlled to quality standards appropriate to their intended use and as required by the marketing authorization.

"Herbal Medicinal Product" Includes plant-derived material preparations with therapeutic or any other human health benefits which contain raw or processed ingredients from one or more plants and materials or organic or animal origin.

"Institutional Review Board/Independent Ethics Committee (IRB/IEC)" An independent body constituted of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

"Investigational Product" 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 authorization when used or assembled 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.

"Investigator's Brochure" A collection of data consisting of all the information known prior to the clinical trial concerning the clinical and non clinical data on the investigational product(s). There should be adequate data to justify the nature, scale and duration of the proposed trial.

"Lot Release Certificate (LRC)" An official document that authorizes the manufacturer to release a specific lot of a product.

"Medical Device" As defined in Part Seven, Section 149 of the Public Health Act 2012, Act 851.

"Placebo" A medication with no active ingredients or a procedure without any medical benefit.

"Principal Investigator / Investigator" The person responsible for the conduct of the clinical trial at the clinical trial site, who is entitled to provide health care under the laws of the Country where that clinical trial site is located.

"Protocol Amendment" A written description of a change(s) to or formal clarification of a protocol.

"Protocol" A document that describes the objective(s), design, methodology, statistical considerations and the organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents.

"Research Institution" Any public or private entity, agency, medical or dental facility where clinical trials are conducted.

"Serious Adverse Event (SAE)" means any untoward medical occurrence that at any dose results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity or is a congenital anomaly/birth defect (ICH definition 1997).

"Sponsor" An individual, company, institution or organization which takes responsibility for the initiation, management and/or financing of a trial. This excludes an individual company, institution or organization which has been requested to provide money for a trial and does not benefit in any way from the results of the trial.

"Vulnerable population" An individual whose willingness to volunteer in a clinical trial may be unduly influenced by the expectations, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate.
Examples are pregnant women, cognitively impaired subjects, children and prisoners.

Research concerning vulnerable population should be conducted in line with provisions made in Food and Drugs Authority's GCP Guidelines.

3.0. REQUIREMENTS

3.1 Clinical Trial Application

A Clinical Trial Application made to The Authority to conduct a clinical trial shall be accompanied by the following:

3.1.1. Covering Letter

3.1.2. A non-refundable Application Fee as per the prescribed Fee Schedule.

3.1.3. A Clinical Trial Protocol

3.1.4. Completed Food and Drugs Authority Application Forms for Conducting Clinical Trials signed by authorized persons

3.1.5. A proof of registration with a Clinical Trials Registry (approved by The Authority)

3.1.6. Investigator's Brochure (COA, GMP)

3.1.7. Ethics Committee / Institutional Review Board Approval

3.1.8. Insurance Cover

3.1.9. Financial Declaration

3.1.10. DSMB Charter

3.1.11. Sponsor/PI Contractual Agreement

All clinical trial application documents shall be submitted in hard and soft copies (1 each).

3.1.1. Cover Letter

Addressed to the Chief Executive Office as follows:

The Chief Executive Officer
Food and Drugs Authority
Head Office
P.O. Box CT 2783
Cantoments, Accra Ghana.
Tel: (+233-302) 233200, 235100
Fax: (+233-302) 229794, 225502
Email: fda@fdaghana.gov.gh

3.1.2. Application Fees

An application shall be accompanied by a non-refundable application fee as specified in the Food and Drugs Authority Fee Schedule.

3.1.3. Application Form to Conduct a Clinical Trial

Two (2) copies of completed application forms signed by all participating investigators shall contain at least the following:

3.1.3.1. Name of trial

3.1.3.2. Sponsor's details

3.1.3.3. Clinical trial registration number

3.1.3.4. CVs of investigators

3.1.3.5. Investigator's current work load

3.1.3.6. Study Pharmacist's details

3.1.3.7. Signed declaration by the Sponsor or authorized person.

3.1.4. Clinical Trial Protocol and Trial Amendment

3.1.4.1. General Information

This shall include:

3.1.4.1.1. Protocol title, protocol identifying number, and date. Any amendment(s) should also bear the amendment number(s) and date(s).

3.1.4.1.2. Name and address of the Sponsor and monitor (if other than the Sponsor)

3.1.4.1.3. Name and title of the person(s) authorized to sign the protocol and the protocol amendment(s) for the Sponsor.

3.1.4.1.4. Name, title, address, and telephone number(s) of the Sponsor's medical expert (or dentist when appropriate) for the trial.

3.1.4.1.5. Name and title of the Principal Investigator(s) who is (are) responsible for conducting the trial, and the address and telephone number(s) of the trial site(s).

3.1.4.1.6. Name, title, address, and telephone number(s) of the other investigators designated by the PI to be responsible for some aspects of the study.

3.1.4.1.7. Name(s) and address (es) of the clinical laboratory (ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

3.1.4.1.8. Contractual agreement between the investigator and Sponsor.

3.1.4.1.9. A clear statement on compensation and benefits package for clinical trial participants.

3.1.4.1.10. Publication policy

3.1.4.2. Background Information

This shall include:

3.1.4.2.1. Name and description of the investigational product(s).

3.1.4.2.2. A summary of findings from nonclinical studies that potentially have clinical significance to the trial

3.1.4.2.3. Summary of findings from clinical trials that are relevant to the trial.

3.1.4.2.4. Summary of the known and potential risks and benefits, if any, to human subjects.

3.1.4.2.5. Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).

3.1.4.2.6. A statement that the trial shall be conducted in compliance with the protocol, GCP and the applicable regulatory requirement(s).

3.1.4.2.7. Description of the population to be studied.

3.1.4.2.8. References to literature and data that are relevant to the trial and that provide background for the trial.

3.1.4.2.9. Signed declaration by the applicant and all investigators that they are familiar with and understand the protocol and shall comply with principles of Good Clinical Practice (GCP) as determined by the Food and Drugs Authority in the conduct of the trial.

3.1.4.2.10. Explanation of the trial being conducted in Ghana and not in the host country of applicant or Sponsor.

3.1.4.3. Trial Objectives and Purpose

3.1.4.3.1. Explanation of the trial being conducted in Ghana and not in the host country of applicant or Sponsor.

3.1.4.3.2. A detailed description of the objectives and the purpose of the trial

3.1.4.3.3. Aim of the trial and reason for its execution.

3.1.4.4. Trial Design

The scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design. A description of the trial design should include:

3.1.4.4.1. A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.

3.1.4.4.2. A description of the type/design of trial to be conducted (e.g. double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages.

3.1.4.4.3. A description of the measures taken to minimize/avoid bias, including: Randomization and Blinding.

3.1.4.4.4. A description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s).

3.1.4.4.5. Description of the dosage form, packaging, and labeling of the investigational product(s) and sample of label to be used for investigational product.

3.1.4.4.6. The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.

3.1.4.4.7. Quantities of investigational medicines and comparators

3.1.4.4.8. A detailed description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial and entire trial.

3.1.4.4.9. Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.

3.1.4.4.10. Maintenance of trial treatment randomization codes and procedures for breaking codes.

3.1.4.4.11. The identification of any data to be recorded directly on the CRFs (i.e. no prior written or electronic record of data), and to be considered to be source data.

3.1.4.4.12. Number of human subjects to be involved in the trial and the statistical justification.

3.1.4.4.13. Specifications and instructions for anticipated deviations from the protocol.

3.1.4.5. Selection and withdrawal of subjects

3.1.4.5.1. Subject inclusion criteria.

3.1.4.5.2. Subject exclusion criteria.

3.1.4.5.3. Subject withdrawal criteria (i.e. terminating investigational product treatment/trial treatment) and procedures specifying:

3.1.4.5.3.1. When and how to withdraw subjects from the trial/investigational product treatment.

3.1.4.5.3.2. The type and timing of the data to be collected for withdrawn subjects.

3.1.4.5.3.3. Whether and how subjects are to be replaced.

3.1.4.5.3.4. The follow-up for subjects withdrawn from investigational product treatment/trial treatment.

3.1.4.6. Treatment of Subjects

3.1.4.6.1. The treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial.

3.1.4.6.2. Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.

3.1.4.6.3. Procedures for monitoring subject compliance.

3.1.4.6.4. Description of treatment applied to control group(s) or control period(s), placebo, and other therapy and any other treatment that may be given concomitantly including measures to be implemented to ensure the safe handling of the products.

3.1.4.6.5. Description of diagnostic devices or kits applied to be used in the clinical trial.

3.1.4.6.6. Description of special analyses and/or tests or procedure to be carried out.

3.1.4.7. Assessment of Efficacy

3.1.4.7.1. Specification of the efficacy parameters.

3.1.4.7.2. Methods and timing for assessing, recording, and analyzing of efficacy parameters.

3.1.4.7.3. Clear procedures for interim assessment of trial.

3.1.4.8. Assessment of Safety

3.1.4.8.1. Specification of safety parameters.

3.1.4.8.2. The methods and timing for assessing, recording, and analyzing safety parameters.

3.1.4.8.3. Procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses.

3.1.4.8.4. The type and duration of the follow-up of subjects after adverse events.

3.1.4.8.5. Provision for dealing with all adverse events. Copy of form to be used to report adverse event.

3.1.4.8.6. Criteria for the termination of the trial

3.1.4.9. Statistics

3.1.4.9.1. A description of the statistical methods to be employed, including timing of any planned interim analysis.

3.1.4.9.2. The number of subjects planned to be enrolled. In multicentre trials, the numbers of enrolled subjects projected for each trial site should be specified.

3.1.4.9.3. Reason for choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification.

3.1.4.9.4. The level of significance to be used.

3.1.4.9.5. Criteria for the termination of the trial.

3.1.4.9.6. Methods for data analyses and evaluation of results.

3.1.4.9.7. Procedure for accounting for missing, unused, and spurious data.

3.1.4.9.8. Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in protocol and/or in the final report, as appropriate).

3.1.4.9.9. The selection of subjects to be included in the analyses (e.g. all randomized subjects, all dosed subjects, all eligible subjects, evaluable subjects).

3.1.4.10. Ethics

General ethical consideration relating to the trial and informed consent sheet or form or otherwise to be given to patients or volunteers.

3.1.4.11. Data Handling and Record Keeping

3.1.4.11.1. Procedure for keeping a list of participating volunteer/patients and detailed records indicated on the case report form (CRF) for each individual taking part in the trial.

3.1.4.11.2. A clear statement on composition and benefit package for clinical trial participants

3.1.4.11.3. All clinical and experimental data (electronic or paper) shall be kept in a secured place for a period of 5 years and 20 years for New Drug Application (NDA) after completion of the trial and be made readily available for review upon request by The Authority.

3.1.4.12. Publication of clinical trial report

3.1.4.12.1. Publication policy, if not addressed in a separate agreement.

3.1.4.12.2. Publication policy, including a plan for the publication of the results (publishing plan)

3.1.5. Protocol amendments

3.1.5.1. Any amendment to the trial protocol, trial arrangements and investigational product shall be submitted to the institutional review Authority(s) that originally approved the protocol and The Authority for approval by these bodies before such amendments are carried out.

3.1.5.2. If such amendments are necessary to protect the life of subjects, an urgent amendment may be carried out but the investigator shall inform the independent ethics committee and The Authority of such amendments with an immediate phone call, followed by a written report within forty-eight (48) hours.

3.1.5.3. Reports of all amendments shall include but not be limited to the following:

3.1.5.3.1. Reasons for the amendments.

3.1.5.3.2. Possible consequences for subjects already included in the trial.

3.1.5.3.3. Possible consequences for the evaluation of the report.

3.1.5.3.4. All amendment shall attract a fee which shall be determined as per Food and Drugs Authority Fee Schedule

3.1.6. Investigator's Brochure

Investigators Brochure containing information on the following but not limited to:

3.1.6.1. Chemical, physical and pharmaceutical properties and formulations,

3.1.6.2. Preclinical, pharmacological and toxicological data,

3.1.6.3. Human pharmacological and clinical data with the substance concerned and any other supporting documentation sufficient to establish quality, safety and efficacy where applicable.

3.1.6.4. Marketing experience in countries where the investigational product is being marketed or approved. Where appropriate there should be discussions of published reports.

3.1.6.5. Sample of label to be used for the investigational products.

3.1.6.6. Clear instructions on storage and handling of investigational products.

3.1.6.7. An updated investigator's brochure should be submitted at least once a year, or whenever it is updated within this period. Additional information and any changes that have been incorporated in the updated investigator's brochure should be highlighted for ease of review and evaluation.

3.1.6.8. Good Manufacturing Practice (GMP) certificate/statement from the country of manufacture for the product/ placebo issued by the competent recognized Authority.

3.1.7. Ethical Committee / Institutional Review Board's Approval

3.1.7.1. Ethical Clearance for all phases of clinical trials in humans shall be sought from the national ethics approving body, Ghana Health Service, Ethical Review Committee or Institutional Review Board (IRB) or Institutional Ethics Committee (IEC) or a recognized independent ethics committee of each of the proposed institution(s) or centre(s) where the trial is to be conducted.

3.1.7.2. Submissions to The Authority and to the review authorities or ethics committees can be done in parallel.

3.1.7.3. Original copy of approval letter/certificate from the applicant's Institutional Review Board (IRB) or Institutional Ethics Committee (IEC) or recognized independent ethics committee and the committees as listed in 3.1.7.1 above. In the case of multicentre studies, an approval from each institution's review authority shall be required.

3.1.8. Insurance Cover

3.1.8.1. All subjects must be satisfactorily insured against possible injuries that might arise during the conduct of the clinical trial.

3.1.8.2. For all Sponsor-initiated trials, a valid insurance certificate for the duration of the study must be provided prior to study initiation.

3.1.8.3. Sponsors and Principal Investigators shall ensure insurance cover for clinical trial participants and shall submit as evidence a Certificate of insurance cover for participants.

3.1.9. Financial Declaration

3.1.9.1. The financial aspects of the trial should be documented in an agreement between the Sponsor and the Principal Investigator/Contracted Research Organization/Institution.

3.1.9.2. A declaration must be signed by both the Sponsor and the Principal Investigator which states that there are sufficient funds available to complete the study.

3.1.10. Data Safety Monitoring Board/Committee (DSMB/C) or Independent Data-Monitoring Committee (IDMC) or Data Monitoring Committee (DMC)

3.1.10.1. An independent data-monitoring committee that may be established by the Sponsor to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the Sponsor whether to continue, modify, or stop a trial.

3.1.10.2. The Sponsor shall include charter of work, membership and curriculum vitae of the DSMB when applicable.

3.1.10.3. It is recommended that for trials conducted in Ghana, one member of the DSMB is a Ghanaian.

3.2. Responsibilities of Sponsors and Investigators

Sponsors and Principal Investigators shall have as their primary concern the protection of the life, health, privacy and dignity of the patients or healthy volunteers who participate in such trials.

3.2.1 Sponsor

Submission to The Authority for approval:

Before initiating a clinical trial(s) in Ghana, the Sponsor and the Principal Investigator must obtain approval from The Authority to begin the trial(s). The protocol should be submitted in duplicate. It is the responsibility of both the Sponsor and the PI to ensure that the protocol satisfies the requirements of the protocol checklist.

3.2.2. Investigator

A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.

The Principal Investigator shall ensure that a qualified pharmacist supervises the management of the investigational product.

3.2.3. Qualification of Principal Investigators

Principal Investigator(s) directly in charge of a trial and at each site in a multi-centre trial shall be in good standing with the Ghana Medical and Dental Council and should be responsible for the proper conduct of the trial and must;

3.2.3.1. Be medically qualified and clinically competent

3.2.3.2. Be sufficiently experienced in clinical evaluation of medicinal products

3.2.3.3. Be experts in the pathology and the clinical handling of the particular disease or condition under study.

3.2.3.4. Have evidence of Good Clinical Practice training organized by the Authority of not more than 2 years. First time Principal Investigators shall be required to participate in the next GCP training of the Authority as a prerequisite for a Clinical Trial approval. A Sponsor's GCP certificate shall not be considered for his respective trial.

3.2.3.5. Performance of Principal Investigators in regulatory compliance assessment with regards to previous clinical trials conducted would have an impact on the suitability/adequacy of the Principal Investigator for new clinical trial applications.

3.2.3.6. Provide evidence of such qualifications specified by the applicable regulatory requirement(s).

3.2.3.7. Non-medically qualified scientists may participate as co-investigators or in other roles, but not as Principal Investigators.

3.2.3.8. A Veterinary Surgeon may be the Principal Investigator or clinician for zoonotic studies.

3.3. Responsibilities of the Authority

3.3.1. The Authority shall approve a clinical trial by issuing a Clinical Trial Certificate in a format as may be prescribed by The Authority for the initiation and conduct of clinical trials in Ghana. The approval process shall involve establishing adequate procedures and/or requirement for review of the clinical trial application. The Authority may require protocol revisions whenever it deems necessary.

3.3.2. The Authority may renew or amend a Clinical Trial Certificate issued if adequate justification for the renewal or amendment is given by an applicant.

3.3.3. A Clinical Trial Certificate issued shall be revoked if conditions for which the certificate was issued are violated.

3.3.4. The Authority shall order the person conducting the clinical trial to stop or suspend the trial immediately if at any stage during the conduct of a clinical trial The Authority is satisfied that it is in the public interest to do so.

3.3.5. The Authority shall act as a Secretariat to the CT-TAC that has been established by Section 150 of the Public Health Act

3.3.6. The Authority shall monitor a clinical trial from the beginning to the end in order to ensure adequate protection of the general public against the risk or adverse events from authorized clinical trials. This is to satisfy itself that the specific and general conditions to which the trial was authorized are being strictly adhered to by the person(s) conducting the trial and that the trial will achieve its objectives.

3.3.7. The Authority shall conduct on-site inspections to ensure:

3.3.7.1. the safety of clinical trial participants,

3.3.7.2. the quality and reliability of data obtained in a trial, and

3.3.7.3. the facilities used continue to be acceptable throughout the clinical investigation.

3.3.8. The Authority shall assess Investigators' compliance to regulatory requirements to ascertain the competence of the Investigator to conduct clinical trials in Ghana.

3.4. Reporting and Managing Adverse Events

The Sponsor of a clinical trial and Principal Investigators participating in a clinical trial are responsible for proper reporting of Serious Adverse Events (SAEs).

The Sponsor should expedite the reporting of all adverse drug events (AEs) that are both serious and unexpected to The Authority

Reporting should occur within the timeframe and format specified by The Authority.
(Refer to Appendix I)

3.4.1. Any serious adverse event to the investigational product shall receive immediate medical attention and reported to The Authority within forty-eight (48) hours.

3.4.2. The SAE report form shall be completed and detailed information such as laboratory results submitted to enable causality assessment report by CT-TAC.

3.4.3. All fatal cases shall be accompanied by a formal autopsy report.

3.4.4. In exceptional circumstances where a formal autopsy is not practicable, provision of a verbal autopsy report shall be prior approved by The Authority and shall be given with ample reasons.

3.4.5. The verbal autopsy conducted and the report submitted shall be in accordance with W.H.O Standard Verbal Autopsy Method for Investigating Causes of Death in Infants and Children (ref. WHO/CDS/CSR/ISR/99.4).

3.4.6. Any frequent adverse event to the product shall receive immediate medical attention and reported to The Authority within seven (7) days.

3.4.7. The Principal Investigator 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.

3.5. Clinical Trial Reports

3.5.1. Progress Report

3.5.1.1. The Authority should be informed in writing on the exact date of commencement of the study.

3.5.1.2. Quarterly reports of the progress of a clinical trial starting from the date of issuance of the clinical trial certificate shall be submitted to The Authority in the recommended format. (Refer to APPENDIX II)

3.5.1.3. Quarterly progress reports must be submitted to The Authority within 21 days after the end of the previous quarter. A quarter shall be considered as a three months beginning from the date of initiation of a specific clinical trial.

3.5.1.4. If the trial does not begin or is delayed as per the date of commencement on the Clinical Trial Certificate issued, The Authority shall be informed of the new date of commencement within ninety (90) days of issuance of the Clinical Trial Certificate.

Failure to inform the Authority of the commencement or otherwise of the study within this period shall have regulatory implications including but not limited to the payment of administrative charges for the re-issuance of the Clinical Trial Certificate on its expiration.

3.5.1.5. If the trial is interrupted before its purpose is achieved, the reason shall be conveyed in writing to The Authority within ten (10) working days. This shall include:

3.5.1.5.1. Justification for the premature ending or of the temporary halt of the trial;

3.5.1.5.2. Number of patients receiving treatment at the time of the study termination;

3.5.1.5.3. Proposed management of patients receiving treatment at the time of halt or study termination;

3.5.1.5.4. Implications of the discontinuation on the evaluation of the final results.

3.5.1.6. The Principal Investigator/Sponsor shall notify in writing, The Authority not later than 30 days after the completion of a clinical trial and submit preliminary report on the ethical evaluation of the trial.

3.5.2. DSMB Report

Duly signed and authenticated DSMB reports and/or minutes shall be forwarded to The Authority upon request.

3.5.3. Final Report

In addition to the report referred to above, the person who conducted the trial shall, not later than 90 days after the completion of the trial, compile and submit to the Authority a comprehensive formal report conforming to the ICH E3 Guideline for the Structure and Content of Clinical Study Reports.

The report shall include a short but comprehensive summary of the essential findings of the trial and of its methodology and course.

The Final report shall be submitted in hard and soft copies (1 each).

Publication of the report in a scientific journal or other medium for the purpose of disseminating the information obtained to stakeholders may be encouraged only after 30 days of acknowledgement of receipt by the Authority.

3.6. Procedure for Importing Products for Clinical Trial

3.6.1. Approval to import products for clinical trials shall only be granted to recognized clinical research entity whose protocol has been approved by The Authority to conduct clinical trial in accordance with these guidelines.

3.6.2. An application for importation of investigational products, placebo and trial products, shall receive prior approval from The Authority.

3.6.3. Application to import investigational product and placebo shall be made to The Authority by submitting:

3.6.3.1. Letter stating the quantities of each investigational product, placebo and trial related products to be imported.

3.6.3.2. Certificate of analysis of investigational product and placebo for all batches to be imported.

3.6.3.3. Lot Release certificate (where applicable) for all batches to be imported

3.6.4. On approval of Section 2.17.2, an application for import permits must be processed through the electronic GC NET system as pertains at the approved ports of entry for medicines and medical devices (Tema Harbour and Kotoka International Airport).

3.6.5. The Principal Investigator shall notify the Authority within 48 hours through drug.safety@fdaghana.gov.gh of each respective consignment of investigational product and placebo batches received on site. The notification shall include the following details: Name of product(s), Quantities received and Batches received

3.6.6. All import permit applications shall bear the full name and address of the innovator, the Sponsor and the recognized clinical research entity, the name/description of the investigational product, placebo and quantity to be imported.

3.6.7. Both the investigational medicinal product and the placebo shall be appropriately labelled with the approved labels to indicate they are samples for the conduct of clinical trials only.

3.6.8. Products imported may be inspected by officials of The Authority at the port of entry before they are released to the recognized clinical research entity.

3.6.9. The Authority may order for destruction or re-exportation of the products intended for clinical trials if The Authority has any reason to believe that there is a protocol violation resulting in the termination of the study.

3.6.10. The above notwithstanding, all other statutes governing importation procedures and tax liabilities in Ghana shall apply to imported products regulated by The Authority

3.6.11. The Principal Investigator shall document the source, proof of purchase, quantities purchased and Certificate of Analysis for each batch of Investigational Products and Placebo purchased locally.

3.7. Good Clinical Practice Inspections

3.7.1. The Authority reserves the right to inspect and interrupt any trial for which authorization has been given, as and when necessary.

3.7.2. Periodic Good Clinical Practice (GCP) Inspections of the trial sites shall be conducted to ensure that the facilities used continue to be acceptable throughout the clinical investigation

3.7.3. GCP inspections shall be conducted in accordance with Food and Drugs Authority - GCP guidelines (Refer to the Food and Drugs Authority GCP Guidelines)

3.8. Phases of Clinical Trials

The application shall indicate the phase of clinical trial that is intended; see Appendix III of these Guidelines.

4.0. TIMELINES

For timelines relating to the submission of serious adverse events (SAE), refer to Appendix Ia of these Guidelines.

5.0. SANCTIONS

A person who contravenes these Guidelines or sections is liable to regulatory sanctions which shall be imposed by the Authority. These sanctions may include but not limited to any of the underlisted:

5.1. Suspension of an on-going clinical trial.

5.2. Revocation of a clinical trial certificate issued (stopping of a trial/recall of all investigational products).

5.3. Vary a clinical trial.

6.0. PENALTIES

A person who contravenes these Guidelines commits an offence and is liable on summary conviction to penalties in line with the provisions of Section 165, Part 8, of the Public Health Act, 2012, Act 851.

7.0. APPENDICES

7.1. APPENDIX Ia: Serious Adverse Events (SAE) Reporting Timelines

Type of ADR Report	Time Frame For Reporting	Format
REPORTS FROM SITES IN GHANA		
Serious Adverse Events	Immediately where possible and in any event, within 48 hours after becoming aware of the information	A Serious Adverse Events form conforming to the CIOMS format or previously approved by the Food and Drugs Authority must be completed and submitted after the site becomes aware of an event. Electronic submissions must be E2B compliant.
• Follow-up reports	Immediately when any of the underlisted occurs: i. Change in the severity of SAE initially reported. ii. Whenever there is any new development on an initially reported SAE. iii. When the SAE resolves.	Follow-up reports should include an assessment of the importance and implication of any findings. All fatal cases must be followed up with formal autopsy report[1.]
• Frequent adverse events (greater than or equal to 1% but less than or equal to 10%)	Immediately where possible and in any event, within 7 days after becoming aware of the information	Line listing
Non Serious Adverse Events	On request and where applicable, submitted as part of an application for registration	Individual reporting in accordance with the data elements specified in the ICH guidance Document E2A

REPORTS FROM FOREIGN SITES (For multicentre studies with Ghana as a participating country)		
Serious Events	Immediately where possible and in any event, within 7 days after becoming aware of the information.	Line listing Reports should include an assessment of the importance and implication of any findings.
Foreign regulatory decisions that affect the safety or use of the product	7 days	Detailed report Records with respect to all adverse events in respect of the drug that have occurred inside or outside the country, including information that specifies the indication for use and the dosage form of the drug at the time of the adverse event may be added.
OTHER REQUIREMENTS		
Literature reports that affect the safety of the product	7 days	Detailed report and / or copy of the publication Records with respect to the enrolment of clinical trial subjects including information sufficient to enable all clinical trial subjects to be identified and contacted in the event that the sale of the drug may endanger the health of the clinical trial subjects or other persons may be added.
Notification of change in nature, severity or frequency of risk factors	28 days	Complete and accurate records with respect to each change made to the Investigator's Brochure, including the rationale for each change and documentation that supports each change

New information impacting on risk benefit profile of product or conduct of trial	7 days	Communicate with appropriate scientific and medical judgments being applied to each situation. Additional information may include copies of diagnostic test results, laboratory reports or medical record progress notes
Periodic Safety Update Reports (PSUR)	• On request by The Authority • Within 30 days when it is a condition of registration for a new medicinal product	As a Follow Up Report including copies of diagnostic test results, laboratory reports or medical record progress notes

APPENDIX Ib: OTHER TIMELINES

ACTION	REFERENCE	TIMELINE
Notification for the implementation of an urgent amendment necessary to protect the life of subjects	3.1.5.2	Immediate phone call, followed by a written report within forty-eight (48) hours
Quarterly progress reports	3.5.1.3	Within 21 days after the end of the previous quarter. A quarter in this instance is considered as three months beginning from the date of initiation of a specific clinical trial.
Notification of Trial initiation	3.5.1.4	Immediately trial commences or within ninety (90) days of issuance of the Clinical Trial Certificate if the trial does not begin or is delayed as per the date of commencement on the Clinical Trial Certificate issued. Failure of notification within the stipulated time would invalidate the Clinical Trial Certificate issued. A new certificate would attract

		administrative fees.
Notification of interruption of an approved trial before achievement of its purpose.	3.5.1.5	Within ten (10) working days
Submission of preliminary report on the ethical evaluation of the trial after completion.	3.5.1.6	Not later than 30 days after the completion of a clinical trial
Final Report of Clinical Trial as per ICH E3 Guideline (unless otherwise specified on clinical trial certificate)	3.5.3	Not later than 90 days after the completion of the trial

PROCESSING OF SUBMITTED DOCUMENTS BY THE FDA

ACTIVITY	TIMELINE****
Processing of Clinical Trial applications	60 days
Processing of import permits for Investigational Products	10 days
Processing of quarterly progress and safety reports	15 days
Notification of receipt of electronic submissions including SAE reports	5 days
Communicating GCP Inspection findings	21 days
Processing of applications for protocol amendment	30 days
Processing of final Clinical Trial reports	30 days

****Timelines specified are working days and excludes clock stop time

7.2. APPENDIX II: Food and Drugs Authority Clinical Trials Quarterly Progress Report Form

SECTION A: ADMINISTRATIVE INFORMATION			
FOOD AND DRUGS AUTHORITY Clinical Trial Certificate Number: ……	Expected Date of Commencement (as indicated on the certificate): ……..../……./…….	Actual Date(s) of Commencement (at the Study Centre(s): ....……/……./…….	Protocol Number: …… ……
Study Title:			
Reporting Period	From….....to……....		
Principal Investigator:	Name:		
	Address:	Phone: Mobile: E-mail:	
Co-Investigators:	Name(s):	Phone: Mobile: E-mail:	
Other Study Contact (if applicable):	Name: Address:	Phone: Mobile: E-mail:	

SECTION B: STUDY STATUS (Check one category only)
☐ Enrolment has not begun
☐ Actively enrolling subjects
☐ Enrolment closed on: _____(insert date): Subjects are receiving treatment/intervention
☐ Enrolment closed on: _____(insert date): Subjects are in follow-up only.
☐ Analyzing data
☐ Data analysis completed

SECTION C: INFORMATION ON SUBJECTS & STUDY ACTIVITIES	
a. Number of subjects consented and screened.....	
b. Total number of subjects consented and screened who are eligible for the study.....	
c. Number of subjects to which the investigational product(s) has been administered.....	
d. Number of subjects left to be enrolled in the coming months (years).....	
e. Number of participants who have discontinued the study: • by Investigator: • voluntarily: • due to SAE:	
f. Have there been any Serious Adverse Events (SAEs)?	Yes ☐ ☐ No
g. Total number of SAEs:___. (attach line list of SAEs documented for the quarter)	
h. Have these SAEs been reported to the Food and Drugs Authority	Yes ☐ ☐No
i. If No, explain ……..... .....……..... j. Have there been any changes to the protocol since the Food and Drugs Authority approved?	Yes ☐ ☐ No
k. Is this amendment submitted to the Food and Drugs Authority?	Yes ☐ ☐No
l. If No, explain ……..... .....……..….…..... m. Date for the end of the study	
n. Date for the final study report	

SECTION D: COMMENTS (if any)

SECTION E: SIGNATURE	
. _____ .	. _____ .
Signature of Principal Investigator	Date

Return this form and all supporting documentation to:
THE CHIEF EXECUTIVE
FOOD AND DRUGS AUTHORITY
P. O. BOX CT 2783, CANTONMENTS, ACCRA
or submit via e-mail to drug.safety@fdaghana.gov.gh

7.3 APPENDIX III: Phases of Clinical Trials

PHASE I

- Studies preceding this phase would have established the effect and safety of the product in animals. The purpose of this phase is to establish a preliminary evaluation of safety, tolerance and a first outline of how the drug is metabolized and excreted in humans.
- Phase I trials, being the first trials of a new drug in humans, shall be conducted in healthy volunteers, with their informed consent, who shall
  - Be aged between 18 and 65 years and in good mental health and not pregnant or lactating.
  - Not have any illness which could potentially affect the results of the trial, or which could create special conditions for unfavourable effects of the drug.
- The number of volunteers participating in this phase of clinical trials shall not be less than twenty-four (24).

PHASE II

- The purpose of a phase II trial is to demonstrate activity of the drug and to obtain further safety data. It also aims at the determination of effective dose ranges and regimens and provides an optimal background for the design of future therapeutic trials.
- This phase may be an open trial in a small number of informed consenting patients suffering from the disease or condition which the product potentially can treat.
- If the drug is found to be effective at this stage, and the risks considered acceptable, then it progresses to phase III trials.

PHASE III

- This phase consists of wider participants to further determine the therapeutic effects of the drug and possibly the short and long-term safety and efficacy balance of formulations of the drug.
- The effect of treatment with the drug may be compared in this phase with established methods of treatment, if any, or with other control procedures.
- The design of trials in this phase shall, preferably, be randomized, double-blind or cross-over. Other designs may be acceptable for long-term safety studies.
- Generally, the conditions of the trial shall be as close as possible to the normal clinical setting in which the disease for which the drug is intended occurs.

PHASE IV

- Phase IV trials shall be conducted on an approved product already on the market to find out more about the long-term risks, benefits, and optimal use, or to test the product in different populations of people, such as children.
- The trial shall include post-market surveillance.