IOCTB LEARN

GOOD CLINICAL PRACTICE (GCP) INSPECTIONS

Presented by:

Innovation Office & Clinical Trials Branch

Health Products Regulation Group

Health Sciences Authority

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Outline

- Definition of GCP Inspection
- HSA's GCP Inspection Framework
- How to Prepare for a GCP Inspection
- What Happens During and After a GCP Inspection
- Classification of GCP Inspection Findings
- Considerations for Remote / Hybrid GCP Inspections

Learning Objectives

1. Have a clear understanding of the objectives of GCP Inspections
2. Understand the scope and types of GCP Inspections conducted by HSA
3. Learn how to prepare for a GCP Inspection
4. Appreciate what happens during and after a GCP Inspection
5. Understand how GCP Inspection Findings are classified
6. Appreciate the considerations for remote / hybrid GCP Inspections

DEFINITION OF GCP INSPECTION

Definition of GCP Inspection

The act by a **regulatory authority(ies)** of conducting an **official review of documents, facilities, records and any other resources** that are deemed by the authority(ies) to be related to the clinical trial and that may be accessed at the **investigator site, at the sponsor's and/or service provider's (including CRO's) facilities, or at other establishments** deemed appropriate by the regulatory authority(ies). Some aspects of the inspection may be conducted remotely.

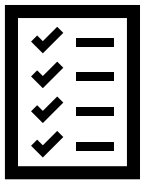
Reference: ICH E6 (R3) GCP Guideline

HSA'S GCP INSPECTION FRAMEWORK

Objectives of GCP Inspections

Safeguard the rights, safety and well-being of trial participants.

Verify the quality and integrity of the clinical trial data submitted to the Regulatory Authority.



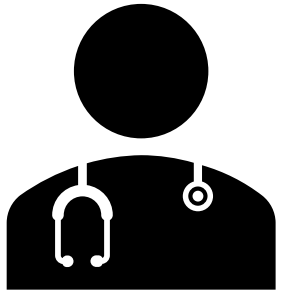
Assess compliance to the protocol and applicable regulations, guidelines and standard operating procedures for clinical trials.

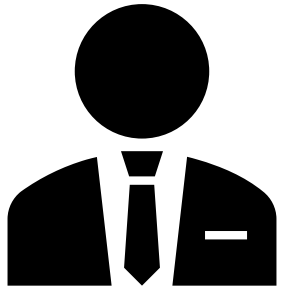
Scope of GCP Inspections

- Clinical trials regulated by the Health Sciences Authority (HSA)
  - Clinical trials that are subject to the requirements of a:
    - Clinical Trial Authorisation (CTA)
    - Clinical Trial Notification (CTN)

- GCP inspections may either be **protocol-specific** or **systems inspections**.

Inspectee





PRINCIPAL INVESTIGATOR (PI)

LOCAL SPONSOR*

**The local sponsor is responsible for all sponsor responsibilities as specified in the applicable clinical trials and clinical research materials regulations and the ICH E6 GCP Guideline.*

**For clinical trials where a Contract Research Organisation is the local sponsor, the global sponsor should provide the necessary support to the local sponsor for the sponsor inspection.*

Types of GCP Inspections

1 ROUTINE

- Selected based on a risk-based approach.
- Typically conducted for ongoing clinical trials.

2 TRIGGERED

- Conducted in response to specific issues or concerns that compromise the goals of GCP.
- Apply to ongoing or completed clinical trials.

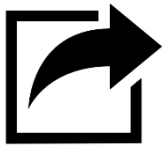
3 PRE-MARKETING APPROVAL APPLICATION

- Apply to completed clinical trials.

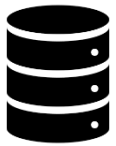
HOW TO PREPARE FOR A GCP INSPECTION

GCP Inspection Preparation

A Notice of GCP Inspection will be sent to the inspectee at least 30 working days prior to the proposed dates for the GCP Inspection.



Submit a GCP Inspection Dossier to HSA within the timeline stipulated in the notice.



Provide direct access to all essential records, including source records, Case Report Forms, Investigator Site File and Trial Master File.

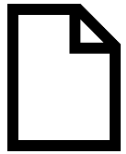
GCP Inspection Preparation

Secure a suitable meeting room for the GCP Inspection.

Assign a separate room for the study staff.

Assign study staff to scribe, retrieve missing essential records and accompany the GCP inspectors on facility tours.

GCP Inspection Preparation



Ensure that study staff are familiar with the protocol, and applicable regulations, guidelines and SOPs.

Ensure that the Investigator Site File and Trial Master Files are complete and current.

Prepare a general overview of the clinical trial.

Prepare a list of the PI's currently active clinical trials.

GCP Inspection Preparation

Ensure that all essential records are attributable, legible, contemporaneous, original, accurate and complete.

Ensure that study staff training records are updated.

Review the IRB / IEC and HSA communications.

Review the informed consent process.

GCP Inspection Preparation

Ensure that study staff have adhered to the approved protocol and amendments, if any.

Verify that adequate medical care by an investigator, who is a qualified practitioner, is provided.

Check that there are adequate source records.

Verify that data has been accurately transcribed from the source records to the Case Report Forms.

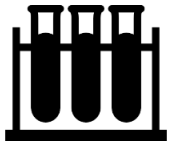
GCP Inspection Preparation

Verify that the Investigational Product is manufactured, labeled, handled and stored in accordance with GMP guideline, protocol, Investigator's Brochure and labeling requirements. Verify that essential records for Investigational Product management are accurate and complete.

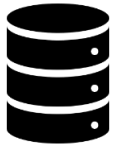
Ensure that all Serious Adverse Events (SAEs) are reported in a timely, accurate and complete manner.

Review site monitoring visit follow-up letters to ensure that all open action items are resolved.

GCP Inspection Preparation



Verify that biological samples have been handled in accordance with the protocol and applicable SOPs.



Ensure that there are provisions for archival of essential records in accordance with applicable regulatory requirements.

WHAT HAPPENS DURING A GCP INSPECTION

GCP Inspection Conduct

Opening Meeting → Interviews → Document Review → Interim Meeting → Closing Meeting

- Introductions

- Presentations
  - *Overview of GCP Inspection Framework by HSA*
  - *Overview of trial conduct by Inspectee, according to the scope of the GCP Inspection*

- Confirmation of agenda, including interim and closing meetings
- Availability of resources, facilities and essential records
- Records access
- Matters relating to confidentiality

GCP Inspection Conduct

Opening Meeting → **Interviews** → Document Review → Interim Meeting → Closing Meeting

SITE INSPECTION

INVESTIGATOR

CLINICAL RESEARCH COORDINATOR

PHARMACIST

MONITOR

GCP Inspection Conduct

Opening Meeting | **Interviews** | Document Review | Interim Meeting | Closing Meeting

SPONSOR INSPECTION

LOCAL SPONSOR REPRESENTATIVE

SUBJECT MATTER EXPERTS RESPONSIBLE FOR THE SCOPE OF THE GCP INSPECTION

GCP Inspection Conduct

SITE INSPECTION	
Investigator Site Staff and Facilities	Safety Assessment and Reporting
Institutional Review Board (IRB) Submissions	Biological Samples Management
Regulatory Authority Submissions	Data Collection and Handling
Trial Participant Recruitment	Monitoring
Informed Consent	Deviations / Noncompliances
Randomisation	Trial suspension / termination / completion
Blinding	Essential Records
Investigational Product (IP) Management	

GCP Inspection Conduct

SPONSOR INSPECTION	
Trial Design	Quality Assurance and Quality Control
Resources	Investigational Product (IP) Management
Service Providers	Safety Assessment and Reporting
Investigator Selection	Data Collection and Handling
Institutional Review Board (IRB) submissions	Monitoring
Regulatory Authority submissions	Deviations / Noncompliance
Sponsor Oversight	Trial suspension / termination / completion
Quality Management	Essential Records

GCP Inspection Conduct

Opening Meeting → Interviews → Document Review → **Interim Meeting** → Closing Meeting

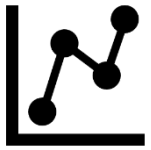
Discuss observations noted from the GCP Inspection.

Provide the inspectee with an opportunity to resolve the observations during the GCP Inspection, where possible.

Re-cap the resolution status of observations on the next business day of the GCP Inspection.

GCP Inspection Conduct

Opening Meeting → Interviews → Document Review → Interim Meeting → **Closing Meeting**



Review classification of GCP Inspection findings.

Discuss the observations noted from the GCP Inspection.

Give inspectee an opportunity to provide clarifications.

Review timelines for receipt of the GCP Inspection Report and submission of the Corrective Action and Preventive Action (CAPA) Plan.

WHAT HAPPENS AFTER A GCP INSPECTION

GCP Inspection Follow-up

GCP Inspection Report

- 20 working days from last date of GCP Inspection.

Corrective Action and Preventive Action (CAPA) Plan

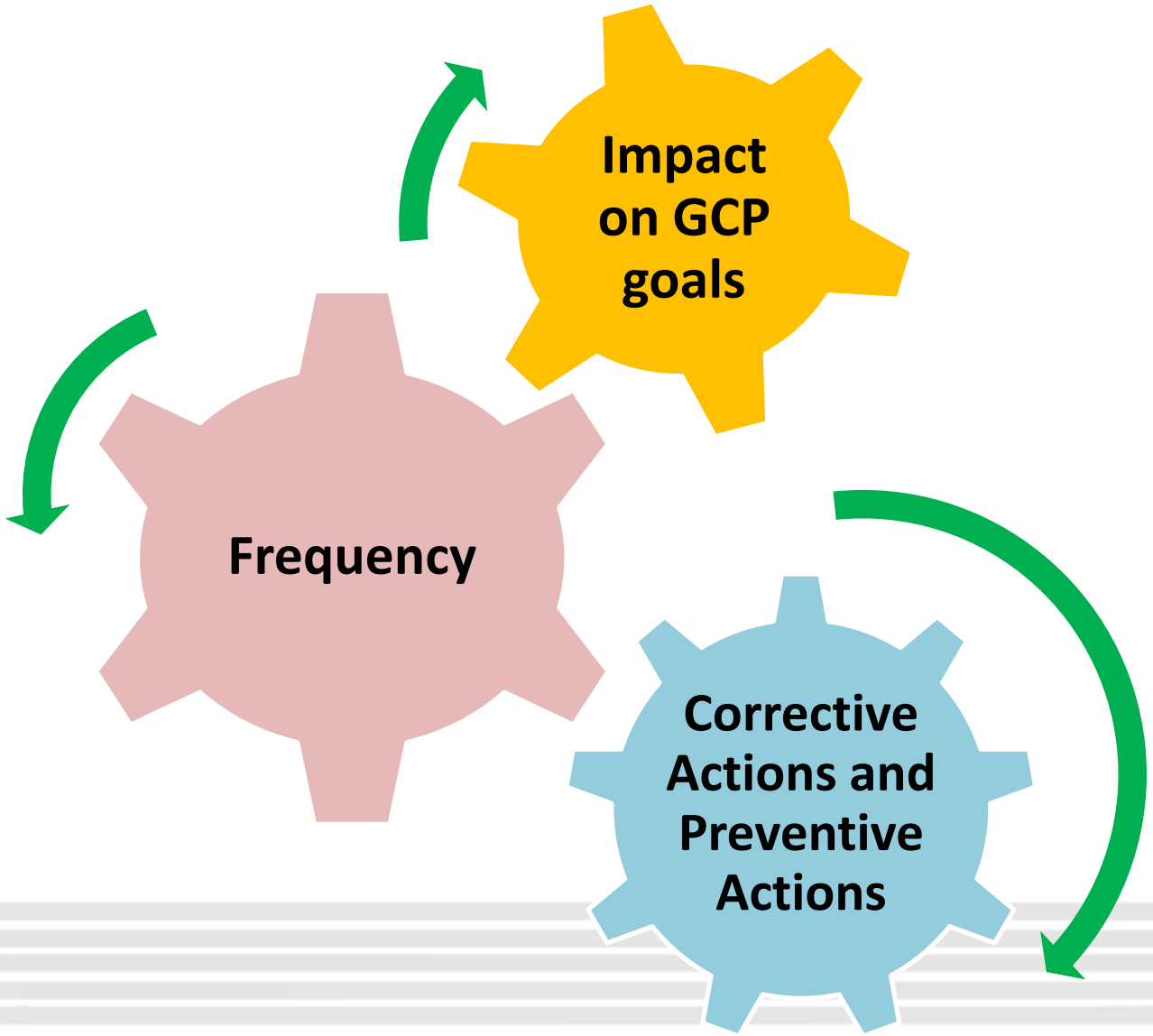
- 30 working days from the receipt of the GCP Inspection Report.

GCP Inspection Closing Letter

- If the CAPA Plan is deemed to be adequate.

Classification of GCP Inspection Findings

- Considerations:

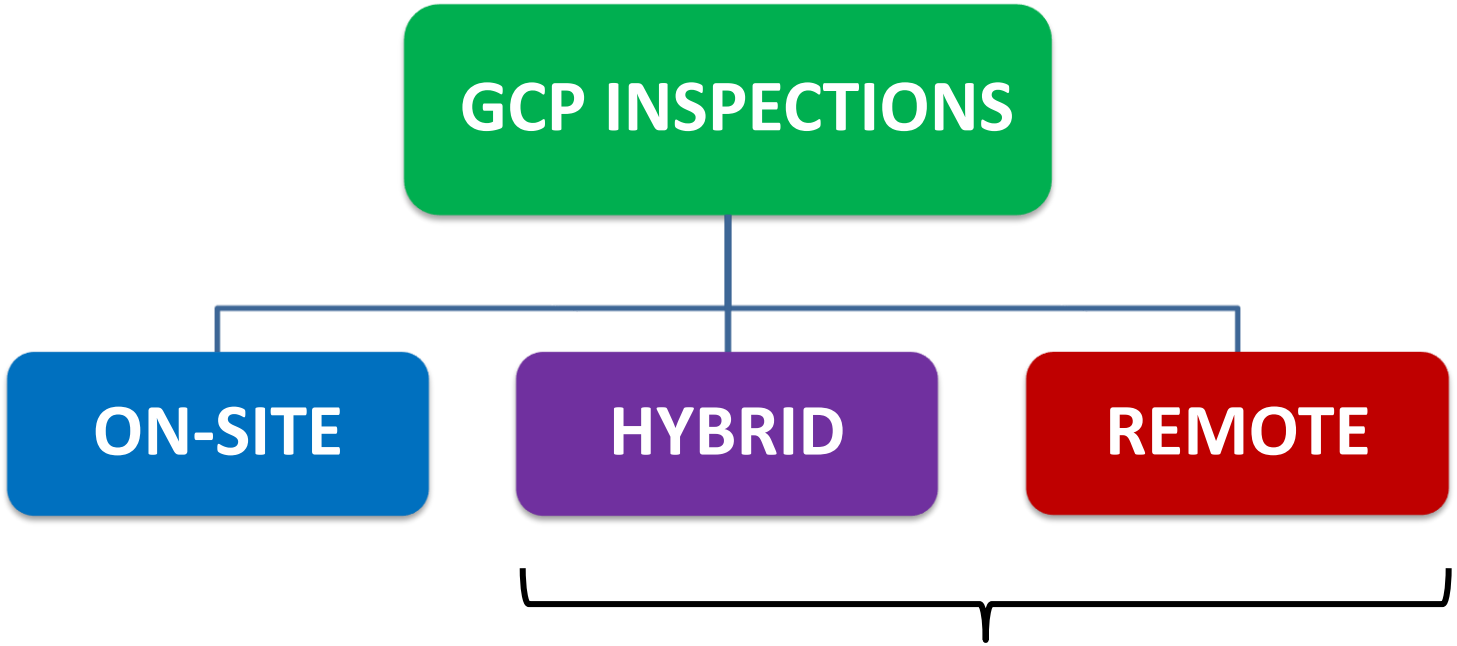


Classification of GCP Inspection Findings

CRITICAL	• Adversely compromise the goals of GCP.
MAJOR	• May adversely compromise the goals of GCP.
OTHER	• Will not be expected to adversely compromise the goals of GCP.
COMMENTS	• For quality improvement or to reduce the potential for deviations / noncompliances.

CONSIDERATIONS FOR A REMOTE / HYBRID GCP INSPECTION

GCP Inspections



- Same objectives, scope and criteria as on-site GCP Inspections.
- Similar procedures as on-site GCP inspections, except for remote interviews and document reviews.

Remote / Hybrid GCP Inspections

- **Considerations for remote / hybrid approaches for GCP Inspections:**
  - Restrictions in the context of a public health emergency;
  - Differing time zones;
  - Scope and objectives of the GCP Inspection;
  - Complexity of the trial-related activities being assessed;
  - Operational feasibility of a remote / hybrid GCP Inspection;
  - Availability of technology and access to computerised systems and file sharing portals to enable stable and secure remote communication, sharing, access and review of essential records, in accordance with applicable data governance policies.

Remote / Hybrid GCP Inspections

- **GCP Inspection activities that may be conducted remotely:**
  - Meetings;
  - Interviews;
  - Review of essential records that are made accessible remotely via computerised systems, in compliance with applicable data governance policies.

Remote / Hybrid GCP Inspections

- **Logistical Arrangements required of the inspectee:**
  - All required attendees are able to participate in the remote / hybrid GCP Inspection, in accordance with the GCP Inspection Agenda;
  - Remote access is provided to the GCP Inspectors for the computerised systems used for the clinical trial (e.g., Investigator Site Files, Trial Master Files, Case Report Forms, Standard Operating Procedures, Patient Reported Outcomes etc.) from GCP Inspection notice to closure;
  - Arrangements are made for the GCP Inspectors to complete the necessary training requirements in order to access the computerised systems used for the clinical trial;
  - A secure file sharing portal is established for document sharing, with downloading functions enabled for the GCP Inspectors;

Remote / Hybrid GCP Inspections

- **Logistical Arrangements required of the inspectee:**
  - In situations where the inspectee is unable to use the proposed video conferencing software, the inspectee should propose an alternative video conferencing software to facilitate communication with the GCP Inspectors during the conduct of the remote / hybrid GCP Inspection, including:
    a) Enabling screen sharing, virtual visits, and break-out rooms; and
    b) Disabling the recording function.

Summary

- Clinical trials regulated by HSA may be subject to GCP Inspections.
- GCP Inspections assess compliance to the regulatory requirements and the principles of GCP, and ensure the rights, safety and well-being of trial participants are safeguarded, and the clinical trial data is credible.
- It is important to always be prepared for a GCP Inspection, than repair from a GCP Inspection.
- If it was never documented, it was never done!

References

- Health Products (Clinical Trials) Regulations
- HSA Regulatory Guidance (GN-IOCTB-11): Guidance on GCP Compliance Inspection Framework
- ICH E6 (R3) Good Clinical Practice (GCP) Guideline

We welcome your enquiries and feedback!

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THANK YOU!