



FOOD AND DRUGS AUTHORITY

15th January 2024

FDA/CTD/GDL - ACT/2024/05

Technical Advisory Committee on Clinical Trials (TAC-CT)

GUIDELINE FOR AUTHORIZATION OF CLINICAL TRIALS OF MEDICINES, FOOD SUPPLEMENTS, VACCINES AND MEDICAL DEVICES IN GHANA

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This guideline replaces 'Guidelines for Authorization of Clinical Trials of Medicines, Food Supplements, Vaccines and Medical Devices in Ghana' (FDA/SMC/CTD/GL-ACT/2013/01)

Document Revision History

Date of Revision	Version Number	Key Changes made and/or reasons for revision
N/A	V 1.0	Initial issue
18 th December 2015	V 2.0	<ol style="list-style-type: none"> 1. Include in the Introduction section, the rationale for developing the Guideline 2. More details/elaboration of the section to include the types of amendments 3. Inclusion of a Section on GMP certificate, stating what it is and when it is required 4. Include the following sections as part of CTA document list <ol style="list-style-type: none"> a. 3.1.7 IMP Dossier b. 3.1.8 GMP Certificate c. 3.1.14 Informed Consent Form and Assent Forms d. 3.1.15 Statistical Analysis Plan 5. Clearly specify which type of ethical clearance may be appropriate in specific situations i.e when GHS-ERC or other IRBs approval is required 6. Inclusion of new section to deal with situations of temporary halt of trials 7. Inclusion of new section to deal with cases of early trial termination 8. Include new Section 3.10.1 which will clearly outline procedures for having pre- and post-approval face-to-face meetings with applicants/clients 9. Include the Clinical Trial Application Process Flowchart to further explain the concept of clock stop 10. Include the Food and Drugs Authority Close-out Report Form
14 th January 2019	V 3.0	<ol style="list-style-type: none"> 1. Inclusion of a paragraph in the introduction which indicates that the FDA relies on and uses relevant CT decisions, reports or information from other NRAs (Well-resourced Regulatory Agencies) or from regional and international bodies. 2. Inclusion of the statement, <i>'The language used in the ICF shall be in English and shall be translated into the local language(s) of the target population'</i> included. 3. Section on procedure for Importing IPs for CT has been elaborated to include appropriate process for destruction of unused, expired, damaged IPs in CTs
6 th January 2020	V 4.0	<ol style="list-style-type: none"> 1. Addition of the criteria for activation of the Reliance pathway 2. Clarifications on the mandate of the Technical Advisory Committee on Clinical Trials with respect to SAE causality assessment

15 th January 2024	V 5.0	<ol style="list-style-type: none"> 1. Addition of the publication of the FDA Public Assessment Report (FAPAR) on Clinical Trial Applications on the FDA website 2. Addition of Sponsor and Monitor/Contract Research Organization Contractual Agreement as part of CTA requirements 3. Addition of Financial disclosure as part of CTA requirements 4. Inclusion of a requirement for Academic trials 5. Inclusion of the criteria for the submission of an updated insurance cover 6. Indication of the FDA's adopted guidelines for First-In-Human trials 7. Use of non-investigational study-related medical devices in trials 8. Additional emphasis on the need for FDA approval before shipment of biological samples 9. Requirements for contracts with local laboratories 10. Addition of the requirements for submission of protocol deviations and interim reports. 11. Revision in the definition for the date of commencement 12. Inclusion of requirements for post-trial access to Investigational Products. 13. Inclusion of the minimum requirements for the content of a GMP Certificate. 14. Inclusion of statement on the signing of clinical trial documents by the appropriate person(s). 15. Rephrased section 3.6.1.2. Quarterly reports of the progress of a clinical trial starting from the date of initiation after the issuance of the clinical trial certificate shall be submitted to The Authority in the recommended format. (Refer to APPENDIX IV).
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Guideline for Authorization of Clinical Trials of Medicines, Food Supplements, Vaccines and Medical Devices in Ghana

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1.0 Introduction (background)

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 humans in Ghana. These Guidelines do not cover veterinary trials.

These Guidelines seek to ensure that clinical trials conducted in Ghana are designed and conducted according to sound scientific principles and ethical standards within the framework of good clinical practice. Compliance with these Guidelines provides the public with assurance that the rights, safety and wellbeing of trial participants are protected.

These Guidelines cover the regulatory requirements for authorization of clinical trials in Ghana.

These Guidelines are addressed to investigators, the pharmaceutical industry, Clinical Research Organizations and sponsors of clinical trials, whether for academic purposes or for generation of data, intended for inclusion in the regulatory submissions for medicinal products. These Guidelines are intended to be applied during all clinical stages of drug development prior to and subsequent to product registration. The same set of rules and requirements must be followed for every clinical trial application, no matter who is organizing and funding the study.

This Guideline is hereby promulgated for information, guidance and strict adherence by all stakeholders/concerned.

Clinical trials shall be categorized as follows:

1. Trials directed by The Authority.
2. Trials initiated by pharmaceutical companies or agencies.
3. Trials initiated by academic and research institutions either locally or as part of an international multi-centre study.

To ensure easy access to medical products, the FDA has developed and implemented alternative /non-routine Clinical Trials Authorization pathway (refer to Appendix III) to the standard approval pathway especially for applications where the Clinical Trial has already

been approved and/or initiated (partly or wholly – phase I/II/III) in a well- resourced setting and by a well-resourced regulatory authority. The Authority relies on and uses relevant Clinical Trial decisions, reports or information from well-resourced regulatory authorities or from regional and international bodies.

That notwithstanding, it is equally important to note that the Authority reserves the right to request for information or material, or define conditions not specifically described in this Guideline or the FDA's *Reliance Policy*, in order to allow the Department to adequately assess the safety, efficacy or quality of a product. The Authority is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

1.1. Legal Basis

In pursuance of the Public Health Act, 2012, Act 851, Part 8, 150-166, this Guideline is 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 humans in Ghana.

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 above.

“Adverse Drug Reaction (ADR)” A response to a medicinal product which is noxious and unintended including lack of efficacy and which occurs at any dosage and can arise from:

- The use of product within the terms of the marketing authorization
- The use of product outside the terms of the marketing authorization, including overdose, off-label use, misuse, abuse and medication errors.
- Occupational exposure.

“Adverse Event (AE)” Adverse event is any untoward medical occurrence in a patient or clinical trial participant administered a medicinal product that may present during treatment with a medicine, but which does not necessarily have a causal relationship with this treatment.

“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 Authority that the clinical trial application has been reviewed and the clinical trial may be conducted within the constraints set forth by an Ethics Review Body, Good Clinical Practice (GCP), and the applicable regulatory requirements.

“Assent” A process by which a child, who is capable of understanding voluntarily, confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the child's decision to participate. Assent is documented by means of a written, signed and dated assent form from the child. As part of the assent process, parents and guardians must give informed consent.

“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).

“Auditor” A person who carries out an audit.

“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 clinical trial processes.

“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 participant(s) being unaware; and double-blinding usually refers to the participant(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

“Case Report Form” A printed, digital or electronic document designed to record all of the required information stated in the protocol. 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, animal and plant products.

“Child” 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, Act 560, 1998.

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

“Clinical Trial” (CT) A research study that test how well new medical approaches work in people. Each study answers scientific questions and tries to find better ways to prevent, screen for, diagnose, or treat a disease. Clinical trials may also compare a new treatment to a treatment that is already available (NIH).

“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 Sponsor’s trial-related duties and functions.

“Data Safety Monitoring Board (DSMB)” An independent data-monitoring committee 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.

“Date of Commencement” For the purpose of the Clinical Trial Certificate and Quarterly Progress Report Form, this is defined as the date when the first participant is consented.

“Drug/Medicine” includes as per the Food and Drugs Act, part 7, Act 851

1. A substance or mixture of substances prepared, sold or represented for use in:
 - i. Restoring, correcting or modifying organic functions in man, and
 - ii. The diagnosis, treatment, mitigation or prevention of disease, disorder of abnormal physical state or the symptoms of it, in man, or

2. Nutritional supplements

“FDA” means Food and Drugs Authority

“Food/Dietary or Nutritional Supplement” 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.

“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 organizations (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” A preparation with therapeutic or any other human health benefits which contains raw or processed ingredients from one or more plants or materials of 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 participants.

“Investigational Product” A product being tested or used as a reference in a clinical trial including a product with a marketing authorization.

“Impartial witness” A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the participant or the participant’s legally acceptable representative cannot read, and who reads the Informed Consent Form and any other written information supplied to the participant.

“Informed Consent” (IC) A process by which a participant voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the participant’s decision to participate. Informed consent is documented by means of a written, signed and dated Informed Consent Form.

“Investigator” A person, regardless of title or position, who is responsible for the design, conduct, or reporting of a clinical trial.

“Investigator’s Brochure” The Investigator’s Brochure (IB) is a compilation of the clinical and nonclinical data on the investigational product(s) that are relevant to the study of the product(s) in human subjects.

“Legal representative” The name given to describe the executor, administrator or the person who looks after another person’s affairs.

“Local Monitor” A person appointed by the Sponsor or CRO to oversee the progress of a clinical trial and of ensuring that it is conducted, recorded and reported in accordance with the SOPs, GCP and the applicable regulatory requirements.

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

“Materials Transfer Agreement” An MTA is a written contract that governs the transfer of tangible research materials or biological samples between parties.

“Medical Device” An instrument, apparatus, implement, a medical equipment, machine, contrivance, implant, in vitro reagent or any other similar or related article, including a component, part or an accessory which is:

1. recognized in the official natural formulary or pharmacopoeia or a supplement to them, or
2. intended for use in the diagnosis of a disease or any other condition, or in the cure, mitigation, treatment or prevention of disease in humans and animals, or
3. intended to affect the structure or a function of the body of the human being or other animal and which does not achieve any of its principal intended purposes through chemical action within the body of the human being or any other animal and which is not dependent on being metabolized for the achievement of any of its principal intended purposes.

“Placebo” An inactive substance or sham form of a therapy administered as a control in testing experimentally or clinically the efficacy of a biologically active preparation or procedure.

“Principal Investigator” A person responsible for the conduct of the clinical trial at the clinical trial site(s), who is entitled to provide health care under the laws of the Country where that clinical trial site(s) is/are 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 during a clinical trial that 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.

“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 resources for a trial and does not benefit in any way from the results of the trial.

“Study Pharmacist” A registered pharmacist appointed by the Sponsor/Principal Investigator to ensure the proper management of pharmaceutical investigational products to be used in the study.

“Suspected Unexpected Serious Adverse Reactions” Any unfavourable occurrence in a trial participant that is judged to have a major impact on their health, was not anticipated and could potentially be due to the intervention under investigation.

“Vaccine” A biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins. The agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and "remember" it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters.

“Vulnerable population” Defined by race/ethnicity, socio-economic status, geography, gender, age, disability status, risk status related to sex and gender, and among other populations identified as at-risk for health disparities. (CDC)

“Well-Resourced Regulatory Authority” The national drug regulatory authorities which are members, or observers or associates of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)

3.0 REQUIREMENTS

3.1. Clinical Trial Application (CTA)

A Clinical Trial Application made to The Authority 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 Completed Food and Drugs Authority Application Forms for Conducting Clinical Trials signed by authorized persons (PI and Sponsor's authorized representative)
- 3.1.4 A Clinical Trial Protocol
- 3.1.5 A proof of registration with Pan African Clinical Trials Registry (PACTR)
- 3.1.6 Investigator's Brochure (IB)
- 3.1.7 Investigational Product (IP) Dossier
- 3.1.8 Good Manufacturing Practice (GMP) Certificate
- 3.1.9 Ethics Committee (EC)/Institutional Review Board (IRB) Approval (at least evidence of submission of application to EC/IRB if final approval is not yet available)
- 3.1.10 Insurance Cover for all study participants
- 3.1.11 Financial Declaration
- 3.1.12 DSMB Membership and signed Charter
- 3.1.13 Sponsor/PI Contractual Agreement
- 3.1.14 Sponsor and Monitor/Contract Research Organization Contractual Agreement
- 3.1.15 Informed Consent and Assent Forms (if applicable)
- 3.1.16 Statistical Analysis Plan (SAP)
- 3.1.17 Materials Transfer Agreement (if applicable)
- 3.1.18 Financial Disclosure

All clinical trial application documents shall be submitted in hard and soft copies (1 each; format of soft copy of documents submitted should be in searchable PDF).

Note:

- a) A Clinical Trial Application shall be rejected if upon preliminary assessment at the time of submission, less than 70% of the required documents as per Section 3.1 are available. This 70% shall include the covering letter, a duly signed protocol, IB, completed FDA application form and application fee.
- b) For Academic Trials, academic supervisors shall make submissions on behalf of their students.
- c) Failure of applicant to address all outstanding issues related to an application within a year renders an application null and void.
- d) The application shall indicate the phase of clinical trial that is intended; see Appendix III of these Guidelines.
- e) With regard to the review of CTAs and amendments
 - i. FDA reviews the documents submitted to assess the quality of the investigational products and determine that the use of the investigational product for the purposes of the clinical trial does not cause any harm to the health or pose undue risk to the health of clinical trial participants or other persons; the clinical trial is not contrary to the best interests of a clinical trial participants, and the objectives of the clinical trial may be achieved.
 - ii. Assessment of documents shall involve evaluators from within the FDA as well as external experts when the need arises.
 - iii. A decision to defer, approve or reject an application shall be done within sixty (60) working days for a routine application (refer to Appendix II), thirty (30) working days for an abridged evaluation after the reliance pathway has been activated, (refer to Appendix III) and twenty-one (21) working days for trials that have to be conducted during emergency situations (refer to Guidelines for Conduct of Clinical Trials during Emergencies).
 - iv. The FDA , during evaluation, reserves the right to seek clarification, additional documentation and/or samples by issuing a formal letter outlining specific queries. The official clock measuring the evaluation's duration shall pause upon the issuance of such queries and will resume only upon receipt of responses.

- v. In the event of a deferral decision resulting in the issuance of queries, the evaluation process shall stop until the FDA receives an official response to the raised queries. After receiving a response, the clock shall restart.
 - vi. Applicants must address all queries within 6 months. Failure to do so within this period will result in the application being treated as a new submission. To facilitate the review process, all queries issued in the same letter must be addressed in a single submission.
 - vii. Non-compliance and non-conformity to the requirements prescribed in these guidelines shall lead to rejection of the clinical trial.
 - viii. In the event of a rejection of an application, an applicant may appeal to the Minister of Health within sixty (60) days in writing. The applicant shall give grounds for review for each reason given for the rejection of the clinical trial based on the information submitted in the application. Where a representation is not submitted by the applicant within the sixty (60) days, the decision of the Authority in respect of the application shall stand.
 - ix. The FDA reserves the right to request information or material, or define conditions not specifically described in this Guideline, in order to allow the Authority to adequately assess the safety, efficacy or quality of the investigational medicinal product.
- f) Regarding Clinical Trials that have already been approved by a well-resourced NRA, the FDA may activate the reliance pathway to facilitate regulatory decisions either on a case-by-case basis or at the explicit request of the Applicant. The Applicant shall submit the full CTA as listed in 3.1 (above) and the full Assessment reports of the CTA submitted to the well-resourced NRA for approval. The application (protocol, IB, nonclinical reports, previous study reports and other relevant documents) shall be identical to that submitted, evaluated and approved by the well-resourced NRA or reference NRA. Refer to FDA's Reliance Policy for details on Reliance Authorization Pathway.
- g) To ensure transparency, summarized review comments on Clinical Trial Applications shall be published as a Public Assessment Report on the Authority's website in a prescribed format outlined in the FDA's Public Assessment Report Guide for Clinical Trials. The status of all clinical trial applications received shall be

updated on the Clinical Trials Registry and published on the FDA website.

3.1.1. Cover Letter

The cover letter shall be addressed as follows:

The Chief Executive Officer
Food and Drugs Authority
Head Office
P.O. Box CT 2783
Cantonments, 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

The application shall be submitted in duplicates and forms signed by all participating investigators.

3.1.4 Clinical Trial Protocol and Trial Amendment

3.1.4.1 Clinical Trial Protocol

1. General Information

This shall include:

- i. Protocol title, protocol identifying number, and date. Any amendment(s) should also bear the amendment number(s) and date(s).
- ii. Name and address of the Sponsor and monitor (if other than the Sponsor)
- iii. Name and title of the person(s) authorized to sign the protocol and the protocol amendment(s) for the Sponsor.
- iv. Name, title, address, and telephone number(s) of the Sponsor's medical expert (or dentist when appropriate) for the trial.

- v. 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).
- vi. Name, title, address, and telephone number(s) of the other investigators designated by the PI to be responsible for some aspects of the study.
- vii. 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.
- viii. Contractual agreement between the investigator and Sponsor.
- ix. A clear statement on compensation and benefits package for clinical trial participants.
- x. Publication policy

2. Background Information

This shall include:

- i. Name and description of the investigational product(s).
- ii. A summary of findings from nonclinical studies that potentially have significance to the clinical trial
- iii. Summary of findings from clinical studies/trials that are relevant to the trial.
- iv. Summary of the known and potential risks and benefits, if any, to human participants.
- v. Summary of the local background rates with respect to the condition for which the intervention is proposed.
- vi. Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).
- vii. Description of the population to be studied.
- viii. A statement that the trial shall be conducted in compliance with the protocol, GCP and the applicable regulatory requirement(s).
- ix. References to literature and data that are relevant to the trial and that provide background for the trial.
- x. 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.

- xi. Justification for the trial is being conducted in Ghana.

3. Trial Purpose and Objectives

- i. Aim of the trial and reason for its execution.
- ii. A detailed description of the objectives and the purpose of the trial.

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:

- i. A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.
- ii. If markers are being used as endpoints, they should be validated.
- iii. 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.
- iv. Number of participants to be involved in the trial and the statistical justification.
- v. A description of the measures taken to minimize/avoid bias, including: Randomization and Blinding.
- vi. A description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s).
- vii. Description of the dosage form, packaging, and labeling of the investigational product(s) and sample of label to be used for investigational product.
- viii. The expected duration of participant participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.
- ix. Quantities and sources of all investigational medicines and/or comparators (whether to be imported or purchased locally).
- x. A detailed description of the "stopping rules" or "discontinuation criteria" for individual participants, parts of trial and entire trial.

- xi. Accountability procedures for the investigational product(s).
- xii. Maintenance of trial treatment randomization codes and procedures for breaking codes.
- xiii. 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.
- xiv. Specifications and instructions for anticipated deviations from the protocol.

5. Selection and withdrawal of participants

- i. Participant inclusion criteria.
- ii. Participant exclusion criteria.
- iii. Participant withdrawal criteria (i.e terminating investigational product treatment/trial treatment) and procedures specifying:
 - a. When and how to withdraw participants from the trial/investigational product treatment.
 - b. The type and timing of the data to be collected for withdrawn participants.
 - c. Whether and how participants are to be replaced.
 - d. The follow-up for participants withdrawn from investigational product treatment/trial treatment.

6. Treatment of Participants

- i. 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 participants for each investigational product treatment/trial treatment group/arm of the trial.
- ii. Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.
- iii. Procedures for monitoring participant compliance.
- iv. 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.

- v. Description of diagnostic devices or kits applied to be used in the clinical trial.
- vi. Description of special analyses and/or tests or procedure to be carried out.

7. Assessment of Efficacy

- i. Specification of the efficacy parameters.
- ii. Methods and timing for assessing, recording, and analyzing of efficacy parameters.
- iii. Clear procedures for interim assessment of trial.

8. Assessment of Safety

- i. Specification of safety parameters.
- ii. The methods and timing for assessing, recording, and analyzing safety parameters.
- iii. Procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses.
- iv. List of adverse events of special interest (AESI) and/or expected adverse events – information shall include;
 - a. Whether the event is related to the intervention or not.
 - b. Rationale for listing each event
 - c. Expected rate or frequency of each event
 - d. Laboratory limits (if applicable)
- v. The type and duration of the follow-up of participants after adverse events.
- vi. Provision for dealing with all adverse events. Copy of form to be used to report adverse event.

9. Statistics

- i. A description of the statistical methods to be employed, including timing of any planned interim analysis.
- ii. The number of participants planned to be enrolled. In multicentre trials, the numbers of enrolled participants projected for each trial site should be

- specified.
- iii. Reason for choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification.
 - iv. The level of significance to be used.
 - v. Criteria for the termination of the trial
 - vi. Methods for data analyses and evaluation of results.
 - vii. Procedure for accounting for missing, unused, and spurious data.
 - viii. 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).
 - ix. The selection of participants to be included in the analyses (e.g. all randomized participants, all dosed participants, all eligible participants, evaluable participants).

10. Ethics

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

11. Data Handling and Record Keeping

- i. 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.
- ii. A clear statement on composition and benefit package for clinical trial participants
- iii. 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.

12. Publication of clinical trial report

- i. Publication policy, if not addressed in a separate agreement.

- ii. Publication policy, including a plan for the dissemination of the results (publishing plan)

3.1.4.2 Protocol Amendments

1. Any amendment to the trial protocol, trial arrangements and investigational product shall be submitted to the IRB/IEC that originally approved the protocol and The Authority for approval before such amendments are carried out.
2. If such amendments are necessary to protect the life of participants, 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. All amendments shall attract a fee which shall be determined as per FDA Fee Schedule
4. The sponsor may make amendments to the protocol after the commencement of the clinical trial. If those amendments are substantial and are likely to have an impact on the safety of the trial participants or to change the interpretation of the scientific documents in support of the conduct of the trial, the sponsor shall notify The Authority of the reasons for, and content of, these amendments.

5. The notion of “amendment”

The following changes do not count as an ‘amendment’:

- i. A change to the documentation submitted to The Authority during the ongoing assessment of the request for authorization by The Authority, and
- ii. A change to the documentation submitted to the Ethics Committee during the ongoing assessment of the request for authorization by the Ethics Committee.
- iii. Safety report (SR) is not per se an amendment and thus does not have to be notified as a substantial amendment to The Authority. However, the sponsor has to verify whether the data presented in the SR requires a change to the documentation submitted with the request for authorization of a clinical trial. If this amendment is substantial, the rules for notification of substantial amendments apply to these changes.
- iv. A change in the contact details of the contact person (e.g. a change of

e-mail or postal address) is not considered as an amendment, if the sponsor and legal representative remain identical. However, the sponsor should ensure that The Authority is aware of this change as soon as possible, in order to allow The Authority to exercise its supervisory function.

6. The notion of “substantial”

- i. Amendments to the trial are regarded as ‘substantial’ where they are likely to have a significant impact on:
 - a. the safety or physical or mental integrity of the clinical trial participants, or
 - b. the scientific value of the trial.
- ii. In all cases, an amendment is only to be regarded as ‘substantial’ when one or both of the above criteria are met.
- iii. The responsibility of assessing whether an amendment is regarded as substantial or not lies with the sponsor.
- iv. The Authority shall however recommend a reassessment of a Sponsor’s classification of an amendment when necessary.
- v. The annual update of the IB is not per se a substantial amendment. However, the sponsor has to verify whether the update relates to changes which are to be considered as substantial. In that case, the rules for notification of substantial amendments apply to the change.
- vi. The sponsor should assess also whether the combination of substantial amendments lead to changes of the clinical trial to an extent that it has to be considered as a completely new clinical trial, which would then be subject to a new authorization procedure.
- vii. Substantial amendments may relate to information relevant for assessment by the Food and Drugs Authority, the Ethics Committee, or both.
- viii. Without prejudice to the above points, The Authority reserves the right to direct for an amendment to the protocol.

7. Format and content of notification

The notification of a substantial amendment should include the following:

- i. A signed cover letter, including a highlighted indication of any special issues related to the amendment and indication where the relevant information or text is in the original application dossier.
- ii. A description of the amendment:
 - a. an extract from the amended documents showing previous and new wording in track changes, as well as the extract only showing the new wording;
 - b. notwithstanding the previous point, if the changes are so widespread or far-reaching that they justify an entire new version of the document, a new version of the entire document. In this case, an additional table should list the amendments to the documents. In this list, identical changes can be grouped.
 - c. The new version should be identified with the date and an updated version number.
- iii. Supporting information including, where applicable:
 - a. summaries of data,
 - b. an updated overall risk/benefit assessment,
 - c. possible consequences for participants already included in the trial,
 - d. possible consequences for the evaluation of the results.

3.1.5 Proof of Registration of the Clinical Trial

As part of a Clinical Trial application, proof of registration of the trial with a Clinical Trial Registry, which is WHO recognized and publicly accessible, shall be submitted. It is mandatory for all trials to be registered with the Pan African Clinical Trials Registry (PACTR).

3.1.6 Investigator's Brochure

Investigator's 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.
- 3.1.6.9 The Investigational Brochure should be prepared from all available information and evidence that supports the rationale for the proposed clinical trial and the safe use of the IP in the trial and be presented in the form of summaries.
- 3.1.6.10 The approved summary of product characteristics (SmPC) may be used in place of the IB if the IP is authorized in Ghana and is used according to the terms of the marketing authorization. If the conditions of use in the clinical trial differ from those authorized, the SmPC should be supplemented with a summary of relevant non-clinical and clinical data that support the use of the IP in the clinical trial. Where the IP is identified in the protocol only by its active substance, the sponsor should elect one SmPC as equivalent to the IB for all medicinal products that contain that active substance and are used at any clinical trial site.

Note:

- ***For the contents of an IB, refer to Section 7.0 of the current version of ICH E6 Guidelines for more details.***
- ***For First in Human trial, refer to the following Guidelines adopted by the Authority:***
 - *EMA guidelines on Strategies to Identify and Mitigate Risks for First-In-Human Clinical Trials with Investigational Medicinal Products should be considered in the design and conduct of FIH trials.*

- *USFDA Guidance for Industry and Reviewers, Estimating the Safe Starting Dose in Clinical Trials for Therapeutics in Adult Healthy Volunteers.*
- *USFDA Guidance on Expansion Cohorts: Use in First-in-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics Guidance for Industry.*

3.1.7 IP Dossier

- 3.1.7.1 The IP dossier (IPD) gives information related to the quality of any IP (i.e. including reference product and placebo), manufacture and control of the IP, and data from non-clinical studies and from its clinical use. However, in many cases where the IP has a marketing authorization, an IPD is not required.
- 3.1.7.2 A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorization but:
1. used or assembled (formulated or packaged) in a way different from the authorized form, or
 2. when used for an unauthorized indication, or
 3. when used to gain further information about the authorized form.
- 3.1.7.3 All study-related medical devices to be used in a trial shall have marketing authorization in Ghana, otherwise, they shall be treated as study Investigational Products (IPs) and the necessary documentation shall be submitted to support the safety and efficacy of the device(s).

3.1.8 GMP Certificate

A GMP certificate from the national competent Authority of the country of origin shall be required when the IP has no marketing authorization in Ghana or has marketing authorization, but its original indication is modified for the purpose of the trial.

- 3.1.8.1 The GMP certificate shall have the underlisted as minimum information:
1. Name and address of the manufacturing site
 2. Name of the Competent/Issuing Authority
 3. Certificate number/Unique identifier
 4. Date of issuance

5. Scope of the certificate
6. Statement of compliance to GMP
7. Signature of the authorized person
8. Validity Period or expiration date

3.1.9 Independent Ethical Committee / Institutional Review Board's Approval

- 3.1.9.1 Ethical Clearance for all phases of clinical trials in humans shall be required to be submitted from the facility(ies)/institution(s) being used in the conduct of the study.
- 3.1.9.2 An ethical approval from the Institutional Review Board (IRB) or Institutional Ethics Committee (IEC) at the facility/institution where the trial would be conducted shall be required. A Ghana Health Service Ethical Review Committee's (GHS-ERC) Approval shall be required for studies being conducted at facility(ies)/institution(s) under the GHS.
- 3.1.9.3 In cases where there is no recognised IRB or IEC at the study facility(ies), an ethics approval from an independent ethics committee shall be submitted with an appropriate justification from the applicant.
- 3.1.9.4 Submissions to The Authority and to the review authorities or ethics committees can be done in parallel.
- 3.1.9.5 In the case of multicentre studies, an approval from each institution's review Authority shall be required.
- 3.1.9.6 In cases where the final ethics approval is not yet available at the time of submission to the Authority, evidence of submission to the EC/IRB shall be required.

3.1.10 Insurance Cover

- 3.1.10.1 Sponsors and Principal Investigators shall ensure appropriate insurance cover for clinical trial participants and shall submit as evidence a Certificate of insurance cover for participants. The insurance policy shall grant specific cover associated with the reimbursement of damages and death caused to participants by the clinical trial activities throughout the entire study period, thus covering any civil liability of investigator and sponsor of the clinical trial, without excluding any damage which may be unintentionally caused by accident and/or be attributed to negligence, imprudence or inexperience.

3.1.10.2 An insurance certificate shall contain at least

1. Insurance company
2. Policy number
3. Initial Date
4. Expiry Date
5. Insured (Policy Holder/Sponsor)
6. Description of activity (purpose of the policy)

3.1.10.3 Information concerning the trial

1. Title of insured protocol and protocol number (if available)
2. Number of trial centres
3. Number of participants (planned number of patients who are expected to take part in the clinical trial)
4. Insured (list all events that are covered by the insurance policy e.g. deaths, permanent and temporary impairment of health conditions, relevant financial consequential losses which are the direct consequence of the trial and which can be traced to the liability of all people operating for the performance of the trial)
5. Exclusions (if provided for that specific protocol, please list all exclusions)

3.1.10.4 Update of Insurance Cover

1. An updated insurance cover for the study shall be submitted to the Authority once the insurance cover/certificate expires or exceeds the validity period of the insurance
2. In the event that the sample size for a trial increases due to an amendment, an updated insurance cover should be submitted to the Authority to include coverage for the additional participants to be recruited.

3.1.11 Financial Declaration

- 3.1.11.1 The financial aspects of the trial should be documented in an agreement between the Sponsor and the Principal Investigator/Contracted Research Organization/Institution.
- 3.1.11.2 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.

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

- 3.1.12.1 An Independent Data Monitoring Committee 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.
- 3.1.12.2 The Sponsor shall include charter of work, membership and curriculum vitae of all the DSMB members when applicable.
- 3.1.12.3 All members of the DSMB shall sign the Charter
- 3.1.12.4 A DSMB/IDMC/DMC Charter shall include
 - 1. Terms of Reference
 - 2. Membership and their CVs
 - 3. Proof of Independence of the Committee
 - 4. Scope of work for Members/responsibilities of the Committee which is to assess the progress of a clinical trial including safety data and the critical efficacy endpoints at intervals, and to recommend to the sponsor whether to continue, modify, or stop a trial.
 - 5. Meeting schedules
 - 6. Standard Operating Procedures of the Committee
 - 7. Document reference numbers with appropriate version numbers and dates
- 3.1.12.5. For trials conducted solely in Ghana, include a Ghanaian DSMB member. In multinational trials, ensure at least one DSMB member from a host country in Africa.

3.1.13 Sponsor/PI Contractual Agreement

The Sponsor/PI Contractual Agreement shall indicate.

- 3.1.13.1. The study title
- 3.1.13.2. Protocol version and date
- 3.1.13.3. Trial site
- 3.1.13.4. Investigational Product
- 3.1.13.5. Definitions of all terms
- 3.1.13.6. Effective date of agreement
- 3.1.13.7. Outline of the Sponsor's responsibilities which shall include
 1. General management of the trial
 2. Provision of adequate funding, resources/logistics and Investigational Products for the study
 3. Insurance for the study participants
- 3.1.13.8. Outline of the PI's responsibilities which shall include
 1. conduct the trial in compliance with GCP, with the applicable regulatory requirement(s), and with the protocol agreed to by the sponsor and given approval/favourable opinion by the IRB/IEC and The Authority
 2. comply with procedures for data recording/reporting
 3. permit monitoring, auditing and inspection
 4. retain all trial related essential documents until the sponsor informs the PI these documents are no longer needed
- 3.1.13.9. Term (period of study duration) and Termination of agreement (conditions for this)
- 3.1.13.10. Confidentiality
- 3.1.13.11. The Sponsor and the PI shall sign this agreement and the protocol.

3.1.14 Sponsor and Monitor/Contract Research Organization (CRO) Contractual Agreement

1. An Agreement duly signed and dated by Sponsor and the Local Monitor or representative of the CRO shall be provided.
2. The agreement shall outline the specific delegated tasks/duties to the CRO or Local Monitor

3. A copy of the signed monitoring plan for the study shall be included in the submission.

3.1.15 Informed Consent and Assent

- 3.1.15.1 The informed consent discussion and the written informed consent form and any other written information to be provided to participants shall include explanations of the following;
 1. That the trial involves research
 2. The purpose of the trial
 3. The trial treatment(s) and the probability for random assignment to each treatment
 4. The trial procedures to be followed, including all invasive procedures.
 5. The participant's responsibilities.
 6. Those aspects of the trial that are experimental, etc
 7. Signature and date of participant, participant's legal representative, impartial witness (where applicable) and person administering Informed Consent.

Refer to section 4.8.10 of the current version of ICH E6 Guidelines for more details

- 3.1.15.2 In trials involving minors, parents/guardians of a minor shall be required to sign an Informed Consent form as above. In addition, an assent form similar to the Informed Consent Form shall also be signed and dated by a minor who is capable of understanding as a confirmation of his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the minor's decision to participate.
- 3.1.15.3 The language used in the ICF shall be in English and may be translated into the local language(s) of the target population.
- 3.1.15.4 The informed consent forms shall have reference numbers (appropriate version number and date)

3.1.16 Statistical Analysis Plan (SAP)

A SAP for the study shall be submitted with the Clinical Trial Application or before data- lock.

Note: Refer to the current version of ICH E9 for further guidance on the development of the SAP

3.1.17 Materials Transfer Agreement (MTA)

- 3.1.17.1 Where applicable, an appropriate MTA which defines the rights, obligations and restrictions for the provider (PI) and the recipient(s) (External Laboratory) with respect to the materials/biological samples and any derivatives to be transferred, as well as any confidential information exchanged with the material shall be provided.
- 3.1.17.2 The MTA shall specify;
- i. The type of materials/samples to be transferred
 - ii. The local laboratory or institution from which the samples shall be transferred
 - iii. The destination of the samples (intermediary and final destination)
 - iv. The type of analyses to be carried out by the recipient(s) of the samples
 - v. Competence of the recipient(s) of the materials/samples for the listed analyses to be carried out
- 3.1.17.3 The MTA at minimum, shall be duly signed and dated by the Sponsor, PI and the recipient(s) of the materials at external laboratory.
- 3.1.17.4 No person shall make arrangements to receive or ship biological samples in a clinical trial without prior approval from The Authority.
- 3.1.17.5 Persons who wish to import or export any biological samples in a clinical trial shall submit an application with proof of payment of the necessary fees and a suitable MTA for approval by The Authority.
- 3.1.17.6 Transfer of biological samples (to and from clinical trial sites) shall only be made upon receipt of The Authority's approval.
- 3.1.17.7 Where local laboratory(ies) is to be used for study-related activity(ies)/analyses, the applicant shall provide a copy of a signed agreement between the Sponsor, PI and the laboratory(ies) specifying;
- i. The obligations and responsibilities of each party.

- ii. The type of samples and analyses to be carried out by the local laboratory(ies).
- iii. Competence of the laboratory(ies) of the materials/samples for the listed analyses to be carried out.

3.1.18. Financial Disclosure

- 3.1.18.1 Principal Investigators shall provide copies of Financial Disclosure forms provided to Study Sponsors regarding their financial interests for the period of their participation in a study, that is, from the date the Investigator entered into agreement with the Sponsor, and for one year following the end of his or her participation in the study.
- 3.1.18.2 The Authority shall be provided with updates if any relevant information changes during the study and for one year following its completion.

3.2 Qualification of Principal Investigators

- 3.2.1 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 shall be responsible for the proper conduct of the trial and must;
 - 3.2.1.1. Be medically qualified and clinically competent
 - 3.2.1.2. Be sufficiently experienced in clinical evaluation of medicinal products
 - 3.2.1.3. Be experts in the particular disease or condition under study
 - 3.2.1.4. Must have evidence of Good Clinical Practice training organized by The Authority within the preceding 2 years. First time Principal Investigators shall be required to participate in a GCP training organized by Authority as a prerequisite for a Clinical Trial approval. GCP training organized by the Sponsor shall not be accepted.
 - 3.2.1.5. The Authority shall assess Investigators' compliance to regulatory requirements to ascertain the competence of the Investigator to conduct clinical trials in Ghana.
 - 3.2.1.6. The Principal Investigator must be resident in Ghana.
 - 3.2.1.7. Provide evidence of such qualifications specified by the applicable regulatory requirement(s).
 - 3.2.1.8. Non-medically qualified scientists may participate as co-investigators or in other roles, but not as Principal Investigators.

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

3.3 Qualifications of Study Pharmacist

3.3.1 Registered as a pharmacist in Ghana.

3.3.2 Must be in good standing with the Pharmaceutical Society of Ghana (PSGH).

3.3.3 Have adequate knowledge in use of the Investigational Product(s).

3.3.4 Must have evidence of Good Clinical Practice training organized by The Authority within the last 2 years.

3.3.5 Must be resident in Ghana.

3.4 Qualifications of Local Monitor, Study Clinician, Study Coordinator, Laboratory Manager, Data Manager

3.4.1 Must be qualified by education, training and experience.

3.4.2 Excellent knowledge in local regulatory requirements.

3.4.3 Must have evidence of Good Clinical Practice training organized by The Authority within the last 2 years.

3.4.4 Must be resident in Ghana

3.4.5 Any change in the local monitor for a study, as well as any other key study personnel should be communicated to the FDA for approval before commencement of their roles.

3.5 Reporting and Managing Adverse Events

- 3.5.1 The Sponsor of a clinical trial and Principal Investigators participating in a clinical trial are responsible for proper reporting of Serious Adverse Events (SAEs).
- 3.5.2 The Sponsor should expedite the reporting of all adverse drug events (AEs) that are both serious and unexpected to The Authority.
- 3.5.3 Reporting should occur within the timeframe and format specified by The Authority. (Refer to APPENDIX I).
 - 3.5.3.1 Any serious adverse event to the investigational product shall receive immediate medical attention and reported to The Authority within forty- eight (48) hours and they shall be processed as follows:
 - 3.5.3.1.1 Acknowledgement of receipt of the report
 - 3.5.3.1.2 Follow-up for clarification, missing or additional information such as laboratory test results where necessary
 - 3.5.3.1.3 Entry of the report into the Authority's Clinical Trial SAE Database where information shall be treated with strict confidentiality.
 - 3.5.3.2 The SAE report form with the necessary detailed information shall be submitted to the TAC to enable causality assessment which may inform regulatory decisions or actions and feedback given to the site when necessary.
 - 3.5.3.3 All fatal cases shall be accompanied by a formal autopsy report.
 - 3.5.3.4 In exceptional circumstances where a formal autopsy is not practicable, prior permission shall be obtained from The Authority for a verbal autopsy.
 - 3.5.3.5 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).

- 3.5.3.6 Any adverse event to the investigational product shall receive immediate medical attention and reported to The Authority within specified timelines.
- 3.5.3.7 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.

3.6 Clinical Trial Reports

3.6.1 Progress Report

- 3.6.1.1 The Authority should be informed in writing on the exact date of commencement of the study within two weeks of commencement of the study.
- 3.6.1.2 Quarterly reports of the progress of a clinical trial starting from the date of initiation after the issuance of the clinical trial certificate shall be submitted to The Authority in the recommended format. (Refer to APPENDIX IV).
- 3.6.1.3 Quarterly progress reports must be submitted to The Authority within 21 calendar days after the end of the previous quarter. A quarter shall be considered as a three-month period beginning from the date of initiation of a specific clinical trial.
- 3.6.1.4 Protocol deviations/violations recorded for the quarter shall be documented and attached to the progress report submitted to the Authority. This shall be accompanied by a corrective action and preventive action (CAPA) for the observed protocol deviation.
- 3.6.1.5 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 actual date of commencement within ninety (90) days of issuance of the Clinical Trial Certificate.
- 3.6.1.6 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.

3.6.1.7 If the trial is terminated before its purpose is achieved by the Sponsor, the reason shall be conveyed in writing to The Authority within ten (10) working days with the necessary documentation. This shall include:

1. Justification for the premature ending or the temporary halt of the trial specifying whether the decision was based on a DSMB report or Interim findings.
2. Number of patients receiving treatment at the time of the study termination.
3. Proposed management/follow-up procedures for patients receiving treatment at the time of halt or study termination.
4. Implications of the discontinuation on the evaluation of the final results.
5. Close-out report within 30 days from the date of termination in the recommended format as per Appendix V
6. Final report within 90 days from the date of termination of the study.

3.6.2 DSMB Report

- 3.6.2.1 Duly signed and authenticated DSMB reports and/or minutes shall be forwarded to The Authority.
- 3.6.2.2 The DSMB reports shall be submitted to the Authority within 10 days from the date of the report.

3.6.3 Interim Reports

- 3.6.3.1 If the approved protocol includes provisions for interim analysis, a comprehensive report on the interim results shall be submitted to the Authority within thirty (30) days of obtaining these results.

3.6.4 Close-out report

- 3.6.4.1 The Principal Investigator/Sponsor shall notify The Authority in writing, not later than 30 days after the completion of a clinical trial.
- 3.6.4.2 A close-out report on the study shall be submitted to The Authority after study completion in the recommended format as per Appendix V.

3.6.4.3 A copy of the disposal certificate issued by The Authority shall be attached to this report.

3.6.5 Final Report

3.6.5.1 In addition to the close-out report, the PI/Sponsor 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.

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

3.6.5.3 Section 16.2 (Patient Data Listings) of the ICH E3 Guideline for the Structure and Content of Clinical Study Reports shall be duly completed and attached to the final report.

3.6.5.4 The Final report shall be submitted in hard and soft copies (searchable pdf).

3.6.5.5 Publication(s) of the study in a scientific journal or other medium for the purpose of disseminating the information obtained to stakeholders shall be encouraged only after 30 days of acknowledgement of receipt of the final report by The Authority.

3.6.6 Temporary Halt of a Trial

3.6.6.1 A temporary halt of a trial is a stoppage of the trial which is not envisaged in the approved protocol and where there is an intention to resume it. A temporary halt can be:

1. due to a substantial amendment, or
2. part of an urgent safety measure. In this case, the notification of the temporary halt of a trial shall be made immediately and, at the latest, in accordance with the deadline set out in the Appendix Ib within 10 days from when the trial is temporarily halted.

3.6.6.2 The reasons and scope, e.g. stopping recruitment or interrupting treatment of participants already included, should be clearly explained.

3.6.6.3 The restart of the trial should be treated as a substantial amendment providing evidence that it is safe to resume the trial.

3.7 Importation and Management of Investigational Products for Clinical Trial

- 3.7.1 An application for importation of investigational products and trial products, shall receive prior approval from The Authority.
- 3.7.2 Approval to import products for clinical trials shall only be granted to recognized clinical research entities whose protocol has been approved by The Authority.
- 3.7.3 An excess of up to ten percent (10%) of the total IPs required for the conduct of the study may be allowed for importation as backup IPs.
- 3.7.4 Application to import investigational products shall be made to The Authority by submitting:
- 3.7.4.1 A letter stating the quantity and source of each investigational products and trial related products to be imported.
 - 3.7.4.2 Certificate of analysis of investigational products for all batches to be imported.
 - 3.7.4.3 Lot Release certificate(s) (where applicable) for all batches to be imported.
- 3.7.5 On approval of Section 3.1, an application for import permit must be processed through the current electronic importation system as pertains at the approved ports of entry for medicines and medical devices in the country.
- 3.7.6 The Principal Investigator shall notify The Authority within 48 hours through an appropriate email clinicaltrials@fda.gov.gh of each consignment of investigational product batches received on site. The notification shall include the following details: Name of product(s), Quantities received, and Batches received.
- 3.7.7 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.
- 3.7.8 The investigational product shall be appropriately labeled with the approved labels to indicate they are samples for the conduct of clinical trials only. The label shall bear the following as the basic information:
- 3.7.8.1 For Clinical Trial purposes ONLY
 - 3.7.8.2 Trial name
 - 3.7.8.3 Expiry date (if applicable)
 - 3.7.8.4 Dosage (if applicable)

3.7.8.5 Investigational Product identity number

- 3.7.9 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.
- 3.7.10 The above notwithstanding, all other statutes governing importation procedures and tax liabilities in Ghana shall apply to imported investigational products.
- 3.7.11 For investigational products purchased locally, the Principal Investigator shall document the source, proof of purchase, quantities purchased and Certificate of Analysis for each batch of Investigational Products.
- 3.7.12 Copies of all documents on investigational products, whether purchased locally or imported shall be kept on site for verification and accountability during GCP inspections.
- 3.7.13 Used, destroyed/broken and expired Investigational Products may be destroyed upon authorization by the Sponsor. To do this:
- 3.7.13.1 Proper reconciliation of all Investigational Products shall be done and verified by or on behalf of the Sponsor explaining any discrepancies satisfactorily if any.
- 3.7.13.2 An official request to dispose of the Investigational Products, indicating the type and quantity of each product to be destroyed, shall be made to the FDA as stipulated in the *Guidelines for Safe Disposal of Defective and Expired Drugs, Cosmetics, Household Chemicals and Medical Devices*.
- 3.7.13.3 The destruction process shall be supervised by Officers of the FDA and representatives of other relevant agencies where applicable, and a destruction certificate issued.

3.8 Post Trial Access to Investigational Products (IPs)

- 3.8.1 In the event that provision is made for post-trial access to study IPs, the study shall request for approval from the Authority for the initiation of post-trial access to study IPs for study participants.
- 3.8.2 The request for approval for the initiation of post-trial access to study IPs shall be supported by adequate safety and efficacy data. The efficacy data must provide evidence of continued clinical benefit to study participants.

3.9 Pre-Submission Meetings

3.9.1 A Clinical Trial applicant/client who wishes to meet with officers of The Authority before submitting an application or during the conduct of a study, shall submit an official letter of request to The Authority indicating:

3.9.1.1 Purpose for the meeting

3.9.1.2 Agenda for the meeting

3.9.1.3 Names of study team expected to meet with The Authority

3.9.2 The Authority shall consider the request and respond appropriately.

3.10 Special Conditions for Clinical Trials

Special conditions shall apply for the conduct of Clinical Trials involving the following:

3.10.1 Paediatric populations (refer to FDA *Guidelines for Conducting Clinical Trials with Paediatric Population*)

3.10.2 Vulnerable Populations (contact the FDA for requirements)

3.10.3 Public Health Emergencies (refer to FDA *Guidelines for Conduct of Clinical Trials During Emergencies*)

3.11 Appeal Process on CTA Decisions

3.11.1 An Applicant may appeal to the Minister of Health within 60 days of a Clinical Trial Application decision.

3.11.2 An appeal application may also be made to the Chief Executive Officer within 30 days of the decision by submitting:

i. An official letter providing justification for the appeal with relevant supporting documents.

ii. An appeal fee as per the FDA approved fee schedule.

3.11.3 An appeal shall be addressed as per the Authority's Guidelines for Appeal Against Regulatory Decisions of the FDA.

4.0 OTHERS

4.1 Timelines

For all timelines, refer to Appendix I of these Guidelines.

4.2 Document Signatures

All clinical trial related documents should be duly signed by the appropriate person(s) and submitted as part of the trial application. Draft documents and documents without the relevant signatures are deemed unacceptable.

4.3 Sanctions

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

- 4.2.1 Timeline to address infractions
- 4.2.2 Warning letters
- 4.2.3 Administrative fines
- 4.2.4 Suspension of an on-going clinical trial.
- 4.2.5 Revocation of a clinical trial certificate (stopping of a trial/recall of all investigational products).
- 4.2.6 Dissociation of study data/results

4.4 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.

5.0 APPENDICES
APPENDIX I: TIMELINES

APPENDIX Ia: Serious Adverse Events (SAE) Reporting Timelines

Type of Safety Report	Time Frame For Reporting	Format
REPORTS FROM SITES IN GHANA		
<p>Serious Adverse Events including Suspected Unexpected Serious Adverse Reactions</p> <ul style="list-style-type: none"> • Follow-up reports 	<p>Immediately where possible and in any event, within 48 hours after becoming aware of the information</p> <p>Immediately when any of the underlisted occurs:</p> <ul style="list-style-type: none"> 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. 	<p>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.</p> <p>Electronic submissions must be compliant with current version of E2B system.</p> <p>Follow-up reports should include an assessment of the importance and implication of any findings.</p> <p>All fatal cases must be followed up with formal autopsy report¹.</p>

• Frequent adverse	Immediately where possible	Line listing
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events (greater than or equal to 1% but less than 10% of the total events)	and in any event, within 7 days after becoming aware of the information	
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 participants including information sufficient to enable all clinical trial participants to be identified and contacted in the event that the sale of the drug may endanger the health of the clinical trial participants 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

Development/Periodic Safety Update Reports (D/PSURs)	<ul style="list-style-type: none"> • To be submitted annually or when new information becomes available • 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
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APPENDIX Ib: OTHER TIMELINES

ACTION	REFERENCE	TIMELINE
Notification for the implementation of an urgent amendment necessary to protect the life of participants	3.1.4.2	Immediate phone call, followed by a written report within forty-eight (48) hours
Notification of commencement of study	3.6.1.1	Within 2 weeks of commencement of the study
Quarterly progress reports	3.6.1.3	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	3.6.1.4	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.	3.6.1.6	Within ten (10) working days
Submission of preliminary report on the ethical evaluation of the trial after completion.	3.6.3.1	Not later than 30 days after the completion of a clinical trial
Notification of temporary halt of an approved trial where there is an intention to resume it.	3.6.5.1	Within ten (10) working days
Submission of close-out report	3.6.4.1	Within thirty (30) days after the completion / termination of a trial
Final Report of Clinical Trial as per ICH E3 Guideline (unless otherwise specified on clinical trial certificate)	3.6.4.1	Not later than 90 days after the completion of the trial

Submission of Corrective actions and Preventive actions (CAPA) after receipt of inspection report.	Sec. 5.9 of FDA GCP Guideline	Within the deadline period stipulated on the cover letter for the GCP Inspection report.
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APPENDIX Ic: Processing Of Submitted Documents by the FDA

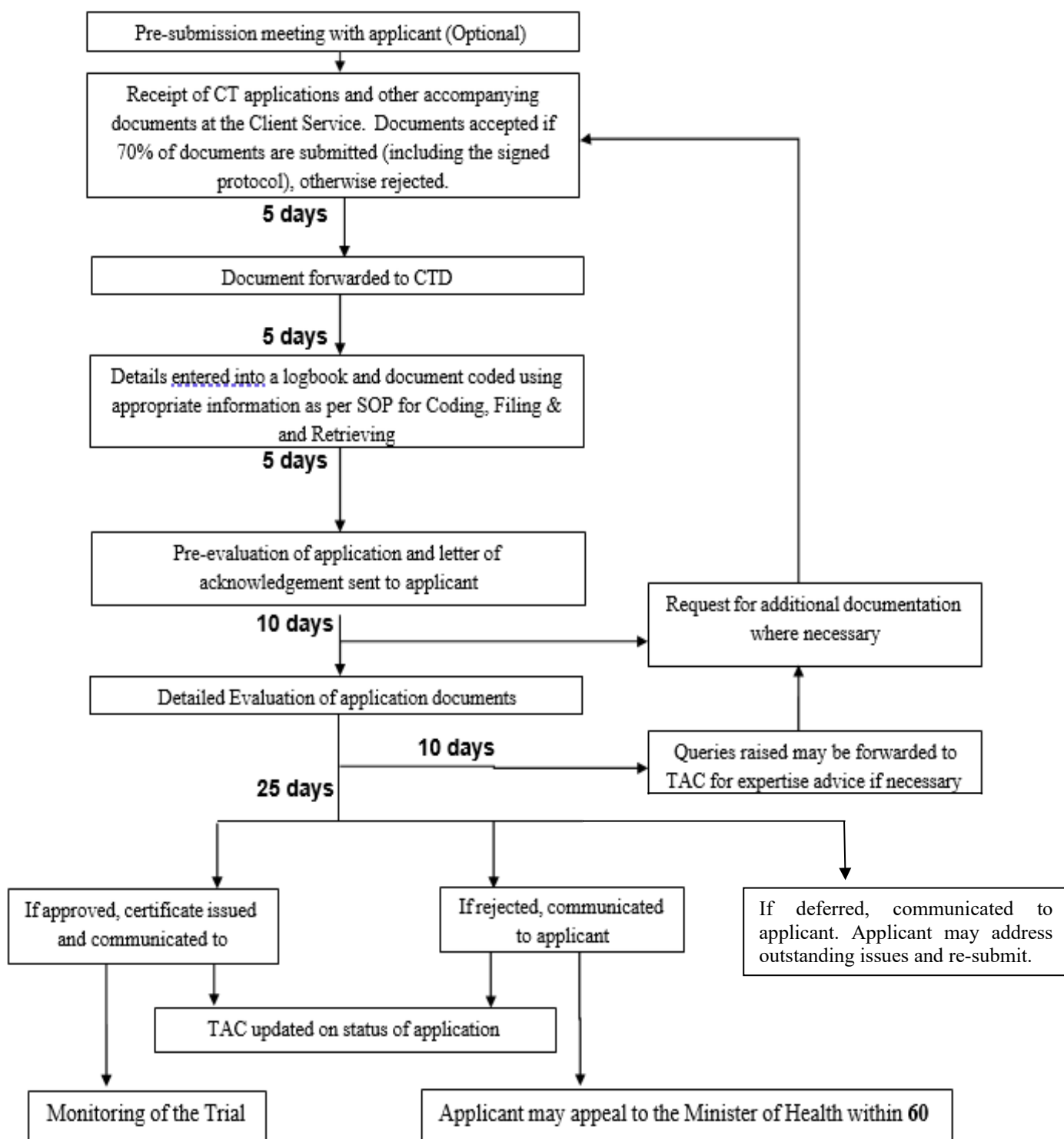
ACTIVITY	TIMELINE****
Processing of Clinical Trial applications – routine pathway	60 days
Processing of Clinical Trial applications – reliance pathway	30 days
Processing of import permits for Investigational Products	10 days
Processing of quarterly progress and safety reports	15 days
Notification of 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

APPENDIX Id: Format For Summary Review Comments On Clinical Trial Applications for the FDA Clinical Trial Registry

SECTION	COMMENTS TO BE MADE
<p>Administrative</p> <p>This includes but not limited to:</p> <ul style="list-style-type: none"> Names, contact details of key study personnel CVs and Charters of relevant boards Competencies of facilities and personnel where applicable. Contract agreements Ethical Approvals and Insurance cover for study participants 	<p>Shall include completeness/sufficiency and consistency of information provided as well as submission of all relevant documents</p>
<p>Protocol including study-related procedures and analyses</p>	<p>Shall include consistency and clarity in information provided such as study design, follow-up procedures, regulatory requirements, etc.</p>
<p>Informed Consent Form</p>	<p>Shall include consistency and clarity in information provided including the necessary information on regulatory requirements</p>

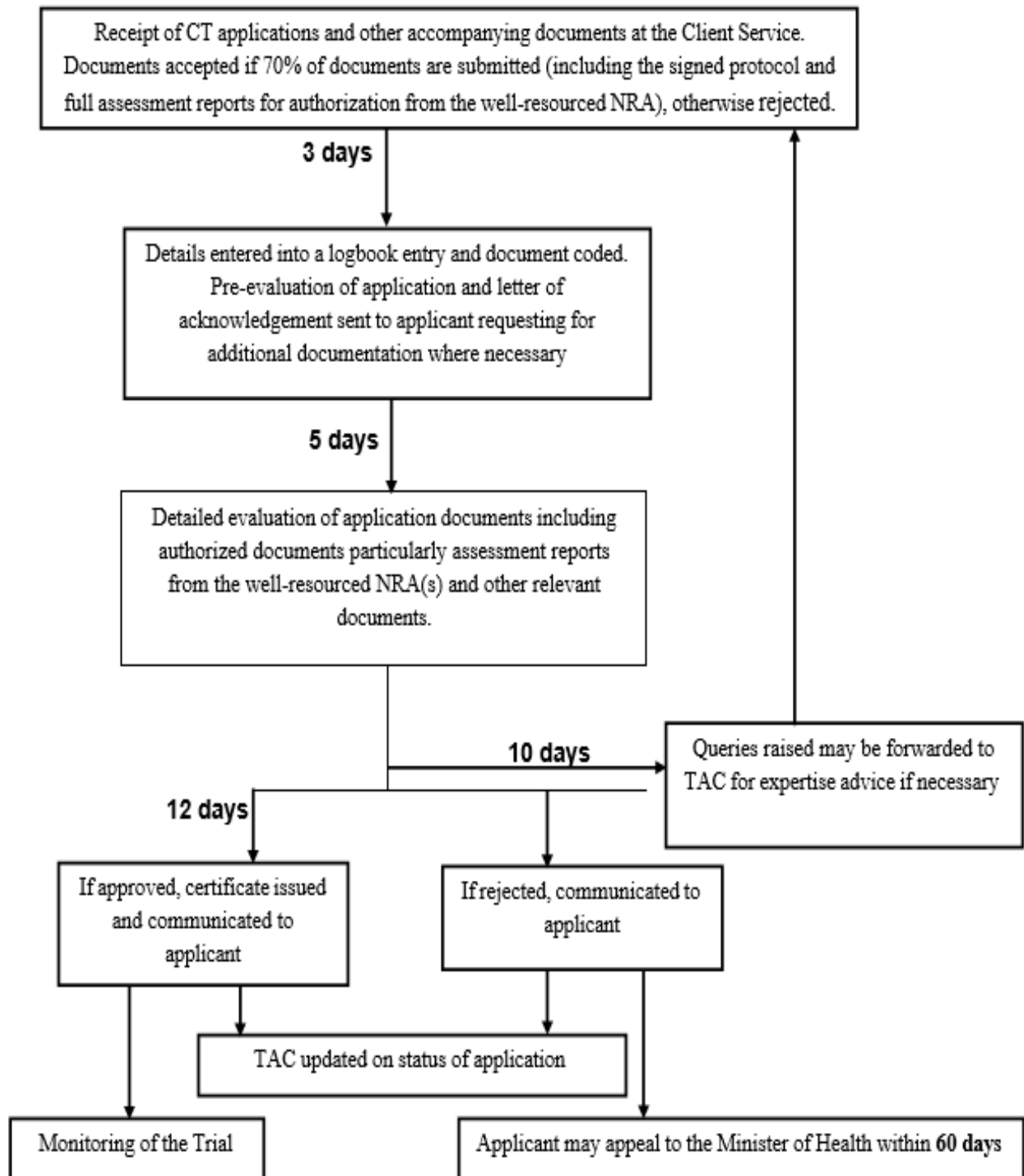
Investigational Products, Investigator's Brochure and Investigational Product Dossier	Shall include consistency and clarity in information provided
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APPENDIX II: Clinical Trial Application Process Flowchart



Note: Application process takes a maximum of 60 working days excluding stop clock time

APPENDIX III: Reliance Evaluation and Authorization Pathway for Clinical Trials



Note: Processing of submissions shall take a maximum of 30 working days excluding stop clock time.

APPENDIX IV: 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:		Phone: Mobile: E-mail:
	Address:		
Co-Investigators:	Name(s):		Phone: Mobile: E-mail:
Other Study Contact (if applicable):	Name:		Phone: Mobile: E-mail:
	Address:		

SECTION B: STUDY STATUS (Check one category only)	
<input type="checkbox"/>	Enrolment has not begun
<input type="checkbox"/>	Actively enrolling participants
<input type="checkbox"/>	Enrolment closed on: (insert date): Participants are receiving treatment/intervention
<input type="checkbox"/>	Enrolment closed on: (insert date): Participants are in follow-up only.
<input type="checkbox"/>	Analyzing data
<input type="checkbox"/>	Data analysis completed

SECTION C: INFORMATION ON PARTICIPANTS & STUDY ACTIVITIES	
a.	Number of participants consented and screened.....
b.	Total number of participants consented and screened who are eligible for the study.....
c.	Number of participants to which the investigational product(s) has been administered.....
d.	Number of participants 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 <input type="checkbox"/> <input type="checkbox"/> 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	
i. If No, explain	Yes <input type="checkbox"/> <input type="checkbox"/> No
.....	
.....	
j. Have there been any changes to the protocol since the Food and Drugs Authority approved?	Yes <input type="checkbox"/> <input type="checkbox"/> No
k. Is this amendment submitted to the Food and Drugs Authority?	
l. If No, explain	Yes <input type="checkbox"/> <input type="checkbox"/> No
.....	
.....	
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
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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 clinicaltrials@fda.gov.gh

APPENDIX V: Food and Drugs Authority Close-out Report Form

I. SITE INFORMATION

Protocol Title:

Protocol Identification number:

Clinical Trial Certificate number:

Name and address of Clinical Site:

Name, address, telephone number and e- mail address of Principal Investigator: Name, address, telephone number and e- mail address of Sponsor:

Date of last recruitment:

Reason for closure:

Date(s) of Report:

Clinical Site Personnel Involved with the Study:

NAME	TITLE	CONTACT
	Local monitor	
	Site Coordinator	
	Pharmacist	
	Other	

II. CLINICAL SITE CLOSE- OUT CHECKLIST

Instructions: Please provide comment (s) for each of the items listed below. Additional sheets may be attached if necessary.

OBJECTIVE	COMMENTS
1. All regulatory and other essential documents (refer to Appendix VII of FDA Guidelines for the Authorization of Clinical Trials, FDA/SMC/CTD/GL-ACT/2013/01) are up-to-date and on file	<i>Provide list of documents on file at the site</i>
2. Notification of all relevant oversight bodies of closure of study	
3. Signed, informed consent is on file for each study participant	<i>Provide list of participants (use codes/ study IDs)</i>

OBJECTIVE	COMMENTS
4. Documentation of all protocol violations/ deviations and/ or appropriate note- to- files in the relevant essential document	<i>Provide list</i>
5. Appropriate follow- up and reporting of all SAEs to FDA	<i>Provide number of SAEs reported. Summary of outcome for SAEs listed is relevant</i>
6. Completion of all Case Report forms for each participant	
7. Entry/ submission of all relevant data into database/ to sponsor/ coordination center. If not complete, indicate the timeline for accomplishing this and document in the comments section	
8. Status of all outstanding data edits, queries or delinquent forms and timeline for their resolution	
9. Tentative date for submission of full Clinical Study Report (not FDA timelines, Appendix VII FDA/SMC/CTD/GL-ACT/2013/01)	
10. Requirements for retention of study records. Indicate if each requirement has been fulfilled	
11. Drug accountability <ul style="list-style-type: none"> • Quantity of IPs received • Quantity of IPs utilized in the study • Quantity of IPs destroyed (attach copy of destruction certificate (s)) • Quantity of IPs onsite/ returned to sponsor 	
12. Status/ shipment/ analyses of all participant specimen according to protocol requirements (including plans for future shipments or period of time they will be stored on- site)	

13. If blinded study drug was used, confirm that the tear-off labels were not opened. For any that were opened, documentation should be obtained noting the reason for unblinding

Additional comments:

- III. STATUS OF PAST OBSERVATIONS/ RECOMMENDATIONS MADE DURING MONITORING/ GCP INSPECTIONS: (Have corrective measures been implemented for all observations and recommendations?), Provide summary of measures implemented for each point)**
- IV. OUTSTANDING ISSUES OR ACTIVITIES TO BE IMPLEMENTED: (Include problems identified, if any, and recommendations/ action items for corrections)**

Prepared by: _____ Date: _____

(Signature)

APPENDIX VI: Phases of Clinical Trials

Phase I

These are the first trials of a new active ingredient or new formulations in man, often carried out in healthy volunteers. Their purpose is to establish a preliminary evaluation of safety, and a first outline of the pharmacokinetic and, where possible, a pharmacodynamic profile of the active ingredient in humans. These trials are tested in a small group of people.

Phase II

These trials are performed in a limited number of subjects 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 patients suffering from a disease or condition 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. These trials are tested in a larger group of people.

Phase III

Trials in larger (and possibly varied) patient 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 randomized 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 Studies performed after marketing of the pharmaceutical product. Trials in phase IV are carried out on the basis of the product characteristics on which the marketing authorization 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. After a product has been placed on the market, clinical trials designed to explore new indications, new methods of administration or new combinations, etc. are normally considered as trials for new pharmaceutical products.

APPENDIX VII

ESSENTIAL DOCUMENTS FOR THE CONDUCT OF A CLINICAL TRIAL

1.0 Introduction

Essential Documents are those documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements.

Essential Documents also serve a number of other important purposes. Filing essential documents at the investigator/institution and sponsor sites in a timely manner can greatly assist in the successful management of a trial by the investigator, sponsor and monitor. These documents are also the ones which are usually audited by the sponsor's independent audit function and inspected by the regulatory Authority(ies) as part of the process to confirm the validity of the trial conduct and the integrity of data collected.

The minimum list of essential documents which has been developed follows. The various documents are grouped in three sections according to the stage of the trial during which they will normally be generated: 1) before the clinical phase of the trial commences, 2) during the clinical conduct of the trial, and 3) after completion or termination of the trial. A description is given of the purpose of each document, and whether it should be filed in either the investigator/institution or sponsor files, or both. It is acceptable to combine some of the documents, provided the individual elements are readily identifiable.

Trial master files should be established at the beginning of the trial, both at the investigator/institution's site and at the sponsor's office. A final close-out of a trial can only be done when the monitor has reviewed both investigator/institution and sponsor files and confirmed that all necessary documents are in the appropriate files.

Any or all of the documents addressed in this guideline may be participant to, and should be available for, audit by the sponsor's auditor and inspection by the regulatory Authority(ies).

2.0 Before the Clinical Phase of the Trial Commences

During this planning stage, the following documents should be generated and should be on file before the trial formally starts

No.	Title of Document	Purpose	Located in Files of	
			Investigator	Sponsor
1.	INVESTIGATOR'S BROCHURE	To document that relevant and current scientific information about the investigational product has been provided to the investigator	X	X
2.	SIGNED PROTOCOL AND AMENDMENTS, IF ANY, AND SAMPLE CASE REPORT FORM (CRF)	To document investigator and sponsor agreement to the protocol/amendment(s) and CRF	X	X
3.	INFORMATION GIVEN TO TRIAL PARTICIPANT			
i.	- INFORMED CONSENT FORM (including all applicable translations)	To document the informed consent	X	X
ii.	- ANY OTHER WRITTEN INFORMATION	To document that participants will be given appropriate written information (content and wording) to support their ability to give fully informed consent	X	X
iii.	- ADVERTISEMENT FOR PARTICIPANT	To document that recruitment measures are appropriate and not coercive	X	

	RECRUITMENT (if used)			
4.	FINANCIAL ASPECTS OF THE TRIAL	To document the financial agreement between the investigator/institution and the sponsor for the trial	X	X
5.	INSURANCE STATEMENT (where required)	To document that compensation to participant(s) for trial-related injury will be available	X	X
6.	SIGNED AGREEMENT BETWEEN INVOLVED PARTIES , e.g.: - Investigator/institution and sponsor - Investigator/institution and CRO - Sponsor and CRO - Investigator/institution and Authority(ies) (where required)	To document agreements	X X X X	X X X (where required)
7.	DATED, DOCUMENTED APPROVAL/FAVOURABLE OPINION OF INSTITUTIONAL REVIEW BOARD (IRB) /INDEPENDENT	To document that the trial has been participant to IRB/IEC review and given approval/favourable opinion. To identify the version number and date of the document(s)	X	X

	<p>ETHICS COMMITTEE (IEC) OF THE FOLLOWING:</p> <ul style="list-style-type: none"> - Protocol and any amendments - CRF (if applicable) - Informed consent form(s) - Any other written information to be provided to the participant(s) - Advertisement for participant recruitment used) - Participant compensation (if any) - Any other documents given approval/ favourable opinion 			
8.	<p>INSTITUTIONAL REVIEW BOARD/ INDEPENDENT ETHICS COMMITTEE COMPOSITION</p>	<p>To document that the IRB/IEC is constituted in agreement with GCP</p>	X	X (where required)
9.	<p>REGULATORY AUTHORITY(IES) AUTHORIZATION/</p>	<p>To document appropriate authorization /approval /notification by the regulatory Authority(ies) has been obtained prior to</p>	X	X (where required)

	APPROVAL/ NOTIFICATION OF PROTOCOL (where required)	initiation of the trial in compliance with the applicable regulatory requirement(s)		
10.	CURRICULUM VITAE AND/OR OTHER RELEVANT DOCUMENTS EVIDENCING QUALIFICATIONS OF INVESTIGATOR(S) AND SUB-INVESTIGATOR(S)	To document qualifications and eligibility to conduct trial and/or provide medical supervision of participants	X	X
11.	NORMAL VALUE(S) /RANGE(S) FOR MEDICAL/ LABORATORY/ TECHNICAL PROCEDURE(S) AND/OR TEST(S) INCLUDED IN THE PROTOCOL	To document normal values and/or ranges of the tests	X	X
12.	MEDICAL/ LABORATORY/ TECHNICAL PROCEDURES /TESTS	To document competence of facility to perform required test(s), and support reliability of results	X (where required)	X

	<ul style="list-style-type: none"> - Certification or - Accreditation or - Established quality control and/or external quality assessment or - Other validation (where required) 			
13.	SAMPLE OF LABEL(S) ATTACHED TO INVESTIGATIONAL PRODUCT CONTAINER(S)	To document compliance with applicable labelling regulations and appropriateness of instructions provided to the participants	X	
14.	INSTRUCTIONS FOR HANDLING OF INVESTIGATIONAL PRODUCT(S) AND TRIAL-RELATED MATERIALS (if not included in protocol or Investigator’s Brochure)	To document instructions needed to ensure proper storage, packaging, dispensing and disposition of investigational products and trial-related materials	X	X
15.	SHIPPING RECORDS FOR INVESTIGATIONAL PRODUCT(S) AND TRIAL-RELATED MATERIALS	To document shipment dates, batch numbers and method of shipment of investigational product(s) and trial-related materials. Allows tracking of product batch, review of shipping conditions, and accountability	X	X

16.	CERTIFICATE(S) OF ANALYSIS OF INVESTIGATIONAL PRODUCT(S) SHIPPED	To document identity, purity, and strength of investigational product(s) to be used in the trial	X	
17.	DECODING PROCEDURES FOR BLINDED TRIALS MASTER	To document how, in case of an emergency, identity of blinded investigational product can be revealed without breaking the blind for the remaining participants' treatment	X (a third party if applicable)	X
18.	RANDOMISATION LIST	To document method for randomization of trial population		X (a third party if applicable)
19.	PRE-TRIAL MONITORING REPORT	To document that the site is suitable for the trial (may be combined with 20)		X
20.	TRIAL INITIATION MONITORING REPORT	To document that trial procedures were reviewed with the investigator and the investigator's trial staff (may be combined with 19)	X	X

3.0. During the Clinical Conduct of the Trial

In addition to having on file the above documents, the following should be added to the files during the trial as evidence that all new relevant information is documented as it becomes available

	Title of Document	Purpose	Located in Files of	
			Investigator	Sponsor
21.	INVESTIGATOR'S BROCHURE UPDATES	To document that investigator is informed in a timely manner of relevant information as it becomes available	X	X
22.	ANY REVISION TO: - Protocol/amendment(s) and CRF - Informed consent form any other written - Information provided to participants - Advertisement for participant recruitment (if used)	To document revisions of these trial related documents that take effect during trial	X	X
23.	DATED, DOCUMENTED APPROVAL/ FAVOURABLE OPINION OF INSTITUTIONAL REVIEW BOARD (IRB) /INDEPENDENT ETHICS COMMITTEE (IEC) OF THE FOLLOWING: -Protocol amendment(s) -Revision(s) of: - informed consent form - any other written information to be	To document that the amendment(s) and/or revision(s) have been participant to IRB/IEC review and were given approval/favourable opinion. To identify the version number and date of the document(s).	X	X

	<p>provided to the participant</p> <ul style="list-style-type: none"> - advertisement for participant recruitment if used) -Any other documents given approval/favourable opinion -Continuing review of trial (where required) 		
24.	<p>REGULATORY AUTHORITY(IES) AUTHORIZATIONS/ APPROVALS/ NOTIFICATIONS WHERE REQUIRED FOR:</p> <ul style="list-style-type: none"> - Protocol amendment(s) and other documents 	<p>To document compliance with applicable regulatory requirements</p>	<p>X (where required) X</p>
25.	<p>CURRICULUM VITAE FOR NEW INVESTIGATOR(S) AND/OR SUB-INVESTIGATOR(S)</p>	<p>(see 10)</p>	<p>X X</p>
26.	<p>UPDATES TO NORMAL</p>	<p>To document normal values and ranges that</p>	<p>X X</p>

	VALUE(S)/RANGE(S) FOR MEDICAL/ LABORATORY/ TECHNICAL PROCEDURE(S)/TEST(S) INCLUDED IN THE PROTOCOL	are revised during the trial (see 11)		
27.	UPDATES OF MEDICAL/LABORATORY/ TECHNICAL PROCEDURES/TESTS - Certification or - Accreditation or - Established quality control and/or external quality assessment or - Other validation (where required)	To document that tests remain adequate throughout the trial period (see 12)	X (where required)	X
28.	DOCUMENTATION OF INVESTIGATIONAL PRODUCT(S) AND TRIAL-RELATED MATERIALS SHIPMENT	(see 15)	X	X
29.	CERTIFICATE(S) OF ANALYSIS FOR NEW	(see 16)	X	X

	BATCHES OF INVESTIGATIONAL PRODUCTS			
30.	MONITORING VISIT REPORTS	To document site visits by, and findings of, the monitor	X	X
31.	RELEVANT COMMUNICATIONS OTHER THAN SITE VISITS - Letters - Meeting notes - Notes of telephone calls	To document any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, adverse event (AE) reporting	X	X
32.	SIGNED INFORMED CONSENT FORMS	To document that consent is obtained in accordance with GCP and protocol and dated prior to participation of each participant in trial. Also to document direct access permission (see 3)	X	
33.	SOURCE DOCUMENTS	To document the existence of the participant and substantiate integrity of trial data collected. To include original documents related to the trial, to medical treatment, and history of participant	X	
34.	SIGNED, DATED AND COMPLETED CASE REPORT FORMS (CRF)	To document that the investigator or authorized member of the investigator's staff confirms the observations recorded	X (copy)	X (original)

35.	DOCUMENTATION OF CRF CORRECTIONS	To document all changes/additions or corrections made to CRF after initial data were recorded	X (copy)	X (original)
36.	NOTIFICATION BY ORIGINATING INVESTIGATOR TO SPONSOR OF SERIOUS ADVERSE EVENTS AND RELATED REPORTS	Notification by originating investigator to sponsor of serious adverse events and related reports in accordance with 3.4 of FDA Guidelines for Conducting Clinical Trials in Ghana	X	X
37.	NOTIFICATION BY SPONSOR AND/OR INVESTIGATOR, WHERE APPLICABLE, TO REGULATORY AUTHORITY(IES) AND IRB(S)/IEC(S) OF UNEXPECTED SERIOUS ADVERSE DRUG REACTIONS AND OF OTHER SAFETY INFORMATION	Notification by Sponsor and/or Investigator, where applicable, to regulatory authorities and IRB(s)/IEC(s) of unexpected serious adverse drug reactions and of other safety information in accordance with 3.3.14 and 3.2.12.8 of FDA Guidelines for GCP in Ghana and 3.4 of FDA Guidelines for Conducting Clinical Trials in Ghana.	X (where required)	X
38.	NOTIFICATION BY SPONSOR TO INVESTIGATORS OF SAFETY INFORMATION	Notification by sponsor to investigators of safety information of findings that could affect adversely the safety of participants, impact the conduct of the trial, or alter the IRB/IEC's approval/favourable opinion to continue the trial.	X	X

39.	INTERIM OR ANNUAL REPORTS TO IRB/IEC AND AUTHORITY(IES)	Interim or annual reports provided to IRB/IEC in accordance with approving IRB/IEC requirements and to Authority(ies) in accordance with 3.5.1.2 and 3.5.1.3 of FDA Guidelines for Conducting Clinical Trials in Ghana	X	X (where required)
40.	PARTICIPANT SCREENING LOG	To document identification of participants who entered pre-trial screening	X	X (where required)
41.	PARTICIPANT IDENTIFICATION CODE LIST	To document that investigator/institution keeps a confidential list of names of all participants allocated to trial numbers on enrolling in the trial. Allows investigator/institution to reveal identity of any participant	X	
42.	PARTICIPANT ENROLMENT LOG	To document chronological enrolment of participants by trial number	X	
43.	INVESTIGATIONAL PRODUCTS ACCOUNTABILITY AT THE SITE	To document that investigational product(s) have been used according to the protocol	X	X
44.	SIGNATURE SHEET	To document signatures and initials of all persons authorized to make entries and/or corrections on CRFs	X	X

45.	RECORD OF RETAINED BODY FLUIDS/ TISSUE SAMPLES (IF ANY)	To document location and identification of retained samples if assays need to be repeated	X	X
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4.0. After Completion or Termination of the Trial

After completion or termination of the trial, all of the documents identified in sections 2.0 and 3.0 of Appendix II should be in the file together with the following

	Title of Document	Purpose	Located in Files of	
			Investigator/	Sponsor
46.	INVESTIGATIONAL PRODUCT(S) ACCOUNTABILITY AT SITE	To document that the investigational product(s) have been used according to the protocol. To document the final accounting of investigational product(s) received at the site, dispensed to participants, returned by the participants, and returned to sponsor	X	X
47.	DOCUMENTATION OF INVESTIGATIONAL PRODUCT DESTRUCTION COMPLETED	To document destruction of unused investigational products by sponsor or at site	X (if destroyed at site)	X
48.	PARTICIPANT IDENTIFICATION CODE LIST	To permit identification of all participants enrolled in the trial in case follow-up is required. List should be kept in a confidential manner and for agreed upon time	X	
49.	AUDIT CERTIFICATE (if available)	To document that audit was performed		X

50.	FINAL TRIAL CLOSE-OUT MONITORING REPORT	To document that all activities required for trial close-out are completed, and copies of essential documents are held in the appropriate files		X
51.	TREATMENT ALLOCATION AND DECODING DOCUMENTATION	Returned to sponsor to document any decoding that may have occurred	X	
52.	FINAL REPORT BY INVESTIGATOR TO IRB/IEC WHERE REQUIRED, AND WHERE APPLICABLE, TO THE REGULATORY AUTHORITY(IES)	To document completion of the trial	X	
53.	CLINICAL STUDY REPORT	To document results and interpretation of trial	X (if applicable)	X