NATIONAL DRUG AUTHORITY

Safe Drugs Save Lives

GUIDELINES ON GOOD CLINICAL PRACTICE IN THE CONDUCT OF CLINICAL TRIALS INVOLVING HUMAN PARTICIPANTS

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PRESENTATION OUTLINE

- Introduction
- Regulatory framework
- Principles of GCP
- Brief overview of the guidelines
- GCP Inspections: Critical areas of non-compliances
- Consequences of Non-compliance with GCP

INTRODUCTION

- Objective of the guidelines is to ensure that drug-related trials in Uganda are conducted in accordance with international ethical and scientific standards.
- The Guidelines on Good Clinical Practice In The Conduct Of Clinical Trials Involving Human Participants have been adapted from the ICH GCP guidelines, E6(R2), with some modifications to suit local requirements.
- Compliance with these guidelines;
  - facilitates mutual acceptance of clinical data by international regulatory authorities
  - Provides assurance that rights safety and well being of participants are protected

Regulatory Framework

- The National Drug Policy and Authority (NDP/A) Act.
  - Section 40
  - Section 64
- The NDP/A (Conduct of Clinical Trials) regulations, 2014.
  - Regulation 7: Authorization of clinical trials
  - Regulation 14: Protection of subjects
  - Regulation 15: Responsibilities of a sponsor
  - Regulation 16: Responsibilities of the principal investigator

GOOD CLINICAL PRACTICE (GCP)

ICH GCP E6(R2) Definition:

- A Standard for the **design, conduct , performance, monitoring, auditing, recording, analyses and reporting of clinical trials** that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial subjects are protected.
- There are 13 principles of GCP that summarize the requirements for GCP in the conduct of a clinical trial (**section 1.3 of the draft guidelines**). These are Internationally recognized.

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- Principle #1:
  - Clinical Trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirements.

Overview of Guidelines

1. Introduction
2. Protection of study participants
3. Responsibilities of the principal investigator
4. Responsibilities of the sponsor
5. Data management
6. Clinical Trial protocol and protocol amendments
7. Investigator's Brochure

Section 1: Introduction

This section provides details on the scope and purpose of the guidelines, principles of GCP, roles of parties involved and procedures for review and approval of applications

Key GCP Principles:

Principle #4 and #5

Considerations for approval of applications

- Relevance of the clinical trial
- Suitability of the principal investigator
- Quality of the facilities to be used for the clinical trial
- Informed consent process
- Clinical trials insurance
- Etc

2. Protection of Participants

Key GCP Principles:

Principle #2, #3, #11

Considerations

- All medical research involving human participants must undergo an independent ethical review.
  - the UNCST Guidelines for Research Involving Humans as Research participants, 2014
- For research involving vulnerable persons and groups, there is need for special protection of their rights and welfare.
  - CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects, 2016

3. Responsibilities of the PI

Key GCP Principles:

Principle #7, #9, #12, #6

Considerations

- PI should be well qualified to conduct the trial.
- Responsible for the clinical trial site.
- Provide adequate care to the participants for any adverse events
- Be responsible for and accountable for the investigational medicinal product
- Comply with ethical principles while obtaining informed consent.
- Responsible for data management at the trial site (collection, ensuring quality, recording, maintenance and retrieval)
- Others as specified in the guidelines

4. Responsibilities of a Sponsor

Key GCP Principles:

Principle #13, #8, #3

Considerations:

- Maintain quality assurance and quality control systems for the conduct of clinical trials.
- Provide insurance for participants against any clinical trial related injuries or harm.
- Update the investigator's brochure.
- Appoint monitors and ensure that trials are adequately monitored.
- The sponsor is responsible for supplying the investigational medicinal product.
- Others as specified in the guidelines

5. Data Management

Key GCP Principles:

Principle #10, #11

Considerations:

- Quality control should be applied to each stage of data handling to ensure that all data is reliable and has been processed correctly.
- Final study report should have all aspects of the trial that are consistent with the data generated during the trial.
- Records should be maintained both during and after the conduct of the clinical trial for verification purposes.

6. Protocol and Protocol amendments

Key GCP Principles:

Principle #5, #6

This section provides details on the content of clinical trial protocol.

Considerations

- The study endpoints should be measurable and where it has inference to the standard of practice, should not below the standard of practice.
- For multi-site studies, especially multi-country studies, a site specific protocol should be provided in addition to the general protocol.
- The protocol should have received IRB/IEC approval.
- Protocol amendments: Refer to the guidelines on conduct of clinical trials in Uganda.

7. Investigator's Brochure

Key GCP Principles:

Principle #4

This section provides details on the content of an investigator's brochure. It is a compilation of the clinical and non-clinical data on the IMP that is relevant to the study of the product in human participants.

Considerations

- The information in the IB should support the use of the IMP in the trial
- It should also provide insight in the clinical management of the participants

GCP INSPECTIONS

Types

1. Routine inspections
2. For-cause / Triggered inspections
3. Follow-up / Re-inspections

Critical areas of non-compliances

A. Investigational Medicinal product
B. Quality control and quality assurance
C. Trial management

A. Investigational Medicinal Products

Common findings

- Discrepancy in IMP accountability records
  - Shipping records vs IMP accountability logs
  - IMP accountability logs vs Participant specific accountability logs
  - Inconsistent units of measure e.g batch/lot, pack/unit size
- IMP Integrity
  - Temperature monitoring: Excursions, QA/QC of data recorded
  - Storage conditions
- Premises
  - Controlled access to storage area
  - Separation of different categories of medicines e.g expired, returned.

Quality Assurance / Quality Control

Common findings

1. This responsibility seldom appears on the Delegation of Duties log.
2. Most data collection tools have no provision for this process.
3. There is limited or no monitoring being carried out.
4. Equipment are not calibrated and/or verified routinely.
5. Standard Operating Procedures not in place for critical activities.
6. Lack of job aides or tools to guide research staff in making clinical decisions

Trial Management

Common findings

1. No trial organogram or other document
2. No records of regular meetings or mechanisms of communication within the team or between investigators for multi-site studies.
3. Absence of evidence of staff job descriptions (in relation to the Delegation log) & training
4. Absence of records of re-training on the protocol or on specific activities when protocol deviations are documented

Consequences of Non-compliances noted following GCP findings

- CAPA Report
- Warning letter
- Suspension of clinical trial
- Termination of clinical trial
- Penalty specified in the Act.
- The Authority may share findings of the inspection with other regulatory bodies (UNHRO, UNCST, FRECU, REC of record)

Thank you for listening

Comments