

HEALTH
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REGULATORY GUIDANCE

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CLINICAL TRIALS GUIDANCE

ALTERNATIVE MEASURES FOR
INVESTIGATIONAL PRODUCT MANAGEMENT FOR
CLINICAL TRIALS OF LOCALLY REGISTERED
PRODUCTS

GN-IOCTB-08 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.

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REVISION HISTORY

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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

1. INTRODUCTION	5
1.1. Purpose	5
1.2. Background	5
1.3. Scope	5
2. IP RECEIPT.....	6
3. IP STORAGE.....	7
4. IP DISPENSING AND ACCOUNTABILITY.....	8
5. IP DESTRUCTION	8
6. REFERENCES	9

1. INTRODUCTION

1.1. Purpose

The purpose of this guidance is to provide alternative measures for Investigational Product (IP) management for clinical trials of locally registered therapeutic products¹ or locally registered Class 2 cell, tissue or gene therapy products (CTGTPs)^{1,2}, whereby the hospital pharmacy is used for IP management.

1.2. Background

Investigational Product (IP) management remains a perennial stumbling block for sponsors and investigators, resulting in numerous GCP Inspection Findings. The objective of this guideline is to help sponsors and investigators overcome the challenges in IP management, without compromising the principles of Good Clinical Practice (GCP).

1.3. Scope

1.3.1. This guidance applies to clinical trials where:

- (a) a Clinical Trial Certificate (CTC), Clinical Trial Authorisation (CTA) or Acceptance of Clinical Trial Notification (CTN) has been issued by HSA;
- (b) the investigational product is a locally registered therapeutic product or locally registered Class 2 CTGTP; and
- (c) the hospital pharmacy is used for IP management.

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.

1.3.2. These alternative measures will only be applicable to IP receipt, storage, dispensing, accountability, return and destruction.

1.3.3. These alternative measures will not be applicable to the need to maintain Standard Operating Procedures for IP Management, IP Repackaging, and IP Labelling.

2. IP RECEIPT

2.1. The investigator should maintain records of the delivery of the IP to the site and the inventory at the site (ICH GCP Sections 2.12, 4.6.3, 8.2.14, 8.2.15, 8.3.8).

2.1.1. Thus, the investigator should maintain IP shipment receipts and IP inventory logs.

2.2. Alternative measures for IP Receipt

2.2.1. The IP is usually sourced from the hospital pharmacy stock or from pharmaceutical companies.

(a) IP sourced from hospital pharmacy stock

IP Inventory Logs may not be required to be maintained if the IP is sourced from the hospital pharmacy stock. If the hospital pharmacy does not have a system of tracking the batch number and expiry date of the IP, this information may be tracked on the IP Dispensing Log. It would be recommended to file copy of the product insert of the IP in the Investigator Site File.

(b) IP sourced from pharmaceutical company

IP Inventory Logs should be maintained if the IP is sourced from a pharmaceutical company. It would be recommended to file the IP

Shipping Records, IP Receipts, IP Inventory Logs and Product Insert of the IP in the Investigator Site File.

3. IP STORAGE

3.1. The investigator should ensure that the IP is stored as specified by the Sponsor and in accordance with applicable regulatory requirements (ICH GCP Sections 2.12, 4.6.4, 8.2.14).

3.1.1. Thus, the investigator should ensure that the IP is stored in an area where the access is secure and limited; and maintain IP Storage Temperature Records.

3.2. Alternative Measures for IP Storage

3.2.1. Separate IP Storage Temperature Records may not be required if the existing hospital pharmacy system for temperature monitoring is utilized. It would be recommended to ensure that the temperature monitoring system is calibrated and maintained regularly; an alarm system is available for temperature excursions; and a copy of the temperature monitoring records is filed in the Investigator Site File.

3.2.2. If the hospital pharmacy does not monitor the storage temperature of medicinal products stored at ambient temperatures, it would be recommended that an alarm system should be available to detect temperature excursions.

4. IP DISPENSING AND ACCOUNTABILITY

4.1. The investigator should maintain records of the use of the IP by each trial participant; that the trial participants were provided the doses specific by the protocol; and reconcile all IP received from the sponsor (ICH GCP 2.12, 4.6.3, 4.6.5, 4.6.6, 8.2.14, 8.3.23, 8.4.1).

4.1.1. Thus, the investigator should maintain IP Dispensing and Accountability Records.

4.2. Alternative Measures for IP Dispensing and Accountability

4.2.1. IP Dispensing and Accountability Logs may not be required if the protocol does not require the determination of compliance with the IP. It would be recommended to document the batch number and expiry date of the IP on the prescription or alternative document.

4.2.2. If Pharmacy Technicians or nurses are involved in IP dispensing or administration in accordance with routine clinical practice, a Pharmacist or Nurse Manager should be delegated to be a part of the study team; and the Pharmacy Technicians or nurses should be trained on the study protocol and perform IP dispensing or administration under active supervision by the Pharmacist or Nurse Manager. It would be recommended to file the training records in the Investigator Site File.

5. IP DESTRUCTION

5.1. The investigator should maintain records of return and/or destruction of the IP (ICH GCP 2.12, 4.6.3, 4.6.5, 4.6.6, 8.2.14, 8.4.2).

5.1.1. Thus, the investigator should maintain IP Return and/or Destruction Records.

5.2. Alternative Measures for IP Return and Destruction

5.2.1. IP Destruction Records may not be required if the existing hospital pharmacy system for destruction of pharmaceutical waste is utilized. It would be recommended to document and file the IP Returns in the Investigator Site File.

6. REFERENCES

- (i) Health Products (Clinical Trials) Regulations
- (ii) Medicines (Clinical Trials) Regulations
- (iii) Health Products (Clinical Research Materials) Regulations
- (iv) Medicines (Medicinal Products as Clinical Research Materials) Regulations
- (v) ICH E6 (R2) Good Clinical Practice (GCP) Guidelines

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