

HEALTH  
SCIENCES  
AUTHORITY

REGULATORY GUIDANCE

01 MAR 2021

**CLINICAL TRIALS GUIDANCE**  
**GUIDANCE ON GCP COMPLIANCE INSPECTION**  
**FRAMEWORK**

GN-IOCTB-11 Rev. No. 002



## **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.

## **CONTACT INFORMATION**

For further information, please contact:

Innovation Office & Clinical Trials Branch

Health Products Regulation Group

Health Sciences Authority

11 Biopolis Way, #11-01, Helios

Singapore 138667

Email: [HSA\\_CT@hsa.gov.sg](mailto:HSA_CT@hsa.gov.sg)

Website: [www.hsa.gov.sg](http://www.hsa.gov.sg)

**REVISION HISTORY**Guidance Version (Version Date)

GN-CTB-3-001A-001 (02 May 2017)

GN-IOCTB-11 Rev. No. 002 (01 Mar 2021)

**SUMMARY OF AMENDMENTS**

- Added a new category of health products, i.e., Cell, Tissue and Gene Therapy Products (CTGTPs), that is regulated under the Health Products Act
- Amended the term “subjects” to “trial participants”

---

**TABLE OF CONTENTS**

<b>1. INTRODUCTION .....</b>	<b>6</b>
1.1. Purpose .....	6
1.2. Background .....	6
1.3. Scope .....	6
1.4. Definitions.....	7
<b>2. OBJECTIVES OF GCP INSPECTIONS .....</b>	<b>7</b>
2.1. Objectives of Protocol-specific GCP Inspections.....	7
2.2. Objectives of Systems GCP Inspections .....	7
<b>3. GCP INSPECTION CRITERIA .....</b>	<b>8</b>
<b>4. TYPES OF GCP INSPECTIONS .....</b>	<b>8</b>
4.1. Routine GCP Inspections .....	8
4.2. Triggered GCP Inspections .....	9
4.3. Pre-marketing approval application GCP Inspections.....	9
<b>5. TYPES OF INSPECTEES.....</b>	<b>9</b>
<b>6. GCP INSPECTION PROCESS.....</b>	<b>9</b>
<b>7. GCP INSPECTION PREPARATION .....</b>	<b>10</b>
7.1. Notice of GCP Inspection .....	10
7.2. GCP Inspection Dossier .....	10
7.3. GCP Inspection Preparation Checklist.....	10
<b>8. GCP INSPECTION CONDUCT .....</b>	<b>10</b>
8.1. Opening Meeting .....	10
8.2. Interviews with Study Staff.....	10
8.3. Visit to Site Facilities.....	11
8.4. Document Review.....	11

---

8.5. Closing Meeting .....	11
8.6. GCP Inspection Follow-up .....	11
8.6.1. Grading of GCP Inspection Findings .....	11
8.6.2. GCP Inspection Report.....	12
8.6.3. Corrective Action and Preventive Action Plan .....	12
8.6.4. GCP Inspection Closure .....	12
<b>9. REFERENCES .....</b>	<b>12</b>

## 1. INTRODUCTION

### 1.1. Purpose

The purpose of this document is to provide guidance to the industry on the overview of the GCP 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 (R2) Good Clinical Practice (GCP) Guidelines 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<sup>1</sup> and Class 2 Cell, Tissue and Gene Therapy Products (CTGTPs)<sup>1,2</sup> that are subject to the requirements for a Clinical Trial Authorisation (CTA) or a Clinical Trial Notification (CTN);
- (ii) Clinical trials of Medicinal Products<sup>3</sup> that are subject to the requirements of a Clinical Trial Certificate (CTC).

---

<sup>1</sup> Therapeutic Product and CTGTP are defined in the First Schedule to the Health Products Act.

<sup>2</sup> 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.

<sup>3</sup> Medicinal Product is defined in the Medicines Act.

### **1.4. Definitions**

Inspections are defined by the ICH E6 GCP 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 located at the site of the trial, at the sponsor's and/or contract research organisation's (CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority(ies).

## **2. OBJECTIVES OF GCP INSPECTIONS**

GCP Inspections may either be protocol-specific or systems. Examples of clinical trial systems that may be inspected include informed consent, investigational products, pharmacovigilance, biological samples, monitoring etc.

### **2.1. Objectives of Protocol-specific 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.

### **2.2. Objectives of Systems GCP Inspections**

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

### 3. GCP INSPECTION CRITERIA

Compliance to the following standards will be determined during GCP Inspections:

#### Prior to 1 Nov 2016

- (i) Protocol
- (ii) Medicines (Clinical Trials) Regulations
- (iii) Singapore Guideline for Good Clinical Practice Guidelines (SGGCP)
- (iv) Applicable Sponsor / Contract Research Organization (CRO) / Site Standard Operating Procedures (SOPs) for clinical trials

#### From 1 Nov 2016

- (i) Protocol
- (ii) Applicable clinical trial and clinical research material regulations\*
- (iii) ICH E6 (R2) Good Clinical Practice Guidelines (ICH E6 (R2) GCP)
- (iv) Applicable Sponsor / Contract Research Organization (CRO) / Site 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*

### 4. TYPES OF GCP INSPECTIONS

GCP Inspections can either be routine, triggered or conducted in response to a pre-marketing approval application.

#### **4.1. Routine GCP Inspections**

Routine GCP Inspections are done announced and apply to ongoing clinical trials.



## 4.2. Triggered GCP Inspections

Triggered GCP Inspections may be triggered as a result of requests or complaints or reports to HSA on suspected violations of the regulations. Such types of inspections may be done announced and apply to ongoing or completed clinical trials.

## 4.3. Pre-marketing approval application GCP Inspections

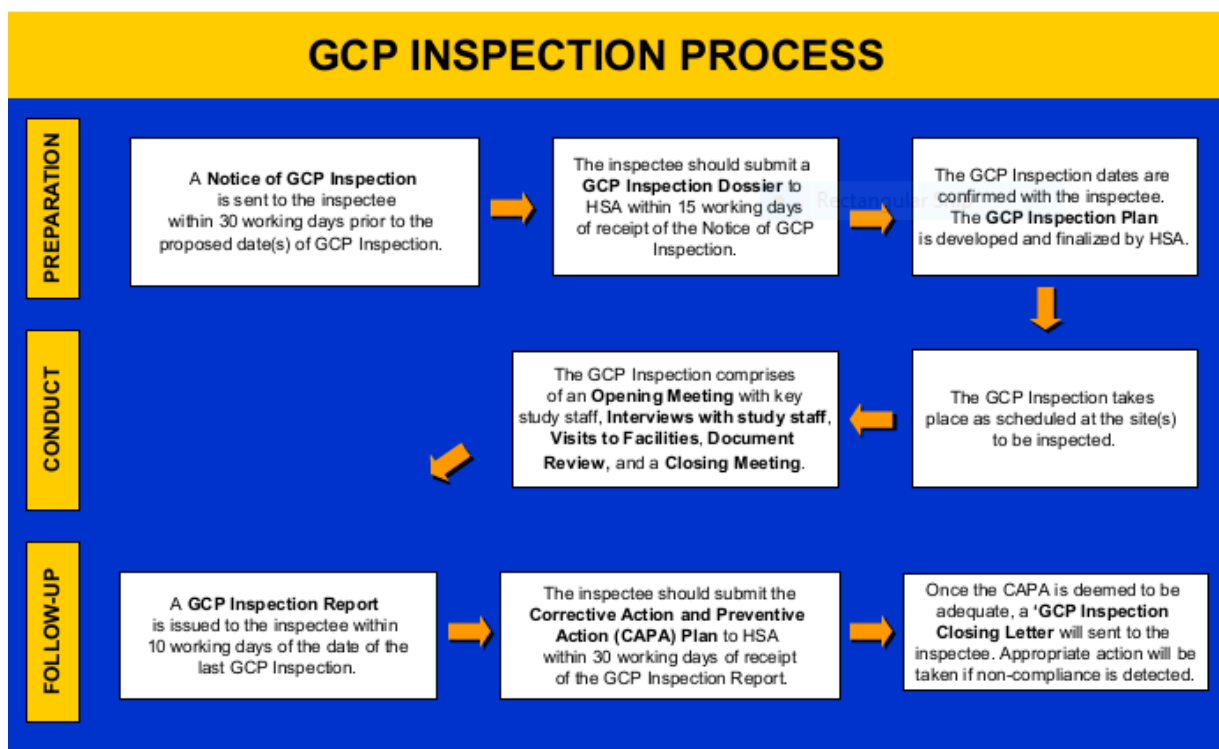
Pre-marketing approval application GCP inspections are usually done announced and apply to completed clinical trials.

## 5. TYPES OF INSPECTEES

The inspectees in a GCP Inspection may either be the Principal Investigator and/or the Sponsor.

## 6. GCP INSPECTION PROCESS

The GCP Inspection Process is summarized in the flowchart below:



## **7. GCP INSPECTION PREPARATION**

### **7.1. Notice of GCP Inspection**

A Notice of GCP Inspection will be sent to the inspectee within 30 working days prior to the proposed date(s) of the GCP Inspection.

### **7.2. GCP Inspection Dossier**

The inspectee will be required to submit a GCP Inspection Dossier to HSA within 15 working days of receipt of the Notice of GCP Inspection, along with relevant essential documents.

### **7.3. GCP Inspection Preparation Checklist**

The inspectee will be provided with a GCP Inspection Preparation Checklist to help the site prepare for the upcoming inspection.

## **8. GCP INSPECTION CONDUCT**

### **8.1. Opening Meeting**

The GCP Inspection will start with an Opening Meeting, where the Compliance Inspectors will explain the GCP Compliance Inspection framework; confirm the agenda; and also confirm that the resources, essential documents and facilities required for the GCP Inspection are available.

The inspectee would be required to present a general overview of the clinical trial at this meeting. Information pertaining to trial participant recruitment, informed consent process, investigational product management, safety reporting, biological sample handling may be included.

### **8.2. Interviews with Study Staff**

During the GCP Inspection, the Compliance Inspectors will interview study staff to determine how the clinical trial is conducted, and review essential documents pertaining to the clinical trial being inspected. Questions relating to study staff,

Institutional Review Board (IRB), Regulatory Authority, Investigator Site Files, Trial Participant Recruitment, Informed Consent, Investigational Product management, Safety Reporting, Biological Samples handling, Source Documents, Case Report Forms, record keeping, monitoring etc. may be asked.

### **8.3. Visit to Site Facilities**

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

### **8.4. Document Review**

The Compliance Inspectors may review essential documents pertaining to study staff, Institutional Review Board (IRB), Regulatory Authority, Investigator Site Files, Trial Participant Recruitment, Informed Consent, Investigational Product management, Safety Reporting, Biological Samples handling, Source Documents, Case Report Forms, record keeping, monitoring etc.

### **8.5. Closing Meeting**

At the end of the GCP Inspection, there will be a Closing Meeting where the Compliance Inspectors will present the GCP Inspection Findings and gradings to the inspectee; ensure that results of the GCP Inspection are clearly understood and acknowledged by the inspectee; and provide an appropriate time frame for the inspectee to present the Corrective Action and Preventive Action (CAPA) Plan.

### **8.6. GCP Inspection Follow-up**

#### **8.6.1. Grading of GCP Inspection Findings**

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

- (i) **Critical:** Conditions, practices or processes that adversely affect the rights, safety or well-being of the trial participants and/or the quality and integrity of data

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

#### **8.6.2. GCP Inspection Report**

Once the GCP Inspection has been completed, it will be sent to the inspectee within 10 working days from the date of the last GCP Inspection. It should be noted that the factual matter contained in the GCP Inspection Report relates to observations noted during the GCP Inspection.

#### **8.6.3. Corrective Action and Preventive Action Plan**

The inspectee should submit a Corrective Action and Preventive Action (CAPA) Plan to HSA within 30 working days of receipt of the GCP Inspection Report.

#### **8.6.4. GCP Inspection Closure**

Once the CAPA is deemed to be adequate, the Compliance 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.

## **9. REFERENCES**

- (i) Health Products (Clinical Trials) Regulations
- (ii) Medicines (Clinical Trials) Regulations
- (iii) ICH E6 (R2) Good Clinical Practice (GCP) Guidelines

# HEALTH SCIENCES AUTHORITY

Health Products Regulation Group  
Blood Services Group  
Applied Sciences Group

[www.hsa.gov.sg](http://www.hsa.gov.sg)

## **CONTACT INFORMATION:**

Innovation Office & Clinical Trials Branch  
Health Products Regulation Group  
Health Sciences Authority

11 Biopolis Way, #11-03, Helios

Singapore 138667

Email: [HSA\\_CT@hsa.gov.sg](mailto:HSA_CT@hsa.gov.sg)

Website: [www.hsa.gov.sg](http://www.hsa.gov.sg)

