HEALTH SCIENCES AUTHORITY

REGULATORY GUIDANCE

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CLINICAL TRIALS GUIDANCE

GUIDANCE ON GCP COMPLIANCE INSPECTION FRAMEWORK

GN-IOCTB-11 Rev. No. 004

HSA
Health Sciences Authority

PREFACE

This document is intended to provide general guidance. Although we have tried to ensure that the information contained here is accurate, we do not, however, warrant its accuracy or completeness. The Health Sciences Authority (HSA) accepts no liability for any errors or omissions in this document, or for any action / decision taken or not taken as a result of using this document. If you need specific legal or professional advice, you should consult your own legal or other relevant professional advisers.

In the event of any contradiction between the contents of this document and any written law, the latter should take precedence.

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REVISION HISTORY

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GN-IOCTB-11 Rev. No. 004 (2 Jan 2026)

SUMMARY OF AMENDMENTS

- Aligned the definition (Section 1.4) and scope of GCP Inspections (Section 5) with the ICH E6 (R3) GCP Guideline
- Expanded the scope of the guidance to include Sponsor Inspections (Section 5.2)
- Aligned the turn-around time for issuing GCP Inspection Reports for Site Inspections and Sponsor Inspections (Sections 7 and 9.7.3)
- Clarified the requirements for direct access to source records (Section 8.3)

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1. INTRODUCTION

1.1. Purpose

The purpose of this document is to provide guidance to the industry on the overview of the GCP Compliance Inspection Framework of the Health Sciences Authority (HSA).

1.2. Background

Clinical trials regulated by HSA must comply with the protocol, applicable clinical trials and clinical research material regulations, ICH E6 Good Clinical Practice (GCP) Guideline and standard operating procedures.

The GCP Compliance Inspection Framework was launched in Sep 2009.

1.3. Scope

This guidance applies to clinical trials regulated by HSA, namely:

(i) Clinical trials of Therapeutic Products[1] and Class 2 Cell, Tissue and Gene Therapy Products (CTGTPs)[1,2] that are subject to the requirements for a Clinical Trial Authorisation (CTA) or a Clinical Trial Notification (CTN);

(ii) Clinical trials of Medicinal Products[3] that are subject to the requirements of a Clinical Trial Certificate (CTC).

[1] Therapeutic Product and CTGTP are defined in the First Schedule to the Health Products Act.

[2] Class 1 and Class 2 CTGTP are defined in the Health Products (Cell, Tissue and Gene Therapy Products) Regulations.

- Class 1 CTGTP means a CTGTP that —
  (a) is the result of only minimal manipulation of human cell or tissue;
  (b) is intended for homologous use;
  (c) is not combined or used with a therapeutic product or a medical device; and
  (d) is assigned by HSA as a Class 1 CTGTP due to a lower health risk to a user of the product.
- Class 2 CTGTP means a CTGTP other than a Class 1 CTGTP.

[3] Medicinal Product is defined in the Medicines Act.

1.4. Definitions

(i) GCP Inspection

A GCP Inspection is defined as 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.

(ii) Remote GCP Inspection

A GCP inspection conducted virtually or at a distance, supported by technology for communicating, sharing, reviewing, accessing computerised systems, without the GCP inspectors being physically present at the location where the activities subject to a GCP inspection have taken place or where the GCP inspection would routinely be hosted.

(iii) Hybrid GCP Inspection

A GCP Inspection performed using a combination of on-site and remote means.

2. TYPES OF GCP INSPECTIONS

GCP Inspections may either be routine, triggered or conducted to support a pre-marketing approval application. A protocol-specific or systems approach may be adopted for GCP Inspections.

2.1. Routine GCP Inspections

Clinical trials for routine GCP Inspections are selected based on a risk-based approach. Some risk considerations may include the phase of the clinical trial, therapeutic area, target trial population, complexity of trial design, and clinical trial experience of the sponsor or Principal Investigator (PI). Routine GCP Inspections are done announced, and apply to ongoing clinical trials.

2.2. Triggered GCP Inspections

Triggered GCP Inspections may be conducted in response to specific issues or concerns that compromise the goals of GCP. Such inspections may be done announced or unannounced, and apply to ongoing or completed clinical trials.

2.3. Pre-marketing approval application GCP Inspections

GCP inspections conducted to support pre-marketing approval applications are usually done announced, and apply to completed clinical trials.

3. TYPES OF INSPECTEE

The inspectee for a GCP Inspection may either be the:

(i) Principal Investigator (PI) of the local investigator site – Such GCP Inspections will be referred to as 'Site Inspections'; and/or

(ii) Local sponsor* of the clinical trial – Such GCP Inspections will be referred to as 'Sponsor Inspections'.

**NB: The local sponsor is responsible for all sponsor responsibilities as specified in the applicable clinical trials and clinical research materials regulations and ICH E6 GCP guideline. For clinical trials where a Contract Research Organisation / CRO is the local sponsor, the global sponsor should provide the necessary support to the local sponsor for the Sponsor Inspection.*

4. OBJECTIVES OF GCP INSPECTIONS

The objectives of GCP Inspections have been summarised below:

4.1. Objectives of Protocol-specific GCP Site Inspections

(i) To safeguard the rights, safety and well-being of trial participants;

(ii) To verify the quality and integrity of the clinical trial data submitted to the Regulatory Authorities;

(iii) To assess compliance to the protocol, applicable regulations, guidelines and standard operating procedures for clinical trials.

4.2. Objectives of Systems GCP Inspections

(i) To safeguard the rights, safety and well-being of trial participants;

(ii) To verify the quality and integrity of the clinical trial data submitted to the Regulatory Authorities;

(iii) To assess compliance to the protocol, applicable regulations, guidelines and standard operating procedures for clinical trials;

(iv) To assess whether a system is suitably designed, controlled, maintained and documented to fulfil the objectives for which it has been set up;

(v) To identify areas for quality improvement.

4.3. Objectives of Sponsor Inspections

(i) To ensure that clinical trials are conducted adequately for the purpose of ensuring the rights, safety and well-being of trial participants, and the data generated in clinical trials are recorded, handled, reported and stored in compliance with the protocol, applicable regulations, guidelines and standard operating procedures for clinical trials.

5. SCOPE OF GCP INSPECTIONS

5.1. Scope of Site Inspections

The scope of Site Inspections may include the following, as summarised in Table 1.

Table 1: Scope of Site Inspections

Main category	Sub-category (where applicable)
Investigator Site Staff and Facilities	• Resources • Delegation • Qualification and Training • Investigator Oversight
Institutional Review Board (IRB) Submissions	• Initial IRB Application • Amendments • Continuing Reviews
Regulatory Authority Submissions	• Initial HSA Application • Clinical Research Material Notification • Substantial Amendments • Trial Status Reports
Trial Participant Recruitment	• Recruitment • Eligibility Assessment • End of trial participation
Informed Consent	• Informed Consent Material • Informed Consent Process
Randomisation	• Randomisation Procedures • Randomisation of Trial Participants
Blinding	• Blinding Safeguards • Unblinding
Investigational Product (IP) Management	• IP Manufacturing • IP Labelling • IP Instructions • IP Receipt • IP Storage • IP Repackaging / Relabelling • IP Dispensing and Accountability • IP Preparation • IP Administration • IP Return / Destruction

Main category	Sub-category (where applicable)
Safety Assessment and Reporting	• Medical Care of Trial Participants • Safety Assessment • Safety Reporting
Biological Samples Management	• Biological Samples Collection • Biological Samples Processing • Biological Samples Storage • Biological Samples Shipment • Biological Samples Destruction
Data Collection and Handling	• Source Records • Case Report Forms • Source Data Review / Source Data Verification • Computerised Systems
Monitoring	• Monitor Selection • Monitoring Plan • Monitoring Procedures • Investigator Site Monitoring
Deviation / Non-compliances	• Deviations / Non-compliances • Serious Breaches • Urgent Safety Measures
Trial Suspension / Termination / Completion	• Management of Trial Participants • Notifications
Essential Records	• Essential Records Access • Management of Essential Records • Essential Records Retention

5.2. Scope of Sponsor Inspections

The scope of Sponsor Inspections may include the following, as summarised in Table 2.

Table 2: Scope of Sponsor Inspections

Main category	Sub-category (where applicable)
Organisation and Personnel	• Organisation • Resources • Allocation of Activities • Qualification and Training
Trial Design	NA
Service Providers	• Selection of Service Providers • Agreements with Service Providers
Investigator Selection	• Selection of Investigators • Agreements with Investigators • Insurance / Indemnification / Compensation
Institutional Review Board (IRB) Submissions	• Initial IRB Application • Amendments • Continuing Reviews
Regulatory Authority Submissions	• Initial HSA Application • Clinical Research Material Notification • Substantial Amendments • Trial Status Reports
Sponsor Oversight	• Trial Oversight • Oversight of Investigators • Oversight of Service providers • Oversight of Trial Committees
Quality Management	• Risk Identification • Risk Evaluation • Risk Control • Risk Communication • Risk Review • Risk Reporting
Quality Assurance and Quality Control	• Quality Assurance • Quality Control
Investigational Product (IP) Management	• IP Information • IP Manufacturing

Main category	Sub-category (where applicable)
	• IP Labelling • IP Instructions • IP Supply and Handling
Safety Assessment and Reporting	• Sponsor Review of Safety Information • Safety Reporting
Data Collection and Handling	• Data Life Cycle • Computerised Systems
Monitoring	• Monitor Selection • Monitoring Plan • Monitoring Procedures • Investigator Site Monitoring • Centralised Monitoring
Deviations / Non-compliances	• Deviations / Non-compliances • Serious Breaches • Urgent Safety Measures
Trial Suspension / Termination / Completion	• Management of Trial Participants • Notifications
Essential Records	• Essential Records Access • Management of Essential Records • Essential Records Retention

6. GCP INSPECTION CRITERIA

Compliance to the following will be determined during GCP Inspections:

(i) Protocol

(ii) Applicable clinical trial and clinical research material regulations*

(iii) ICH E6 Good Clinical Practice Guideline (ICH E6 GCP)

(iv) Applicable Standard Operating Procedures (SOPs) for clinical trials

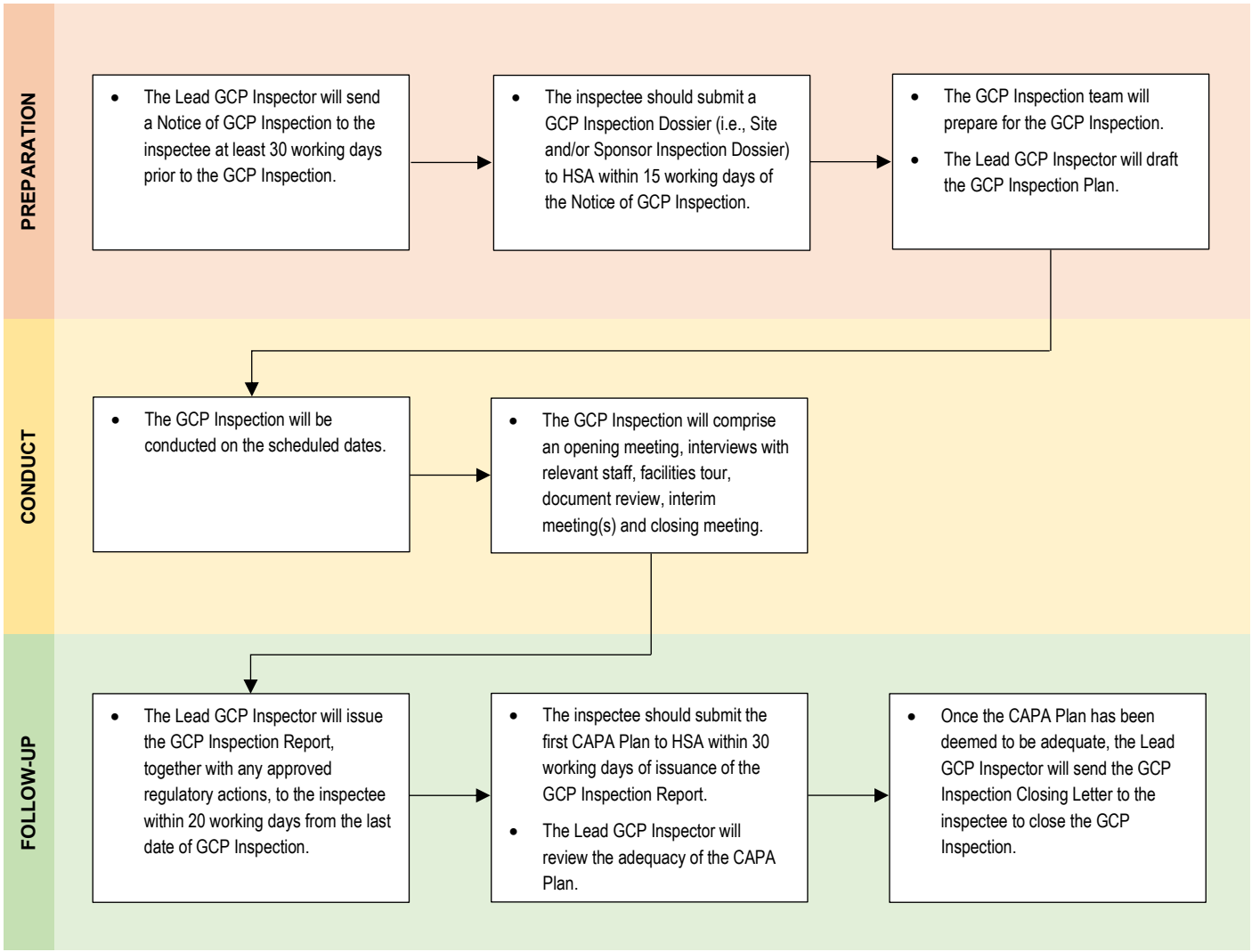
** Examples:*

Health Products (Clinical Trials) Regulations, Medicines (Clinical Trials) Regulations, Health Products (Clinical Research Materials) Regulations, Medicines (Medicinal Products as Clinical Research Materials) Regulations, Health Products (Medical Devices) Regulations

7. GCP INSPECTION PROCESS

The GCP Inspection Process for a routine GCP Inspection is summarised in the flowchart below:

Figure 1. GCP Inspection Process for a routine GCP Inspection



8. GCP INSPECTION PREPARATION

8.1. Notice of GCP Inspection

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

8.2. GCP Inspection Dossier

The inspectee should submit a GCP Inspection Dossier (i.e., Site and/or Sponsor Inspection Dossier) to HSA within 15 working days of the Notice of GCP Inspection, along with relevant essential records.

8.3. Direct access to source records

The inspectee should ensure that direct access* to the participants' source records, including Electronic Medical Records (EMR), is provided to the GCP Inspectors during the conduct of the GCP Inspection. It is important to note that direct access is not synonymous with over-the-shoulder access or provision of printed EMR.

**In accordance with applicable regulations and ICH E6 GCP Guideline,*

(i) Direct access is defined as granting permission to examine, analyse and verify records that are important to evaluation of a clinical trial.

(ii) Direct access to source records is required for trial-related monitoring and audits by sponsors, reviews by the Institutional Review Boards (IRBs), and GCP inspections by Regulatory Authorities to examine, analyse and verify that:

- *a) The rights, safety and well-being of participants are protected;*
- *b) The integrity of the trial data is assured; and*
- *c) The clinical trial is conducted in compliance with the protocol, and applicable regulations, GCP and standard operating procedures (SOPs).*

(iii) By agreeing *to participate in the clinical trial, the participants or their legal representatives have consented to grant direct access to source records to the Monitor, Auditor, IRB and Regulatory Authority.*

(iv) It is the Principal Investigator's responsibility to:

a) Ensure that informed consent materials and informed consent discussion inform the participants or their legal representatives (where applicable) about allowing direct access to source records, based on the understanding that the confidentiality of the participants' medical records will be safeguarded; and direct access is limited for the purpose of reviewing trial activities and/or reviewing or verifying data and records by the regulatory authorities, the sponsor's representatives (e.g., monitors or auditors), and the IRB(s).

b) Provide direct access to all trial-related records for monitoring, audits, IRB reviews and GCP Inspections; and

c) Ensure that the personal data (e.g., NRIC for account creation) of the GCP Inspectors are protected.

(v) It is the sponsor's responsibility to ensure that:

a) Obtain agreement from the investigator / institution and where applicable, service provider, to permit monitoring and audits by sponsors, inspections by regulatory authorities, and reviews by IRB, including providing direct access and facilities of the investigator site and service providers.

b) Ensure that direct access is specified in the protocol or documented agreement that the investigator(s)/institution(s) provide direct access to source records for monitoring, audits, IRB review and GCP Inspections.

c) Ensure that participants have consented to direct access to source records for monitoring, audits, IRB review and GCP Inspections.

(vi) The GCP Inspectors will take reasonable precautions within the constraints of the applicable regulatory requirements to maintain confidentiality of the participants' identities and their data and the sponsor's proprietary information. On this note, it will not be required for the GCP Inspectors to sign a separate Non-Disclosure Agreement (NDA) or Confidentiality Disclosure Agreement (CDA) for direct access.

8.4. Direct access to other trial-related records

The inspectee should provide direct access to the GCP Inspectors for the following trial-related records, where applicable, from submission of the GCP Inspection Dossier to the receipt of the GCP Inspection Closing Letter:

(i) Data Acquisition Tools (e.g., Case Report Forms / CRFs, Interactive Response Technologies / IRTs, Clinical Outcome Assessments / COAs, including Patient Reported Outcomes / PROs and wearable devices, irrespective of media used);

(ii) Investigator Site File (ISF);

(iii) Trial Master File (TMF); and

(iv) Standard Operating Procedures

9. GCP INSPECTION CONDUCT

9.1. Opening Meeting

The GCP Inspection will start with an Opening Meeting, where the GCP Inspectors will share about the GCP Compliance Inspection framework, confirm the agenda (including interim and closing meetings), the availability of resources, facilities and essential records, records access, and matters relating to confidentiality.

The inspectee would be required to present an overview of the trial conduct, in accordance with the scope of the GCP inspection specified in the Notice of GCP Inspection.

9.2. Interviews with relevant staff

During the GCP Inspection, the GCP Inspectors will conduct interviews with the relevant staff.

For Site Inspections, the PI, investigator site staff (e.g., Clinical Research Coordinator, Pharmacist etc.) and Monitor would usually be interviewed.

For Sponsor Inspections, the local sponsor and the Subject Matter Experts responsible for the scope of the GCP Inspection would usually be interviewed. These interview sessions will usually comprise a presentation by the Subject Matter Expert, followed by a question-and-answer session.

9.3. Visit to Facilities

The GCP Inspectors may visit facilities used to conduct the clinical trial being inspected.

9.4. Document Review

The GCP Inspectors will review essential records pertaining to the clinical trial being inspected.

9.5. Interim Meeting

An interim meeting may be conducted during the GCP Inspection to discuss observations noted from the GCP Inspection and provide the inspectee with an opportunity to resolve the observations during the GCP Inspection, where possible.

9.6. Closing Meeting

At the end of the GCP Inspection, there will be a Closing Meeting where the GCP Inspectors will review the classification of GCP inspection findings, discuss the observations noted from the GCP Inspection, and timelines for GCP Inspection Report and Corrective Action and Preventive Action (CAPA) Plan. The inspectee will be given an opportunity to provide clarifications to the observations.

9.7. GCP Inspection Follow-up

9.7.1. Classification of GCP Inspection Findings

The GCP Inspection Findings will be classified as critical, major or other.

(i) **Critical:** Conditions, practices or processes that adversely affect the rights, safety or well-being of the participants, and/or the quality and integrity of data. They may also include a pattern of findings classified as major. Critical findings are considered unacceptable.

(ii) **Major:** Conditions, practices or processes that might adversely affect the rights, safety or well-being of the participants, and/or the quality and integrity of data. Major findings are serious deficiencies and may also include a systematic pattern of other findings that collectively constitute a significant concern.

(iii) **Other:** Conditions, practices or processes that would not be expected to adversely affect the rights, safety or well-being of the participants, and/or the quality and integrity of data.

(iv) **Comments:** The observations might lead to suggestions on how to improve quality or reduce the potential for a deviation or noncompliance from occurring in the future.

9.7.2. Considerations for classification of GCP Inspection Findings

The impact on the goals of GCP, frequency of occurrence, and whether any corrective actions and preventive actions had been taken to effectively address the observations will be considered in the classification of GCP Inspection Findings.

9.7.3. GCP Inspection Report

Once the GCP Inspection has been completed, the GCP Inspection Report will be sent to the inspectee within 20 working days from the last date of the GCP Inspection. It should be noted that the factual matter contained in the GCP Inspection Report relates to observations noted during the GCP Inspection.

9.7.4. Corrective Action and Preventive Action Plan

The inspectee should submit the first Corrective Action and Preventive Action (CAPA) Plan to HSA within 30 working days of issuance of the GCP Inspection Report to address any critical, major or other GCP inspection findings.

The inspectee should ensure that the CAPA Plan is resolved within the stipulated timelines.

9.7.5. GCP Inspection Closure

Once the CAPA Plan is deemed to be adequate, the GCP Inspector will send a GCP Inspection Closing Letter. It is important to note that the GCP Inspection Closing Letter should not be taken as implying a satisfactory state of affairs in documentation, premises, equipment, personnel or procedures not examined during the inspection.

The inspectee should proceed to terminate access to all computerised systems for the GCP Inspectors thereafter.

10. REMOTE / HYBRID GCP INSPECTIONS

10.1. Overview

GCP inspections are typically conducted on-site. However, there may be circumstances in which a GCP Inspection or some aspects of a GCP Inspection may be conducted remotely.

A GCP Inspection that is conducted both on-site and remotely is considered a hybrid GCP Inspection.

The same objectives, scope and criteria for on-site GCP inspections apply to remote or hybrid GCP Inspections.

The procedures for remote or hybrid GCP Inspections are similar to on-site GCP Inspections, except that for remote GCP inspections, meetings, interviews and review of essential records may be conducted remotely.

10.2. Considerations for remote / hybrid approaches

The considerations for remote / hybrid GCP Inspections may include the following:

(i) Investigator site visit restrictions in the context of a public health emergency;

(ii) Differing time zones of parties involved in the GCP inspection;

(iii) Scope and objectives of the inspection;

(iv) Complexity of the trial-related activities being assessed;

(v) Operational feasibility of a remote / hybrid GCP inspection;

(vi) 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.

10.3. GCP inspection activities that may be conducted remotely

In general, the following GCP Inspection activities may be conducted remotely:

(i) Meetings;

(ii) Interviews; and/or

(iii) Review of essential records that are made accessible remotely via computerised systems, in compliance with applicable data governance policies.

10.4. Logistical arrangements

The inspectee should ensure the following in order to facilitate the smooth running of the remote / hybrid GCP Inspection, where applicable:

(i) All required attendees are able to participate in the remote / hybrid GCP Inspection, in accordance with the GCP Inspection Agenda;

(ii) Remote access is provided to the GCP Inspectors for the computerised systems used for the clinical (e.g. Investigator Site Files, Trial Master Files, Case Report Forms, Standard Operating Procedures etc.) from GCP Inspection notice to closure;

(iii) 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;

(iv) A secure file sharing portal is established for document sharing, with downloading functions enabled for the GCP Inspectors; and

(v) In situations where the inspectee is unable to use the proposed video conferencing software, the inspectee should propose using 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.

10.5. Duration of remote / hybrid GCP inspection

The duration of the remote / hybrid GCP inspection may be adjusted, depending on the logistical arrangements.

11. REFERENCES

(i) Health Products (Clinical Trials) Regulations

(ii) Medicines (Clinical Trials) Regulations

(iii) ICH E6 (R3) Good Clinical Practice (GCP) Guideline

HEALTH SCIENCES AUTHORITY

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