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# FOOD AND DRUGS AUTHORITY

## GUIDELINES FOR GOOD CLINICAL PRACTICE IN GHANA

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**1.0 INTRODUCTION**

The purpose of these guidelines is to provide investigators conducting clinical trials in Ghana with clear standards of good clinical practice. The Guidelines seeks to ensure that clinical trials conducted in Ghana are designed and conducted according to sound scientific and ethical standards within the framework of good clinical practice. Compliance with these standards provides the public with assurance that the rights, safety and wellbeing of trial participants are protected and that clinical trial data are credible.

The guidelines were partly derived from the International Conference on Harmonization Good Clinical Practice (ICH GCP) and from the International Ethical Guidelines for Biomedical Research involving human subjects prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with World Health Organization (WHO 2002). It is therefore in line with international best practices as well as the AVAREF Guidelines.

Good Clinical Practice (GCP) is a system of shared responsibilities between clinical investigators, industry/sponsors/monitors, institutions/ethics committees, and government regulators. The Guidelines are therefore addressed to investigators, pharmaceutical, manufacturers and other sponsors of research, drug regulatory authorities, the general public and all, those who have an interest in clinical trials research in Ghana.

These Guidelines will support the regulatory requirements of the Food and Drugs Authority as stipulated in part 8, Act 851 of the Public Health Act 2012. It is therefore critical that research ethics committees, researchers, trial participants, principal investigators of trials and sponsors use these guidelines so as to ensure a standardized and ethical approach to clinical trial conducted in Ghana.

The guidelines are also applicable to academic and contract clinical research and are intended to be applied during all stages of drug development including pre and post product registration and marketing, and they are also applicable, in whole or in part to biomedical research in general. They also provide a resource for editors to determine the acceptability of reported research for publication and specifically, on any study that could influence the use or the terms of registration of a pharmaceutical product.

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

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

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

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

**“Child”** A person who is below eighteen (18) years of age as per the definition of child in the current Children’s Act of Ghana.

**“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 clinical trial site shall start to enroll participants in the clinical trial.

**“Drug/Medicine”** includes as per the Public Health Act, part 7, Act 851,  
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
- iii. Nutritional supplements

**“FDA”** means Food and Drugs Authority

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

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

**“Herbal Medicinal Product”** 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 subjects.

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

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

**“Investigator’s Brochure”** A collection of data consisting of all the information known prior to the clinical trial concerning the clinical and non clinical data on the investigational product(s).

**“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.

**“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 national 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.

An individual designated by the applicant organization to have the appropriate level of authority and responsibility to direct the project or program to be supported by the award. The applicant organization may designate multiple individuals as principal investigators (PIs) who share the authority and responsibility for leading and directing the project, intellectually and logistically.

When multiple PIs are named, each is responsible and accountable to the applicant organization, or as appropriate, to a collaborating organization for the proper conduct of the project or program including the submission of all required reports.

**“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.

**“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 "remember" it, so that the immune system can more easily 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).

### 3.0 RESPONSIBILITIES

#### 3.1 Institutional Review Board/Independent Ethics Committee (IRB/IEC)

The Ethics Committee should consist of:

- 3.1.1 At least 3 professionals in the medical and scientific field with sufficient qualifications and experience.
- 3.1.2 A legal professional
- 3.1.3 A consumer representative who is independent of the institution/trial site. Only those members who are independent of the investigator/sponsor of the trial should make decisions.
- 3.1.4 The Ethics Committee should obtain all the information relating to the trial including, protocol, investigators brochure, patient consent forms, insurance for participants, current CV's for investigators and literature detailing rationale for the study and any other documents that the IRB/ICE may need to fulfill its responsibilities.
- 3.1.5 The Ethics Committee shall consider the following:
  - 3.1.5.1 The suitability of the investigator for the proposed trial in relation to his/her qualifications, experience, supporting staff, and available facilities, on basis of the information available to the Committee.
  - 3.1.5.2 The suitability of the protocol in relation to the objectives of the study. Its scientific efficiency i.e. the potential for reaching sound conclusions with the smallest possible exposure of subjects, and the justification of predictable risks and inconveniences weighed against the anticipated benefits for the subjects and/or others.
  - 3.1.5.3 The adequacy and completeness of the written information to be given to the subjects, their relatives, guardians and, if necessary legal representatives.
  - 3.1.5.4 The means by which initial recruitment is to be conducted and by which full information is to be given, and by which consent is to be obtained. All written information for the subject and/or legal representative must be submitted in its final form.

3.1.5.5 Provision for compensation/treatment in the case of injury or death of a subject if attributed to a clinical trial, and any insurance or indemnity to cover the liability of the investigator and sponsor.

3.1.5.6 The extent to which investigators and subjects may be rewarded/compensated for participation.

3.1.6 The Ethics Committee shall give its opinion and advice in writing clearly identifying the trial, the documents reviewed and the dates of review.

### **3.2 Investigator**

Investigators shall satisfy the following:

3.2.1 The Investigator should be qualified by education, training and experience to assume responsibility for the proper conduct of the trial and should provide evidence of such qualifications and experience through an up to date Curriculum Vitae. The Principal Investigator's qualification should be in accordance with Section 3.2 of the FDA's Guidelines for Authorization of Clinical Trials of Medicines, Food Supplements, Vaccines and Medical Devices in Ghana.

3.2.2 The Investigator should be thoroughly familiar with the characteristics and appropriate use of the investigational product as described in the protocol, current investigator's brochure, in the product information and in other information sources.

3.2.3 Have a clear understanding and willingness to obey the ethical and legal requirements of the trial.

3.2.4 To permit monitoring and auditing of the trial and inspection by the FDA or appointed representatives.

3.2.5 Keep a list of appropriately qualified persons to whom the Investigator has delegated significant trial-related duties.

3.2.6 The Principal Investigator shall ensure that all members of the study team have evidence of GCP training of not more than 2 years. GCP certificates shall be required for key members of the team.

3.2.7 The Investigator should not have been found guilty of any misconduct under the Ghana Medical and Dental Council Decree.

3.2.8 The Principal Investigator must be an appropriately qualified and competent person having practical experience within the relevant professional area, who is resident in the country and who is responsible for the conduct of the clinical trial at a clinical site. A Principal Investigator must have had previous experience as a co-investigator in at least two trials in the relevant professional area.

3.2.9 All investigators in a clinical trial as well as the trial monitor must have had formal training in Good Clinical Practice (GCP) within the last two years.

3.2.10 Upon signing the application, all parties accept the responsibility that all applicable regulations and requirements will be adhered to. Furthermore, all parties are responsible for ensuring that the trial is based on and implemented according to well – founded ethical and scientific principles, which are expressed in the Helsinki Declaration and its current revisions as well as in the local and international guidelines for GCP.

#### 3.2.11 Adequate Resources

3.2.11.1 The Investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.

3.2.11.2 The Investigator should have adequate number of qualified staff and adequate facilities for the duration of the trial to conduct the trial properly and safely.

3.2.11.3 The Investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, investigational product and their trial-related duties and functions.

#### 3.2.12 Medical Care of Trial Subjects

3.2.12.1 A qualified medical practitioner should be responsible for all trial-related medical decisions. The qualified medical practitioner should also be licensed with the Medical and Dental Council of Ghana. The medical care given to, and medical decisions made on behalf of the subjects must always be the responsibility of a qualified medical practitioner or when appropriate a qualified dentist registered with the Medical and Dental Council.

3.2.12.2 During and following a subject's participation in a trial, the Investigator should ensure adequate medical care is provided to a subject for any adverse events including clinically significant laboratory values related to the trial. The subject should be informed when medical care is needed for inter-current illness for which the Investigator becomes aware.

### 3.2.13 Other Investigator Responsibilities

3.2.13.1 Before initiating a trial, the Principal Investigator should have the written and dated approval from the Food and Drugs Authority (FDA) and other relevant bodies.

3.2.13.2 The Investigator should conduct the trial according to the approved protocol.

3.2.13.3 The Investigator shall not implement any deviation from or changes to the protocol and Informed Consent Form without prior review and approval of the FDA except when the changes involve only logistical or administrative aspects of the trial e.g. monitor or telephone number changes or is based on issues relating to the immediate safety of subjects already recruited into the trial.

3.2.13.4 The Investigator shall establish SOPs for investigational products (IP):

1. The IP(s) should be kept by a designated person (a pharmacist) who maintain records of the delivery process and who ensures that the product is processed and stored correctly.
2. The designated person should maintain an inventory of the IP at the site, those used by each subject and the return to sponsor or alternative disposition of unused product(s).
3. The Investigational product(s) should be used only on the subjects participating in the trial.
4. The Investigator should ensure that the IP are used only in accordance with the approved protocol.
5. The Investigator should ensure that if there is blinding, it is maintained but there should be criteria or establishment for breaking of the code.

6. The Investigator or a person designated by the Investigator should explain the correct use of the IP to each subject and should check at appropriate intervals during the trial that each subject is following the instructions. In the case where the IP is administered to the subject the proper administration should be ensured.
- 3.2.13.5 The Investigator shall ensure that the subjects have signed and dated the consent form or given their consent in an acceptable form before participating in the trial.
  - 3.2.13.6 The Investigator shall guarantee the confidentiality of the research data, the trial subjects' details and information provided by Sponsor.
  - 3.2.13.7 The Investigator shall ensure that all data is accurately collected and recorded.
  - 3.2.13.8 The Investigator shall ensure that all serious adverse events are reported promptly to the FDA within timelines specified in the FDA's Guideline for Authorization of Clinical Trials in Ghana. Proper protection procedures or treatments should be administered to trial subjects with serious adverse events.
  - 3.2.13.9 The Investigator shall submit all relevant trial data to the FDA in a timely manner for validation, auditing and inspection.

### **3.3 Sponsor**

- 3.3.1 The Sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, recorded and reported in compliance with the protocol, GCP and regulatory requirements.
- 3.3.2 The Sponsor is responsible for selecting Investigators according to the availability of adequate clinical trial environment facilities and resources. In addition, the Sponsor shall ensure that the investigator has sufficient training, qualifications and capability.
- 3.3.3 The Sponsor shall agree with investigator(s) on the definition, establishment and assignment of responsibilities specified in the protocol. These

responsibilities include data management, unblinding of treatment codes, statistical considerations and preparation of the final clinical report.

Prior to the initiation of the clinical trial, the agreement between the Sponsor and Investigators should be in writing as part of the protocol submitted for FDA's approval or in a separate agreement. The Sponsor, in a written document, may agree to transfer all related activities of the clinical trial to designated research institutions. However, all responsibility for the trial lies with the Sponsor.

- 3.3.4 The Sponsor shall provide an up-to-date Investigator's brochure, which includes information about the products with respect to their physical, chemical, pharmacokinetic and pharmacodynamic properties obtained from animals as well as human subjects and currently available results of relevant clinical trials.

An updated Investigator's Brochure shall be submitted whenever available; at least once year.

- 3.3.5 The Sponsor shall obtain the investigator's/institutions' agreement on the following items:

3.1.5.1 The conduct of the trial in compliance with Good Clinical Practices and with the approved protocol; and to be in compliance with procedures for data recording/reporting and to permit monitoring, auditing and inspection according to the protocol.

3.1.5.2 The Sponsor and all investigators shall sign and date the protocol of the trial to confirm the agreement.

- 3.3.6 The Sponsor shall ensure that sufficient safety and efficacy data from nonclinical studies and/or clinical trials are available to support human exposure by the route, at the dosages for the duration and in the trial population to be studied.

- 3.3.7 The Sponsor shall ensure that the IP's (including active comparator(s) and placebo) is manufactured in accordance with Good Manufacturing Practices and are adequately packed and labelled in a manner that protects the blinding if applicable. In addition the labelling should comply with the regulatory requirements (refer to FDA's Guidelines for Labeling of Products).

- 3.3.8 The Sponsor shall determine for the IP's, acceptable storage temperature and conditions, storage times, reconstitution fluids and procedures and devices for product infusion if any.
- 3.3.9 In blinded trials, the coding system for the IP's shall include a mechanism that permits rapid identification of the products in case of a medical emergency but does not permit undetectable breaks of the blinding.
- 3.3.10 If formulation changes are made to the IP or comparator products during the course of the clinical development, the results of pharmaceutical and pharmacokinetic profile of the product shall be made available to the FDA prior to the use of the reformulated IP in clinical trials.
- 3.3.11 The Sponsor shall appoint qualified and suitable trained individuals to monitor the trial.
- 3.3.12 The Sponsor should provide insurance cover for all trial subjects. The Sponsor's policies and procedures should address the costs of treatment of trial subjects in the event of trial-related injuries.
- 3.3.13 The financial aspects of the trial should be documented in an agreement between the Sponsor and the Investigator/institution.
- 3.3.14 The Sponsor should report to the FDA and all relevant institutions, all adverse events occurring during the course of the trial. The Sponsor should expedite reporting all serious adverse events to the Ethics Committee, the FDA and the Sponsor and the Investigators should immediately undertake appropriate and necessary measures and treatment to protect the trial subjects. (Refer to Guidelines for Authorization of Clinical Trials for timelines).
- 3.3.15 When a trial is prematurely terminated or suspended by the Sponsor/Investigators, the FDA and Ethics Committee and should be informed of the decision to terminate/suspend the trial and the reasons thereof by the Sponsor/Investigators. (Refer to Guidelines for Authorization of Clinical Trials for further details).
- 3.3.16 When the trial is prematurely terminated, the Sponsor should submit a report to the FDA and institution within 30 (thirty) days.

3.3.17 When the trial is completed, the Sponsor should submit a preliminary report to the FDA and institution within 30 (thirty) days.

3.3.18 The external Sponsor should strengthen local capacity for ethical, scientific review, biomedical research and provide healthcare services as described in sections 20, 21 of the International Ethical Guidelines for Biomedical Research involving Human Subjects (CIOMS 2002).

Sponsors and Investigators have an ethical obligation to ensure that biomedical research projects contribute effectively to national or local capacity building. Capacity building may include, but is not limited to, the following activities:

3.2.18.1 Establishing and strengthening independent and competent ethical review processes/committees.

3.2.18.2 Developing technologies appropriate to health-care and biomedical research.

3.2.18.3 Training of research and health-care staff.

3.2.18.4 Educating the community from which research subjects will be drawn.

3.3.19 External Sponsors are ethically obliged to ensure the availability of:

3.2.19.1 health-care services that are essential to the safe conduct of the research

3.2.19.2 treatment of subjects who suffer injury as a consequence of research intervention; and

3.2.19.3 services that are a necessary part of the commitment of a sponsor to make a beneficial intervention or product developed as a result of the research reasonably available to the population or community concerned.

3.2.19.4 The Sponsor shall appoint a Local Monitor to oversee the progress of a clinical trial and to ensure that it is conducted, recorded and reported in accordance with the SOPs, GCP and the applicable regulatory requirements.

***Refer to Section 3.4 of FDA's Guidelines for Authorization of Clinical Trials of Medicines, Food Supplements, Vaccines and Medical Devices in Ghana for the qualification of the Local Monitor***

**3.4 The Authority**

- 3.4.1 The Authority shall approve a clinical trial by issuing a Clinical Trial Certificate in a format as may be prescribed by The Authority for the initiation and conduct of clinical trials in Ghana. The approval process shall involve establishing adequate procedures and/or requirement for review of the clinical trial application. The Authority may require protocol revisions whenever it deems necessary.
- 3.4.2 The Authority may renew or amend a Clinical Trial Certificate issued if adequate justification for the renewal or amendment is given by an applicant.
- 3.4.3 A Clinical Trial Certificate issued shall be revoked if conditions for which the certificate was issued are violated.
- 3.4.4 The Authority shall order the person conducting the clinical trial to stop or suspend the trial immediately if at any stage during the conduct of a clinical trial The Authority is satisfied that it is in the public interest to do so.
- 3.4.5 The Authority shall act as a Secretariat to the CT-TAC that has been established by Section 150 of the Public Health Act.
- 3.4.6 The Authority shall monitor a clinical trial from the beginning to the end in order to ensure adequate protection of the general public against the risk or adverse events from authorized clinical trials. This is to satisfy itself that the specific and general conditions to which the trial was authorized are being strictly adhered to by the person(s) conducting the trial and that the trial will achieve its objectives. The Authority shall therefore process Serious Adverse Events received from clinical trial sites as follows:
- 3.4.6.1 Acknowledgement of receipt of the report
- 3.4.6.2 Follow-up for clarification, missing or additional information such as laboratory test results where necessary
- 3.4.6.3 Entry of the report into the Authority's Clinical Trial SAE Database where information shall be treated with strict confidentiality.
- 3.4.6.4 The SAE report form with the necessary detailed information shall be submitted to the CT-TAC to enable causality assessment which may

inform regulatory decisions or actions and feedback given to the site when necessary.

3.4.7 The Authority shall conduct on-site inspections to ensure:

3.4.7.1 the safety of clinical trial participants,

3.4.7.2 the quality and reliability of data obtained in a trial, and

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

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

#### **4.0 GOOD CLINICAL PRACTICE INSPECTIONS**

In accordance with section 161 of the Public Health Act, 2012, Act 851 The Authority shall conduct GCP inspections.

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

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

4.3 The inspections may be carried out randomly, and/or for specific reasons and shall be either announced or unannounced.

4.4 An inspection would consist of a comparison of the procedures and practices of the principal investigator with the commitments set out in the protocol and reports submitted to The Authority by the investigator or the sponsor.

4.5 During the inspection the FDA shall assure itself that:

4.5.1 The facilities used by the investigator continue to be acceptable for the purposes of the study.

4.5.2 The approved study protocol for the investigation is being followed.

- 4.5.3 Any changes to the protocol have been approved by respective Ethics Committees and The Authority.
- 4.5.4 Accurate, complete and current records are being maintained.
- 4.5.5 Serious adverse events (SAEs) are reported to the sponsor and to the FDA and institutional review board(s) within the stipulated time as specified in these guidelines.
- 4.5.6 The investigator is carrying out the agreed-upon activities, and has not delegated them to other previously unspecified staff.
- 4.6 To facilitate the above The Authority may require the submission of specific data listing before or during the conduct of a GCP inspection.
- 4.7 During an inspection, inspectors:
  - 4.7.1 Should be given easy access to the trial sites and laboratories at all times
  - 4.7.2 Should have easy access to all patient files and raw data utilized for and generated during the trial. All site data and documents including participant files must be available for verification.
- 4.8 All observations and findings shall be verified in order to ensure the credibility of data and to assure that the conclusions that would be presented are derived correctly from the raw data.
- 4.9 Before an inspection, the principal investigator (or the co-investigator) shall be informed of the impending inspection either in writing, by phone or electronically.
- 4.10 An unannounced inspection may however be conducted, if the FDA has reasonable cause to believe that the approved protocol is being violated.

## **5.0 APPENDICES: DETAILS OF AN INSPECTION BY THE FOOD AND DRUGS AUTHORITY**

### **5.1 SELECTION OF CLINICAL TRIALS FOR INSPECTION**

Selection of approved clinical trials for GCP inspection shall be based on benefit to risk ratio considering but not limited to the underlisted:

- 5.1.1 The phase of the clinical trial
- 5.1.2 The nature of the investigational product.
- 5.1.3 The market authorization status of the investigational product
- 5.1.4 The population under study
- 5.1.5 Capacity of trial site
- 5.1.6 Previous experience of FDA with sponsor/principal investigator with respect to compliance to GCP requirements.

## **5.2 WHAT DOES AN INSPECTION INVOLVE?**

The inspection may involve:

- 5.2.1 A comparison of the practices and procedures of the clinical investigator with the commitments made in the application to conduct a clinical trial;
- 5.2.2 A comparison of the data submitted to The Authority with the source data; and/or
- 5.2.3 A system inspection of the sponsor, clinical laboratory or CRO generating data for submission to regulatory authorities. This may include inspection of both the clinical facility and analytical facility.

## **5.3 THE INSPECTION**

Details of the various phases of an inspection, including pre-inspection contact; the opening meeting and the actual inspection are outlined below:

### **5.3.1 Pre-Inspection Contact:**

Where appropriate, appointments for inspection of an investigational site should be made by a telephone call and/or an e-mail. A written confirmation of the inspection date, time and program (if applicable) may be forwarded to the site, the sponsor company or the CRO.

The Local Monitor responsible for the monitoring of the study needs to be present during the inspection. The time span between initial contact and actual inspection shall be as short as possible. Any undue delay of the inspection on the part of the clinical investigator will be investigated.

### **5.3.2 Opening Meeting:**

The purpose of this meeting is for the Inspector(s) to:

- 5.3.2.1 explain the purpose of the inspection, i.e. routine or for -cause,
- 5.3.2.2 outline the scope of the inspection
- 5.3.2.3 obtain a brief review of the organization of the site being inspected.

### **5.3.3 The Inspection Purpose:**

The overall purpose of the conduct of the inspection should be to establish whether the investigator has fulfilled his/her GCP responsibilities. This includes the following:

- 5.3.3.1 To ascertain whether the investigator is thoroughly familiar with the properties of the investigational product(s) as described in the investigator's brochure.
- 5.3.3.2 To ensure that investigator has sufficient time to conduct and complete the clinical study,
- 5.3.3.3 To ensure that the investigator has adequate staff and appropriate facilities (including laboratories) available for the duration of the study, and
- 5.3.3.4 To ensure that other studies do not divert essential participants or facilities away from the study in hand.
- 5.3.3.5 To establish whether the investigator has studied the protocol and whether the assisting personnel have been adequately informed of their responsibilities.
- 5.3.3.6 To determine if The Authority's and Ethics Committee and other relevant approvals have been obtained with stipulated conditions adhered to.

5.3.3.7 To determine in what manner the investigational products are handled and stored, and that investigational products are dispensed to study participants in accordance with the protocol and that any unused products are returned to the Sponsor.

Reconciliation of trial medication must be provided.

5.3.3.8 To ensure that the confidentiality of all information about participants is respected (by all persons involved).

5.3.3.9 To ensure that the investigator observes the following points particularly related to medical care:

In addition, the investigator needs to provide retrospective data on numbers of participants who would have satisfied the proposed entrance criteria during preceding time periods in order to assure an adequate recruitment rate for the study. The investigator also needs to provide an up-to-date curriculum vita.

The Investigator is medically responsible for those participants who are under his/her care for the duration of the study and must ensure that appropriate medical care is maintained after the study. Where appropriate, fully functional resuscitation equipment should be immediately available in case of emergency. Clinical significant abnormal laboratory values or clinical observations must be followed up after completion of the study.

#### **5.4 ESSENTIAL DOCUMENTS FOR THE CONDUCT OF A CLINICAL TRIAL**

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 in addition to other functions not herein mentioned serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements.

The minimum list of essential documents which has been developed are outlined below. The various documents are grouped in three sections according to the stage of the trial during which they will normally be generated (Refer to Appendix II for more details):

5.4.1 Before the clinical phase of the trial commences,

5.4.2 During the clinical conduct of the trial, and

5.4.3 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 study monitor(s) 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 subject to, and should be available for, audit by the sponsor's auditor and inspection by the FDA.

## 5.5 TRIAL PROCEDURES

This part identifies the nature of the information that shall be obtained during each inspection to determine if the clinical investigator is meeting his/her obligation as trialist. This outline provides only the minimal scope of the inspection and the inspector shall extend the inspection as the facts evolve. The inspection conducted shall be sufficient in scope to determine compliance with Good Clinical Practice.

Scientific data shall not be evaluated during the inspection, but only verify documentation and validate data. An inspection may include the following checks:

- 5.5.1 The protocol, included amendments must be signed by the investigator.
- 5.5.2 Ethics Committee and regulatory approval documentation.
- 5.5.3 Validation of signed informed consent documents. Signatures shall be checked against evidence on patient files. It would be determined whether written informed consent was obtained for all participants prior to the entry into the study and whether this was recorded in the participants medical records. A copy of the information presented orally may also be obtained.
- 5.5.4 Participant records shall be verified.
- 5.5.5 The condition, organization, completeness and legibility of the investigator's raw data files may need to be described.

5.5.6 Necessary processes would be put in place to determine whether there is adequate documentation to assure that all inspected participants did exist and were available for the duration of their stated participation in the study.

5.5.7 The raw data in the clinical investigator's records would be compared with the completed case record forms.

The following shall also be determined:

5.5.8 Whether the number and type of participants entered into the study were confined to the protocol limitations

5.5.9 Whether the inclusion and exclusion criteria as specified in the protocol were followed

5.5.10 Observations, information, and data condition of the participants at the time of entering into the trial.

5.5.11 Observations and data on the condition of the participant throughout participation in the investigation, including results of lab tests, development of unrelated illness and other factors which might alter the effects of the test article

5.5.12 Records of exposure of the participant to the test article.

5.5.13 Whether clinical laboratory testing (including ECGs x-rays and other special investigations), as noted in the case reports, can't be evaluated by the presence of completed laboratory reports in the source documents.

5.5.14 The occurrence of adverse reactions would be determined. The reporting of these events to FDA and the Ethics Committee shall be documented.

5.5.15 All persons obtaining raw data or involved in the collection or analysis of such data would be identified.

## **5.6 TRIAL MEDICATION**

With regard to trial medication the following are considered as important in an inspection:

5.6.1 Determination of accounting procedures for the test and comparator drugs.

- 5.6.2 Dates and quantity of trial medication dispensed as well as the recipients must be available as well as corroboration by raw data notations.
- 5.6.3 The blinding of medication, if appropriate, must be validated to ensure protection of the study from bias.
- 5.6.4 It shall be determined whether distribution of the article was limited to those persons under the investigator's direct supervision.
- 5.6.5 The storage area may be inspected.
- 5.6.6 It would be determined whether the test article is a controlled substance and whether it is securely locked
- 5.6.7 Access to the controlled substance must be restricted to the investigator and the responsible pharmacist.

## **5.7 LABORATORY**

The FDA during an inspection would determine the systems and procedures that are followed within an organization that is conducting analysis of samples from clinical trials in compliance with the requirements of Good Clinical Practice (GCP).

Inspections of a laboratory being used to analyze samples from a clinical trial shall be in accordance with provisions outlined in the *Good Clinical Laboratory Practice Guidelines* published by WHO/TDR.

### **5.7.1 Transfer of Biological Samples**

No person shall make arrangements to receive or ship biological samples from a clinical trial without prior approval from The Authority.

Persons who wish to import or export any biological samples from a clinical trial shall submit an application and a suitable Material Transfer Agreement for approval by The Authority. The application must be accompanied with the appropriate clearance from a reputable Ethics Committee or Institutional Review Board in Ghana.

## **5.8 COMPUTER ELECTRONIC DATA SYSTEMS**

If electronic data systems are involved in gathering data, storing data, or transmitting data to the sponsor, these would be identified and their capabilities established. Data should be collected, processed and stored in compliance with the Data Protection Act 2012 (Act

843). The following are important issues to consider in the selection of an appropriate electronic data system:

5.8.1 The source of data entered into the computer

5.8.2 The qualification of the personnel to enter data

5.8.3 At which time/stage should the entering be done

5.8.4 Provision for access to data and computer

5.8.5 Security codes

5.8.6 Procedure and persons responsible for changes and audit trail.

5.8.7 Procedure for submission of data to sponsor? (hard disk, floppy disk, fax, modern network, mail, messenger)

5.8.8 Procedures for corrections (errors, omissions, etc.) in the data received and documentation

***Note: Electronic system must be validated in accordance with Code of Federal Regulations (21 CFR Part 11)***

## **5.9 EXIT MEETING / INSPECTION REPORT**

At the post inspection meeting the inspectors would convey the findings of the inspection to the investigator and the representative of the pharmaceutical company or contract research organization and other key members of the study team. The inspection reports shall eventually reflect discussions had at the exit meeting

The matters discussed at this meeting shall be in line with the report written by the inspectors. Important matters include:

When significant violations of GCP are observed, reports shall contain sufficient narrative and accompanying documentation to support the findings. When it is apparent that the study has been conducted in substantial compliance with the guidelines, an abbreviated report may contain the following shall be compiled:

- 5.9.1 The comparison of raw data recorded in the case report forms to that of the source data, including the number of records compared and what was compared (patient charts, hospital records, lab slips and etc.)
- 5.9.2 A statement about the trial medication accountability records
- 5.9.3 A statement about protocol adherence, which should be characterized and quantified.
- 5.9.4 A statement about the obtaining of informed consent from each participant.
- 5.9.5 A statement identifying the specific individual responsible for each significant aspect of the study.
- 5.9.6 A statement on follow-up of adverse experiences (including death) if any occurred.

If deficiencies were found during the inspection in any of these or in any of the areas it needs to be explained and documentation attached as exhibits.

Inspections conducted 'for-cause' would have full reporting. (A for-cause inspection may be the result of prior knowledge or suspicion of alleged violations of Act 851 of the Public Health Act, 2012 and/or guidelines. A for-cause inspection may concentrate the data verification on specific areas of the study or may expand the data verification to cover multiple studies. This inspection may also result when a study is of singular importance to the approval of registration of a medicine, i.e. one of two adequate and well controlled studies.)