HEALTH SCIENCES AUTHORITY

REGULATORY GUIDANCE

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CLINICAL TRIALS GUIDANCE

CLINICAL RESEARCH MATERIALS

GN-CT-03 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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SUMMARY OF AMENDMENTS

- Administrative changes due to HSA re-organisation

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1. INTRODUCTION

1.1. Purpose

This document provides guidance to local manufacturers, importers and suppliers on the regulatory requirements relating to the import and supply of clinical research materials (CRM). Suppliers include importers, local manufacturers, wholesalers, sponsors, investigators and any persons who supply CRM.

Note: In this Guidance, the term **"Clinical Research Materials (CRM)"** is used to refer to any:

(a) **Therapeutic Product (TP), Cell, Tissue or Gene Therapy Product (CTGTP)** or placebo that meets the definition of "Clinical Research Material" under the *Health Products (Clinical Research Materials) Regulations;*

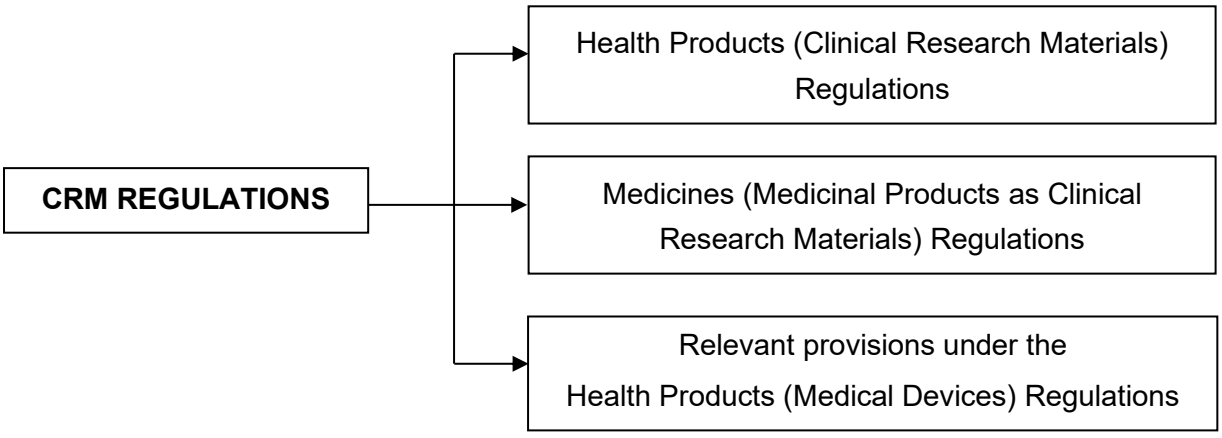
(b) **Medicinal Product (MP)** or placebo that meets the definition of "Clinical Research Material" under the *Medicines (Medicinal Products as Clinical Research Materials) Regulations;*

(c) **Medical Device (MD)** that is referred to in the *Health Products (Medical Devices) Regulations* as a medical device whose planned use is for a clinical purpose in any clinical research;

Please refer to Section 1.3.3 for more details on Clinical Research Materials.

The subsidiary legislation referenced above will be referred to in this Guidance as the **"CRM regulations"** (Figure 1).

Figure 1. Overview of Clinical Research Material (CRM) Regulations



1.2. Background

In 2016, the regulatory controls for therapeutic products[1] (e.g., pharmaceutical drugs and biologics) were transferred from the Medicines Act to the Health Products Act, and clinical trials of therapeutic products were regulated under the Health Products (Clinical Trials) Regulations.

At the same time, the CRM regulations were introduced to facilitate access to CRM for use in clinical research, by streamlining and simplifying the regulatory approach for the import and supply of therapeutic products (TPs), medicinal products (MPs) and medical devices (MDs) for use in clinical research, including clinical trials regulated under the Health Products (Clinical Trials) Regulations and Medicines (Clinical Trials) Regulations (referred to as "regulated clinical trials" in this guidance; see Section 1.3.1). The streamlined approach took the form of a simplified and harmonised regulatory notification system that allowed companies to submit a single notification to facilitate importation of multiple product types (e.g., TP and MD) for use in the same clinical trial.

In 2021, a new category of health products, i.e., cell, tissue and gene therapy products[1] (CTGTPs), was included in the First Schedule of the Health Products Act and regulated under the Act.

CTGTPs are risk-stratified into two classes as follows:

- Class 1 CTGTP[2] 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[2] means a CTGTP other than a Class 1 CTGTP.

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

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

In relation to CTGTPs, CRM means any of the following that is manufactured, imported or supplied for the purpose of being used in any clinical research by way of administration to a subject in accordance with the protocol for the research:

- a Class 2 CTGTP;
- a Class 1 CTGTP for which no notice has been submitted under regulation 4 [manufacturer notification], 7 [importer notification] or 10 [wholesaler notification] of the CTGTP Regulations to manufacture, import or supply by wholesale (as the case may be) a minimally manipulated CTGTP.

Class 1 CTGTP that is imported, manufactured or supplied by wholesale by known dealers (i.e., known manufacturer, known importer, or known wholesaler)[3] are not included in the definition of CTGTP CRM, as they can already be supplied under the CTGTP regulations.

1.2.1. Objectives of CRM Regulations

The key objectives of the CRM regulations include the following:

(a) To facilitate access to CRM;
(b) To require imported or locally manufactured CRM to be of sufficient quality;
(c) To restrict supply of imported or locally manufactured CRM to regulated clinical trials or other IRB-approved clinical research;
(d) To require product tracking and accountability of CRM through record-keeping;
(e) To require appropriate CRM labelling;
(f) To require reporting of unexpected serious adverse drug reactions (USADRs), or medical device adverse events related to the use of CRM; and

[3] "Known manufacturer" means a person who has given notice to the Authority under regulation 4 to manufacture a minimally manipulated CTGTP, until the notice is refused, withdrawn or cancelled;

"Known importer" means a person who has given notice to the Authority under regulation 7 to import a minimally manipulated CTGTP, until the notice is refused, withdrawn or cancelled;

"Known wholesaler" means a person who has given notice to the Authority under regulation 10 to supply by wholesale a minimally manipulated CTGTP, until the notice is refused, withdrawn or cancelled.

(g) To require reporting of CRM product defects

(h) To require disposal/export of imported or locally manufactured CRM after the research/trial ends; and

(i) In the case of a CTGTP CRM, to ensure traceability of the product from the donor or source to its use in patients and vice-versa.

1.3. Scope

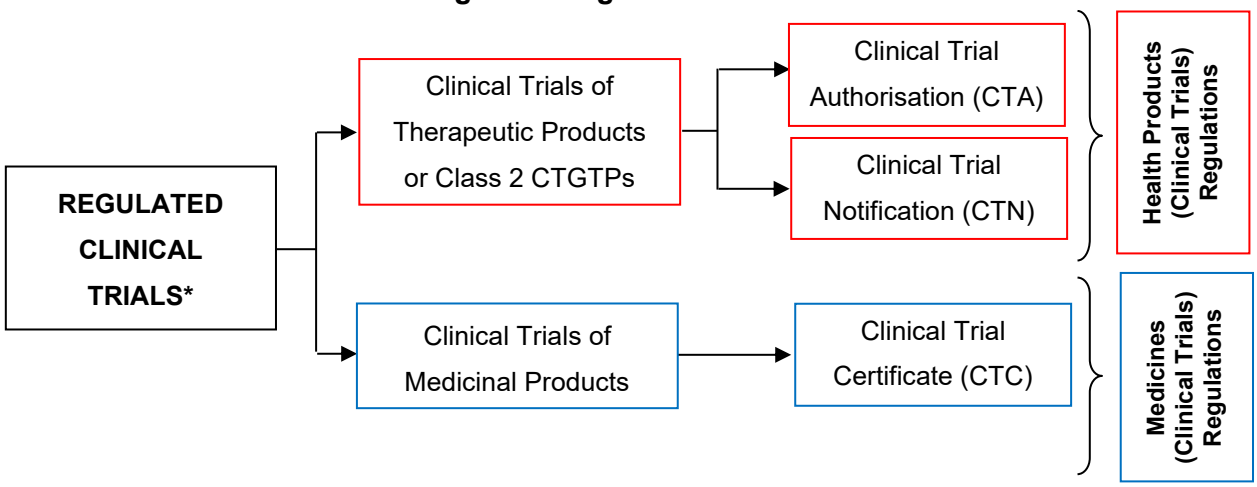
This guidance applies to importers, local manufacturers and suppliers of **CRM** (including importers, local manufacturers, wholesalers and sponsors) for use in **clinical research**, including **regulated clinical trials**.

1.3.1. Regulated Clinical Trial

Regulated clinical trial means a clinical trial that is regulated under the Health Products (Clinical Trials) Regulations or the Medicines (Clinical Trials) Regulations. In other words, a regulated clinical trial is one that requires a Clinical Trial Authorisation (CTA), Clinical Trial Notification (CTN) or Clinical Trial Certificate (CTC).

Regulated clinical trials are typically clinical trials of a therapeutic product (e.g., pharmaceutical drug or biologic), Class 2 CTGTP or medicinal product (e.g. complementary health product intended for treatment or prevention of disease), as shown in Figure 2.

Figure 2. Regulated clinical trials



* For more details on regulated clinical trials, please refer to the *Guidance on Determination of Whether a Clinical Trial Requires CTA, CTN or CTC*.

1.3.2. Clinical Research

Clinical research means any research involving human subjects. This is a broad collective term that comprises **both** the following (See Figure 3):

(a) Regulated clinical trials as outlined in Section 1.3.1; and

(b) Clinical research that is not regulated under the Health Products (Clinical Trials) Regulations or the Medicines (Clinical Trials) Regulations (referred to in this guidance as "other clinical research")

Examples of other clinical research include:

(i) observational clinical trials of therapeutic products, Class 2 CTGTPs or medicinal products;

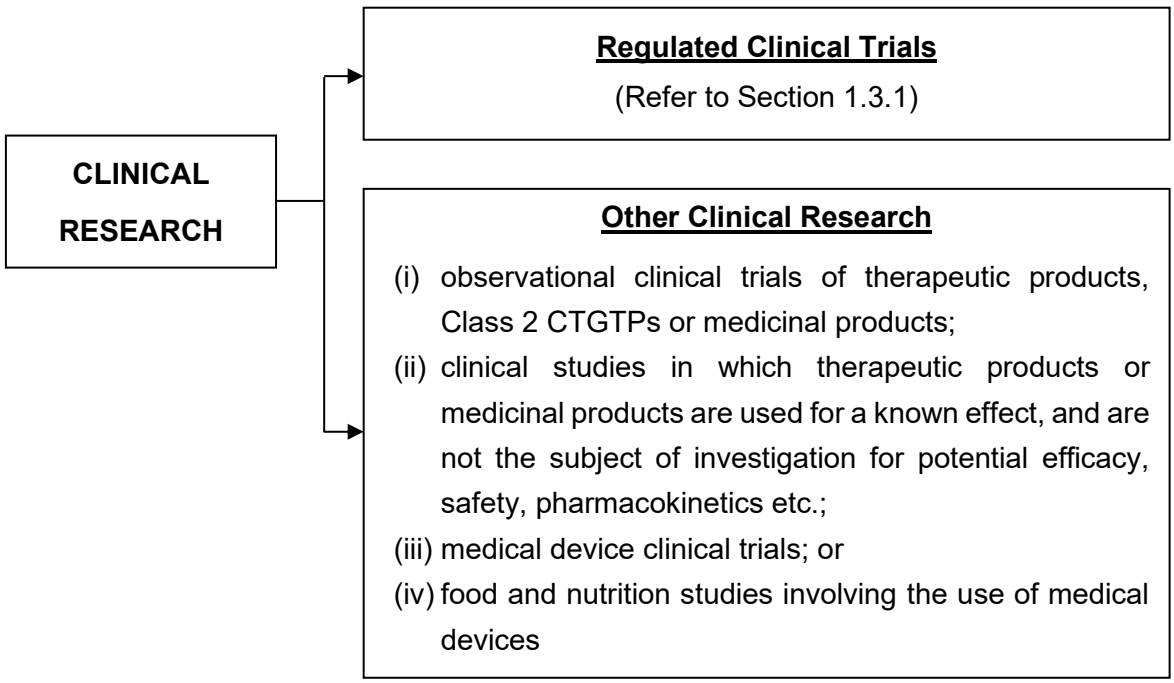
(ii) clinical studies in which therapeutic products or medicinal products are used for a known effect, and are not the subject of investigation for potential efficacy, safety, pharmacokinetics etc.;

(iii) medical device clinical trials; or

(iv) food and nutrition studies involving the use of medical devices.

Other clinical research may be subject to applicable requirements of the Human Biomedical Research Act.

Figure 3. Clinical research



1.3.3. Clinical Research Material (CRM)

CRM means any registered or unregistered TP, MP, MD, applicable CTGTP (refer to Section 1.2), or placebo, that is manufactured, imported or supplied for the purpose of being used in clinical research, by way of administration to a trial participant in accordance with the research protocol or for a clinical purpose.

CRM may be imported, locally manufactured or procured from local commercial sources.

Table 1 provides examples of research material or products that are not regulated under the CRM regulations.

Table 1: Categories or examples of research material or products that are <u>not</u> regulated under the CRM regulations

Category	Examples	Comments / additional notes
Research material that is not a TP, CTGTP, MP or MD	• Human tissue biopsy samples donated for use in laboratory research and not intended for clinical use • Stationery, plastic bags for general use, tablet computers	Since the research material is not a TP, CTGTP, MP or MD, and therefore not a CRM, the requirements of the Health Products Act, Medicines Act and CRM regulations are not applicable. As such, the importer will not require an *Importer's Licence* from HSA in order to import the research material. HSA also need not be notified of the import in accordance with the CRM regulations. If you are unsure as to whether the research material / product to be used is a TP, CTGTP, MP or MD, please submit a Health Products Classification Enquiry via HSA website.
Products excluded from the CRM regulations E.g., MP specified in the First Schedule of the Medicines (MP as CRM) Regulations 2016, Class 1 CTGTPs that are manufactured / imported / supplied by known manufacturers / importers / wholesalers	• Homeopathic medicine • Medicated oil and balm • Quasi-medicinal products • Traditional medicine • Herbal remedy • Raw materials used as ingredients in the preparation or manufacture of any medicinal product, e.g., active pharmaceutical ingredients, intermediates, excipients	The First Schedule of the Medicines (Medicinal Products as Clinical Research Materials) Regulations contains a list of medicinal products excluded from the CRM regulations. This list is aligned to the list of medicinal products exempted from product licence and dealers' licensing requirements. As such, an *Importer's Licence* will not be required under the Medicines Act. HSA also need not be notified of the import in accordance with the CRM regulations. However, if the active pharmaceutical ingredient contains, or is a substance that is listed as a poison under the Poisons Act, a *Form A Poisons licence* will be required.
TP, CTGTP, MP or MD that is intended for **non-clinical** purposes only (e.g., used in laboratory or animal research only and not administered or applied to humans).	• A TP that is imported or locally manufactured for toxicology tests in rats • A drug-coated coronary stent (MD) that is imported or locally manufactured for proof-of-concept studies in monkeys • Clinical trial kits containing TP that are imported for disposal or destruction in Singapore	As the TP, CTGTP, MP or MD is not administered to humans or not intended for a clinical purpose, they are not considered to be CRM. However, the import and supply of the product will be subject to applicable requirements of the Health Products Act, Medicines Act and/or related subsidiary legislation. For TP, companies not holding a valid *Importer's Licence* and are only importing TP for non-clinical purposes will require an *Importer's Licence for Restricted Activity(ies)*. For MD, please refer to *Special Access Routes* for medical devices on HSA website.

Category	Examples	Comments / additional notes
TP, MP or MD that is not intended for **local** clinical research use	• TP imported solely for export for use in regional clinical research (not including Singapore as a trial site) • TP that is locally manufactured for export only	Products that are imported solely for export or manufactured solely for export are not CRM. Therefore, the exceptions and requirements of the CRM regulations are not applicable. For TP, the import-for-export will be governed by the Health Products Act and the Health Products (Therapeutic Products) Regulations. Companies not holding a valid *Importer's Licence* and are only importing TP solely for export will require an *Importer's Licence for Restricted Activity(ies)*. For MD, please refer to *Special Access Routes* for medical devices on HSA website.
TP, MP that is used by participants in the clinical research, but not as an investigational or auxiliary CRM*	Registered TP/MP used as • pre-medication • rescue medication • treatment for trial-related adverse events • concomitant medication for co-morbidities	TP/MP that are not regulated as CRM (i.e., not investigational or auxiliary CRM) will be subject to controls under the Health Products Act, Health Products (Therapeutic Products) Regulations or Medicines Act instead.

* CRM includes both investigational CRM and auxiliary CRM:

- **Investigational CRM** means any CRM that is to be tested or used as a reference in any clinical research.
- **Auxiliary CRM** means any CRM that is used for the needs of any clinical research as described in the protocol, but not as the material to be tested or used as a reference in the research.

The following table provides examples of investigational CRM and auxiliary CRM.

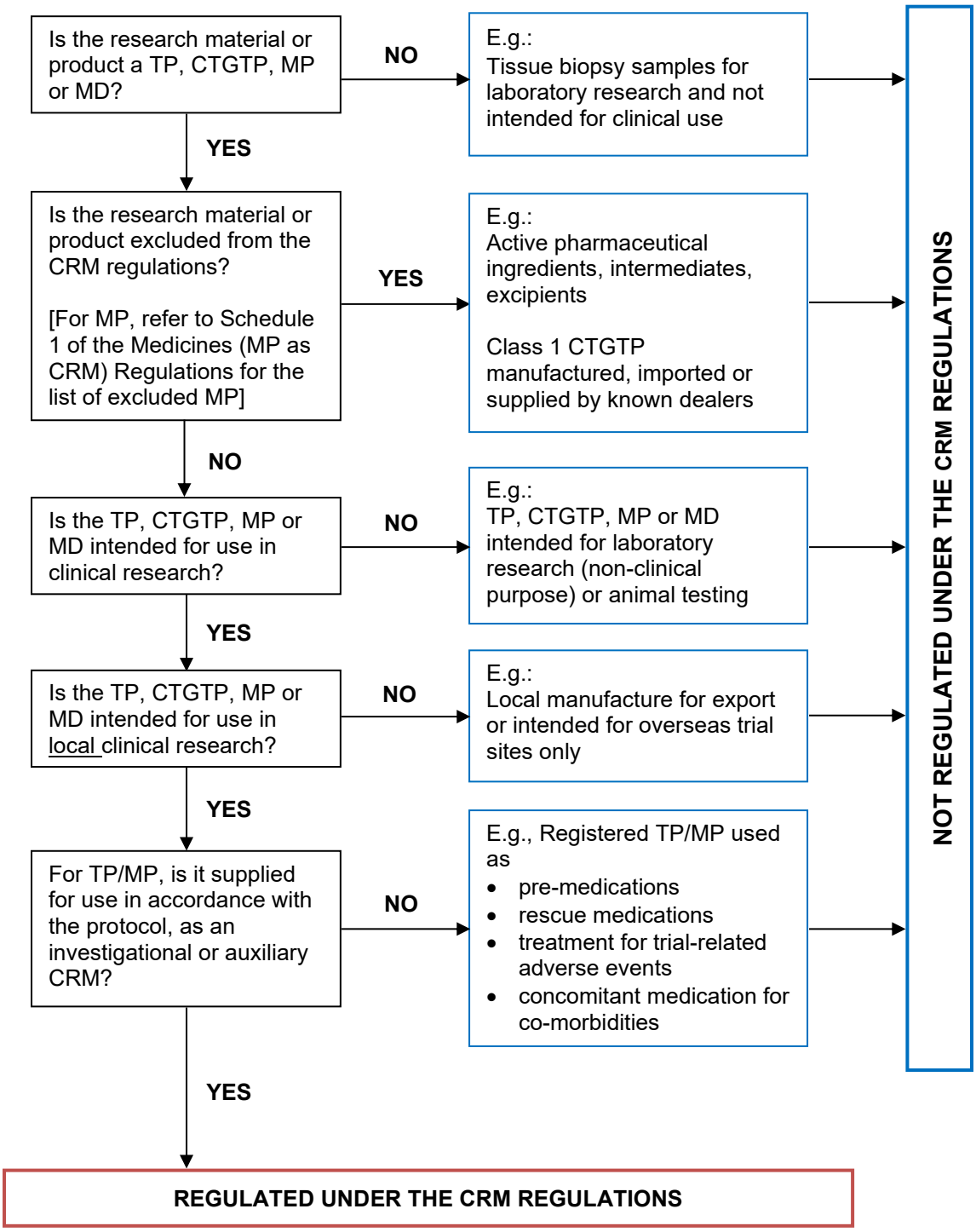
Examples of investigational CRM and auxiliary CRM

Purpose of CRM (TP/MP)	Type of CRM
Test	Investigational CRM
Reference (e.g., active comparator or placebo)	Investigational CRM
Background treatment or standard of care required by the protocol, which is administered for the study indication and relevant to the design of the study	Auxiliary CRM
Challenge agents	Auxiliary CRM
Rescue medications (unregistered)	Auxiliary CRM

Note: The following will not be regulated as CRM since they are typically used in accordance with standard of care: Registered TP/MP used as pre-medication, rescue medication, treatment for trial-related adverse events, concomitant medication for co-morbidities

Figure 4 shows a flowchart to determine if the research material or product is regulated under the CRM regulations.

Figure 4. Flowchart to determine if the research material or product is regulated under the CRM regulations



2. REGULATORY INTENT OF CRM REGULATIONS

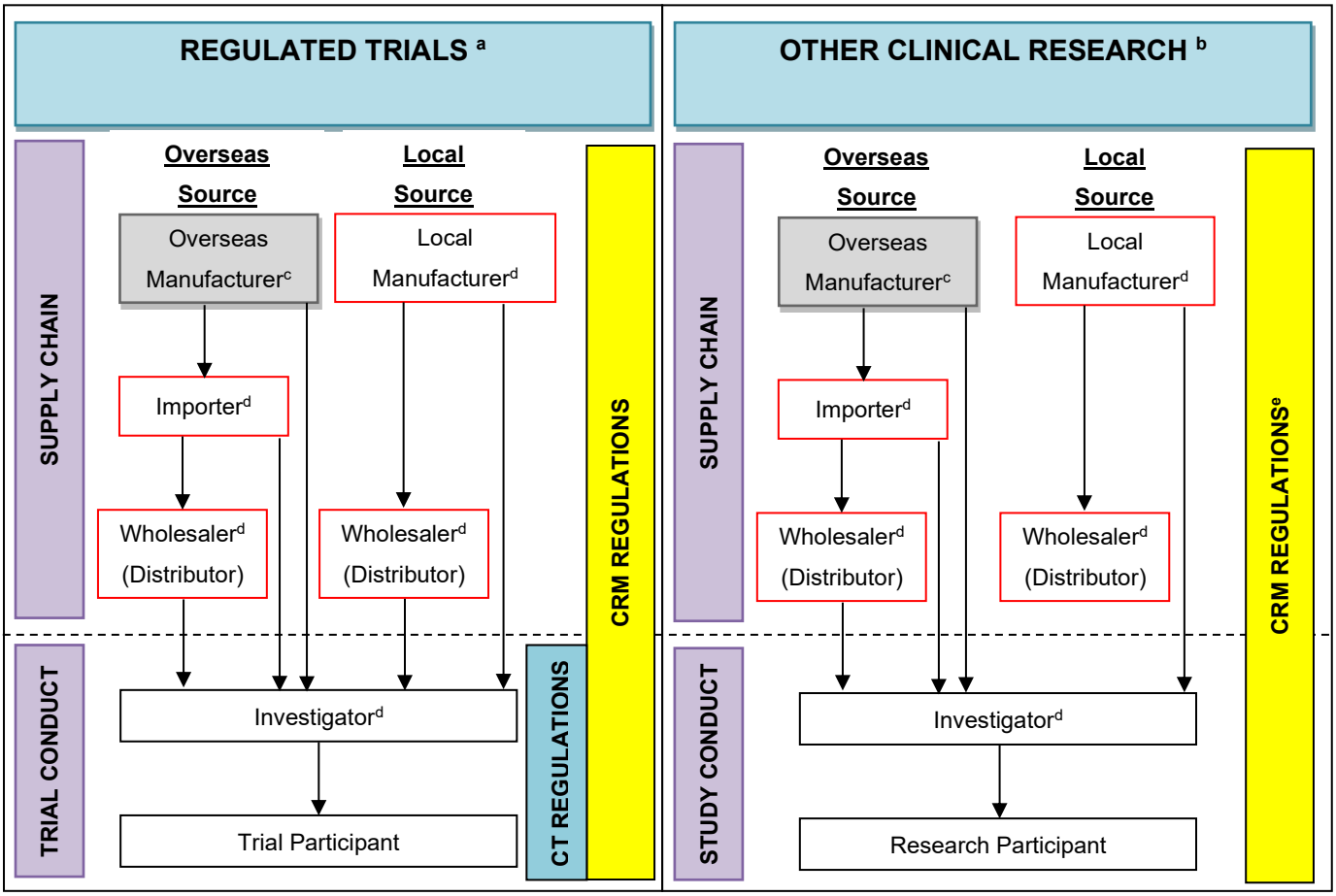
The clinical trial (CT) regulations and CRM regulations differ in their regulatory intent (Figure 5).

(a) The **CRM regulations** are intended to **regulate the product and dealers** (manufacturers, importers, suppliers) and to **safeguard the supply chain** relating to health products/medicinal products that are imported, locally manufactured or supplied for use in clinical research.

(b) The **CT regulations** are intended to **regulate the conduct of regulated clinical trials**, including the parties (e.g., sponsor, investigator) critical to ensuring that clinical trials are conducted in accordance with Good Clinical Practice.

Regardless of whether the clinical research is regulated under the CT regulations, the CRM regulations apply if a CRM is used in the clinical research in accordance with the research protocol.

Figure 5. Regulatory Intent of CRM regulations in relation to the CT regulations



(a) Regulated trials are clinical trials that are regulated under Health Products (Clinical Trials) Regulations or the Medicines (Clinical Trials) Regulations. These are subject to the requirements for a Clinical Trial Authorisation (CTA), Clinical Trial Notification (CTN) or Clinical Trial Certificate (CTC).

(b) Other clinical research include:
- (i) observational clinical trials of therapeutic products, Class 2 CTGTP or medicinal products
- (ii) clinical studies in which therapeutic products or medicinal products are used for a known effect, and are not the subject of investigation for potential efficacy, safety, pharmacokinetics etc.
- (iii) medical device clinical trials
- (iv) food and nutrition studies involving the use of medical devices

(c) Overseas manufacturers are not regulated under the CRM Regulations.

(d) Local manufacturers, importers and wholesalers (distributors) and investigators are suppliers who are regulated under the CRM Regulations. The local sponsor may be any of these parties.

(e) For other clinical research (see footnote b), the CRM Regulations serve to control the CRM product & its supply chain. Although some CRM controls (e.g., record-keeping, safety reporting) apply during the research, these are product-related controls. The conduct of the clinical research may be subject to other applicable requirements, for example, the Human Biomedical Research Act.

3. STRUCTURE OF THIS GUIDANCE

This Guidance is organised into two main sections:

SECTION 4

CRM NOTIFICATION PROCESS

- This section is relevant for importers of CRM, and local manufacturers supplying self-manufactured CRM, without the relevant dealers' licences (i.e., importer's or wholesaler's licence) that are otherwise required to import or supply the self-manufactured CRM.

- Sponsors should be aware of the CRM notification process, since
  - Sponsors of regulated clinical trials should submit the CTA/CTN/CTC application form that includes the CRM notification.
  - Sponsors of other clinical research may be required to endorse the CRM notification that is to be submitted by the importer or local manufacturer.

SECTION 5

DUTIES AND OBLIGATIONS OF IMPORTERS, LOCAL MANUFACTURERS AND SUPPLIERS OF CRM

- Section 5.1 provides guidance on the responsibilities relating to the import and supply of CRM other than a medical device CRM
- Section 5.2 provides guidance on the responsibilities relating to the import and supply of medical device as CRM

4. CRM NOTIFICATION PROCESS

This section applies to:

- **Importers intending to import CRM**
- **Local manufacturers intending to supply self-manufactured CRM**
- **Sponsors of regulated clinical trials or other clinical research for which the CRM will be imported or locally manufactured**

Under the Health Products Act, importers must not import health products (e.g., TP, MD, CTGTP) without a valid importer's licence or importer notification[4]. Similarly, wholesalers must not supply such health products except with a valid wholesaler's licence or wholesaler notification[4], and manufacturers must not manufacture and supply health products without a valid manufacturer's licence or manufacturer notification[4], and wholesaler's licence or wholesaler notification[4], respectively. Such health products must also not be supplied without product registration, or in the case of a Class 1 CTGTP, without product notification. Similar requirements for dealers' licensing apply to MP.

To facilitate access to CRM, the CRM regulations provide exceptions to the requirement for the various dealers' licences and product registration described above. This is on the condition that notice of import (by the importer) or supply (by the local manufacturer) is made to HSA prior to import of CRM, or supply of the CRM by the local manufacturer. This process of notifying HSA is referred to in this Guidance as "CRM notification".

[4] Manufacturers, importers and wholesalers of minimally manipulated CTGTP do not require dealers' licences but are required to notify HSA of their activities.

(a) What are the activities for which CRM notification would be applicable?

(i) Import of CRM

(ii) Supply of locally manufactured CRM by the manufacturer

Note:

- CRM notification is not applicable prior to the import of a registered/licensed CRM, or prior to the supply of a registered/licensed CRM by a local manufacturer, if the importer or local manufacturer has the relevant dealer's licence to import or supply the same product in the commercial setting.
- CRM notification is not applicable prior to import, or prior to supply of a locally manufactured Class 1 CTGTP, by known dealers[5].

(b) Who submits the CRM notification?

(i) Importer

(ii) Local manufacturer

Operationally, for regulated clinical trials, the sponsor submits the CRM notification on behalf of the importer or local manufacturer.

(c) When should CRM notification be submitted?

CRM notification should be submitted

(i) Prior to import of CRM or

(ii) Prior to supply of locally manufactured CRM

(d) How should CRM notification be made to HSA?

CRM notification should be made through the Pharmaceutical Regulatory Information System (PRISM).

[5] "Known dealers" refer to

- Known manufacturer: A person who has given notice to the Authority under regulation 4 to manufacture a minimally manipulated CTGTP until the notice is refused, withdrawn or cancelled;
- Known importer: A person who has given notice to the Authority under regulation 7 to import a minimally manipulated CTGTP until the notice is refused, withdrawn or cancelled;
- Known wholesaler: A person who has given notice to the Authority under regulation 10 to supply by wholesale a minimally manipulated CTGTP until the notice is refused, withdrawn or cancelled.

(e) What is the CRM notification process?

(i) The CRM notification process differs between regulated clinical trials and other clinical research.**For regulated clinical trials,** the CRM notification is made by the sponsor (on behalf of the importer or the local manufacturer)

(ii) **For other clinical research,** the CRM notification is made by the importer or the local manufacturer.

Table 2 summarises the differences in the CRM notification process between regulated clinical trials and other clinical research.

Table 2: Key Differences between the CRM Notification Process for Regulated Clinical Trials and Other Clinical Research

	Regulated clinical trial	Other clinical research
Drafter of the CRM notification form	Sponsor (on behalf of the importer or local manufacturer)	Importer or local manufacturer
Notification form (in PRISM)	Notification is made as part of CTA/CTN/CTC application, or through an amendment to the CTA/CTN/CTC application	Notification is made through the standalone CRM notification form
Endorsement workflow	The draft notification is routed to the importer or local manufacturer for endorsement before routing back to the sponsor for submission	The draft notification is routed to the sponsor for endorsement before routing back to the importer or local manufacturer for submission
Submitter	Sponsor (on behalf of the importer or local manufacturer)	Importer or local manufacturer
Acknowledgment notification	To the importer or local manufacturer, as applicable, and sponsor	To the importer or local manufacturer, as applicable, and sponsor
Validity period of the notification	Valid for the duration of the clinical trial, i.e., study initiation to study completion (i.e. Last Patient Last Visit / LPLV, including remote follow-up)	Valid for 1 year from the date of notification

4.1. Overview of CRM notification process for regulated clinical trials

4.1.1. For regulated clinical trials, the sponsor should submit the CRM notification on behalf of the importer or local manufacturer. This provides assurance that the importer or local manufacturer has indeed been authorised by the sponsor to perform the relevant service of importation or local manufacture.

4.1.2. To streamline the CRM notification process, the sponsor may submit the CRM notification for regulated clinical trials at the time of initial CTA/CTN/CTC application. However, if the CRM-related information or the importer/local manufacturer information is unavailable at the time of CTA/CTN/CTC application, the sponsor may submit the CRM notification later by way of amendment to the CTA/CTN/CTC application.

4.1.3. As part of the CRM notification drafting process, the importer or local manufacturer, as applicable, will be required to endorse the submission electronically. This ensures that the importer or local manufacturer is aware of the submission and agrees to fulfil his responsibilities and obligations as required by the CRM regulations. Upon successful endorsement of the draft notification by the importer or local manufacturer, the local sponsor may proceed to submit the CTA/CTN/CTC application that includes the CRM notification.

4.1.4. Upon successful submission of the CTA/CTN/CTC application that includes the CRM notification, a CRM notification acknowledgement is automatically generated by PRISM and sent to the importer or local manufacturer, as applicable, and the sponsor. This acknowledgement serves as documentary evidence of successful CRM notification. Unlike CTN submissions, HSA does not issue “acceptance of notification” letters for CRM notification submissions.

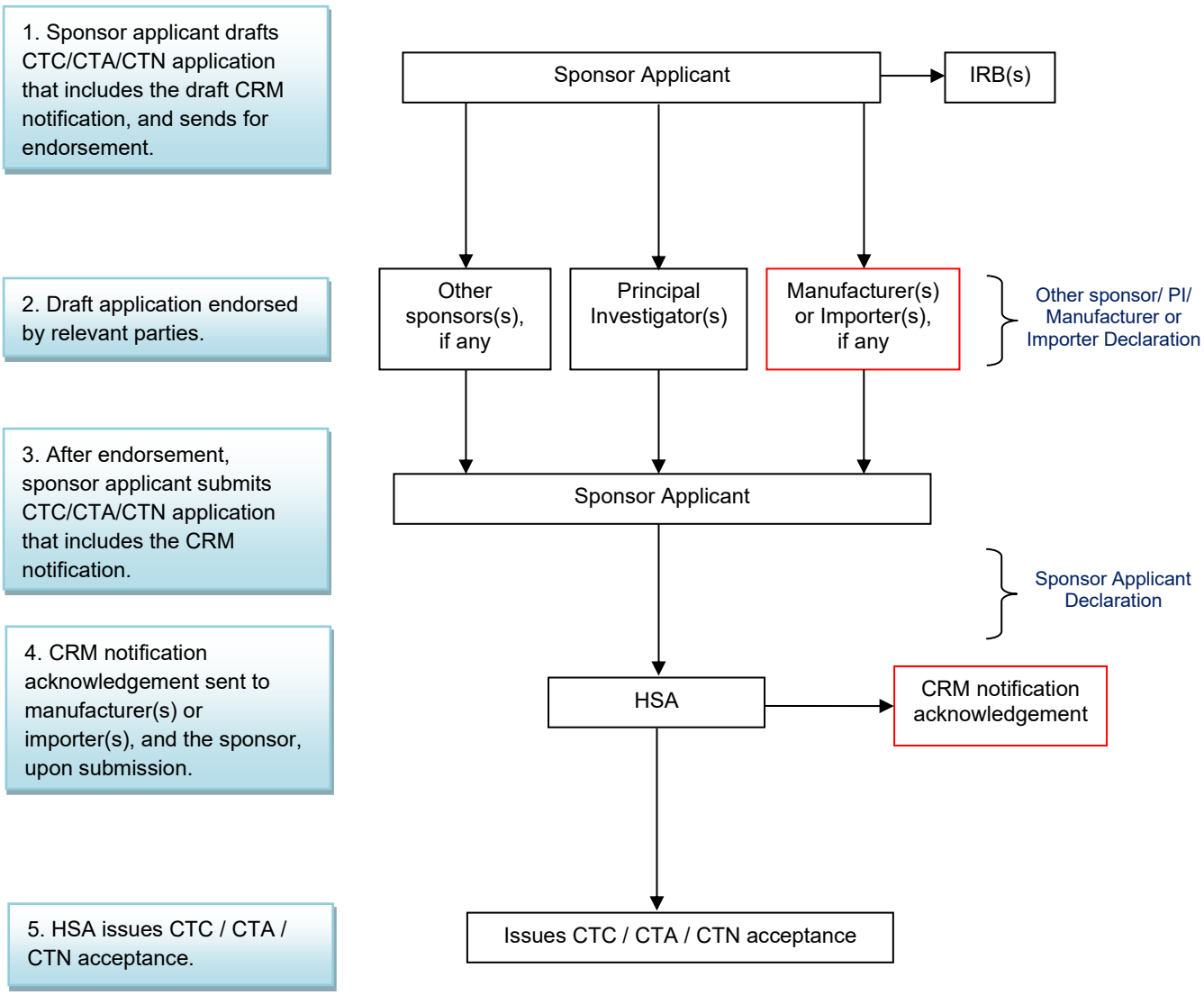
4.1.5. The CRM notification for regulated trials is valid for the duration of the clinical trial, until study completion (i.e., Last Patient Last Visit or LPLV).

4.1.6. Amendments to the CRM notification (e.g., change in quantity of CRM, addition of new importer / manufacturer etc.) may be made as part of an amendment to a CTA/CTN/CTC application.

4.1.7. The imported/supplied CRM should only be used for the clinical trial stated in the CRM notification. HSA approval should be sought for the transfer of the imported/supplied CRM to another clinical trial, or for the CRM to be used for other purposes. If the imported/supplied CRM is transferred for use in another clinical trial, the sponsor receiving the transferred CRM should include the transferred CRM in their CRM notification to HSA, with remarks that it was transferred from an existing clinical trial. This will ensure CRM tracking and accountability, and that the new sponsor receiving the transferred CRM is made aware of their duties and obligations under the CRM regulations. Proper records of the transfer should also be maintained by both sponsors.

4.1.8. Figure 6 provides a summary of the CRM notification process prior to import/supply of CRM for use in regulated clinical trials.

Figure 6. CRM Notification Process for Regulated Clinical Trials



4.2. Overview of CRM notification process for other clinical research

4.2.1. For other clinical research, the importer or the local manufacturer should submit the CRM notification instead of the clinical research sponsor, since an application for CTA/CTN/CTC is not required for such research.

4.2.2. To ensure the accuracy of the clinical research information for which the imported or locally manufactured CRM is to be used, and to provide assurance that the sponsor is aware and agreeable to discharge his duties and obligations under the CRM regulations, the draft notification will be routed to the sponsor for endorsement. The only exception to this endorsement step is when the CRM is imported with the intention of supplying or using it for multiple trials, the sponsors of which have yet to be identified.

4.2.3. The importer or local manufacturer may proceed to submit the notification upon successful endorsement of the draft notification form by the sponsor, if required.

4.2.4. Upon successful submission of the CRM notification, a CRM notification acknowledgement is automatically generated by PRISM and sent to the importer or local manufacturer, as applicable, and the sponsor. This acknowledgement serves as documentary evidence of successful CRM notification. Unlike CTN submissions, HSA does not issue “acceptance of notification” letters for CRM notification submissions.

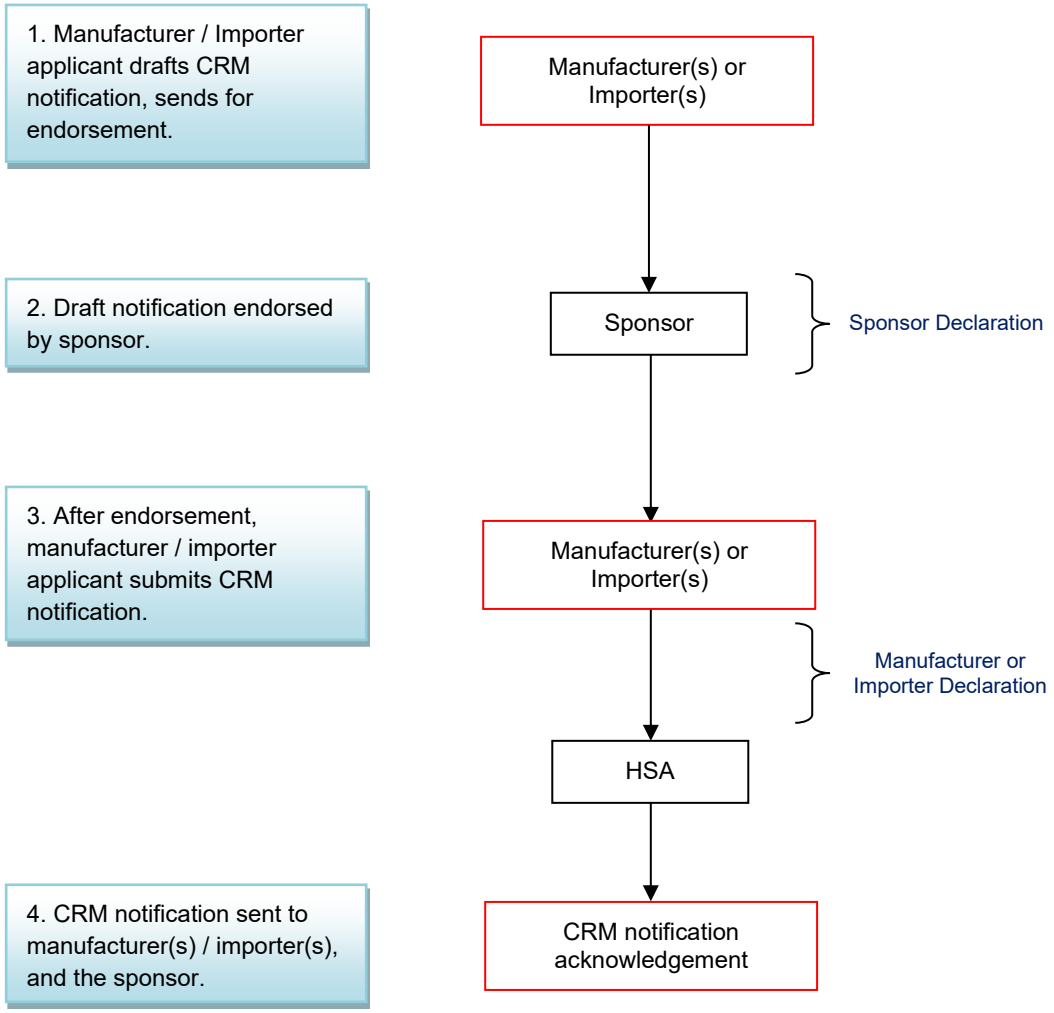
4.2.5. For other clinical research, the CRM notification is valid for 1 year. Extension may be made through PRISM, if required.

4.2.6. Amendments to CRM notification (e.g. change in quantity of CRM, change of Principal Investigator, addition of new importer / manufacturer etc.) may be made through PRISM, if required.

4.2.7. The imported/supplied CRM should only be used for the clinical research stated in the CRM notification. If the imported/supplied CRM is to be transferred to another clinical research, an amendment to the CRM notification may be submitted to include the details of the new clinical research. HSA approval should be sought for the use of imported/supplied CRM for other purposes.

4.2.8. Figure 7 provides a summary of the CRM notification process prior to import/supply of CRM for use in other clinical research.

Figure 7. CRM Notification Process Prior to Import / Supply of CRM for Use in Other Clinical Research



4.3. Additional notes relating to CRM and/or CRM Notification

4.3.1. CRM Obtained from Local Commercial Sources

CRM notification is not applicable for the following scenarios:

- Locally registered/licensed CRM obtained from local commercial sources (e.g. pharmacy, authorised local distributor); or
- Unregistered TP CRM obtained from the stock already available at the hospital pharmacy, or imported via exemption drug route on a named-patient basis or as buffer stock.

4.3.2. Direct Import of CRM

In some situations, the CRM is imported directly to the trial site in Singapore from overseas and it may not be apparent as to whom the local importer is. In such an instance, the local sponsor should assume the role of local importer.

4.3.3. Import of TP, CTGTP or MD for Local vs. Overseas Research Use

Table 3 below summarises the regulatory import route(s) for importing TP, CTGTP or MD for local research use vs. overseas research use.

Table 3: Regulatory import route(s) for importing TP, CTGTP or MD for local research use vs. overseas research use

<table>
<tr><th>Purpose of Import</th><th>Location of Clinical Research</th><th>Regulatory Import Route</th></tr>
<tr><td rowspan="4">Clinical Research</td><td>Local</td><td>TP/MD: CRM Notification</td></tr>
<tr><td rowspan="3">Overseas (Import for Re-export)</td><td>TP: Importer’s Licence (Restricted Activity)</td></tr>
<tr><td>CTGTP: Importer’s Licence</td></tr>
<tr><td>MD: Special Access Route - Import for re-export of unregistered medical devices</td></tr>
<tr><td rowspan="2">Laboratory Analysis of Human Biological Samples from Clinical Research</td><td>Local
(i.e., biological samples from local trial participants)</td><td rowspan="2">MD: CRM Notification</td></tr>
<tr><td>Overseas
(i.e., biological samples from overseas trial participants)</td></tr>
</table>

4.3.4. Import of Unused TP CRM for Destruction

CRM notification is not applicable for the import of unused TP CRM from overseas trial sites for local disposal. However, the company will require a Therapeutic Products Importer's Licence (TPIL) for restricted activity for importing TP for non-clinical use. In addition, the company must comply with duties and obligations outlined in the Health Products (Therapeutic Products) Regulations, such as record-keeping and ensuring that the product is not supplied to the public. The National Environment Agency (NEA) should be notified of the import and an acknowledgement obtained.

4.3.5. Import and Export of CRM that are Psychotropic Substances or Codeine Cough Preparations

4.3.5.1 Import

If the imported CRM is a psychotropic substance, an *import authorisation* will be required for the import of any consignment of psychotropic substance. This *import authorisation* is required in addition to CRM notification (if CRM notification is required), prior to importation of the CRM. This is to fulfil Singapore's obligations under the United Nations Convention on Psychotropic Substances.

4.3.5.2 Export

HSA approval is generally not required for exporting of CRM. However, if the CRM to be exported is a psychotropic substance or a codeine cough preparation, an *export licence* will be required prior to actual export of the CRM.

Please refer to the HSA website for more information on the import and export of psychotropic substances and restricted substances.

4.3.6. Manufacture, Import, Export and Supply of CRM that are Controlled Drugs

4.3.6.1. Manufacture

A *Manufacturer's Licence for Controlled Drugs* is required for a company to manufacture preparations containing Controlled Drugs.

This licence is required in addition to CRM notification (if CRM notification is required), prior to supply of the self-manufactured CRM by the local manufacturer.

4.3.6.2. Import

An *import licence* is required for the import of any consignment of Controlled Drugs into Singapore for legitimate and authorised use of Controlled Drugs. The licence is issued on a per consignment basis and the consignment should be imported into Singapore within 6 months from the date the licence is issued.

This licence is required in addition to CRM notification (if CRM notification is required), prior to importation of the CRM.

4.3.6.3. Export

An *export licence* is required for the export of any consignment of Controlled Drugs out of Singapore. The licence is issued on a per consignment basis and the consignment should be exported out of Singapore within 6 months from the date the export licence is issued.

4.3.6.4. Supply of Controlled Drugs

Companies involved in supply, distribution and wholesale activities of Controlled Drugs require a *Controlled Drug Wholesale Licence*.

Please refer to the HSA website for more information on the licences required for the manufacture, import, export and supply/ distribution/ wholesale of Controlled Drugs.

4.3.7. Importers and Manufacturers of CRM

4.3.7.1. Re-packaging and Re-labelling of CRM

CRM notification is not applicable if the manufacture of the CRM supplied comprises solely the re-packaging or re-labelling of the material. However, the duties and obligations relating to suppliers will be applicable if the repackaged product is supplied locally for use as a CRM.

4.3.7.2. Compounding of TP CRM

Compounding of TP CRM at the local trial site is a manufacturing activity. Hence, CRM notification would be applicable prior to supply of the compounded TP CRM.

4.3.7.3. Manufacturing of CRM that are Radiopharmaceuticals

Radiolabelling a precursor to produce a radiopharmaceutical is considered a manufacturing activity. Hence, CRM notification would be applicable prior to supply of the radiopharmaceuticals as a CRM by the local manufacturer.

4.3.7.4. CRM Notification and Manufacturers

The CRM regulations are for the purpose of controlling the supply chain, namely the import and supply of CRM. They are not intended as the legal instrument to control the manufacturer or manufacture of CRM. As such, successful CRM notification by a local manufacturer (as evidenced by CRM notification acknowledgement) can only be interpreted to mean that the manufacturer may now supply the locally manufactured product without possessing a valid wholesaler’s licence. The acknowledgement of CRM notification should not be misconstrued in any way as HSA’s endorsement of the manufacturer, the manufacturing process or the locally manufactured product.

4.3.7.5. Change of CRM importer/local manufacturer for an existing CRM-N

For regulated clinical trials, the new CRM importer/local manufacturer should be added via an amendment application. As existing CRM records cannot be removed, the CRM quantities specified for the previous CRM importer/local manufacturer may be changed to zero (i.e. 0), if no CRM will be imported/supplied by the previous importer/local manufacturer.

For other clinical research, the new CRM importer/local manufacturer should submit a new CRM notification for the clinical research.

5. DUTIES AND OBLIGATIONS OF LOCAL MANUFACTURERS, IMPORTERS AND SUPPLIERS OF CRM

This section applies to:
LOCAL MANUFACTURERS, IMPORTERS AND SUPPLIERS OF CRM
(includes importer, local manufacturer, wholesaler, sponsor, investigator)

- Section 5.1 provides guidance on the responsibilities relating to the import and supply of CRM other than medical device CRM
- Section 5.2 provides guidance on the responsibilities relating to the import and supply of medical device as CRM

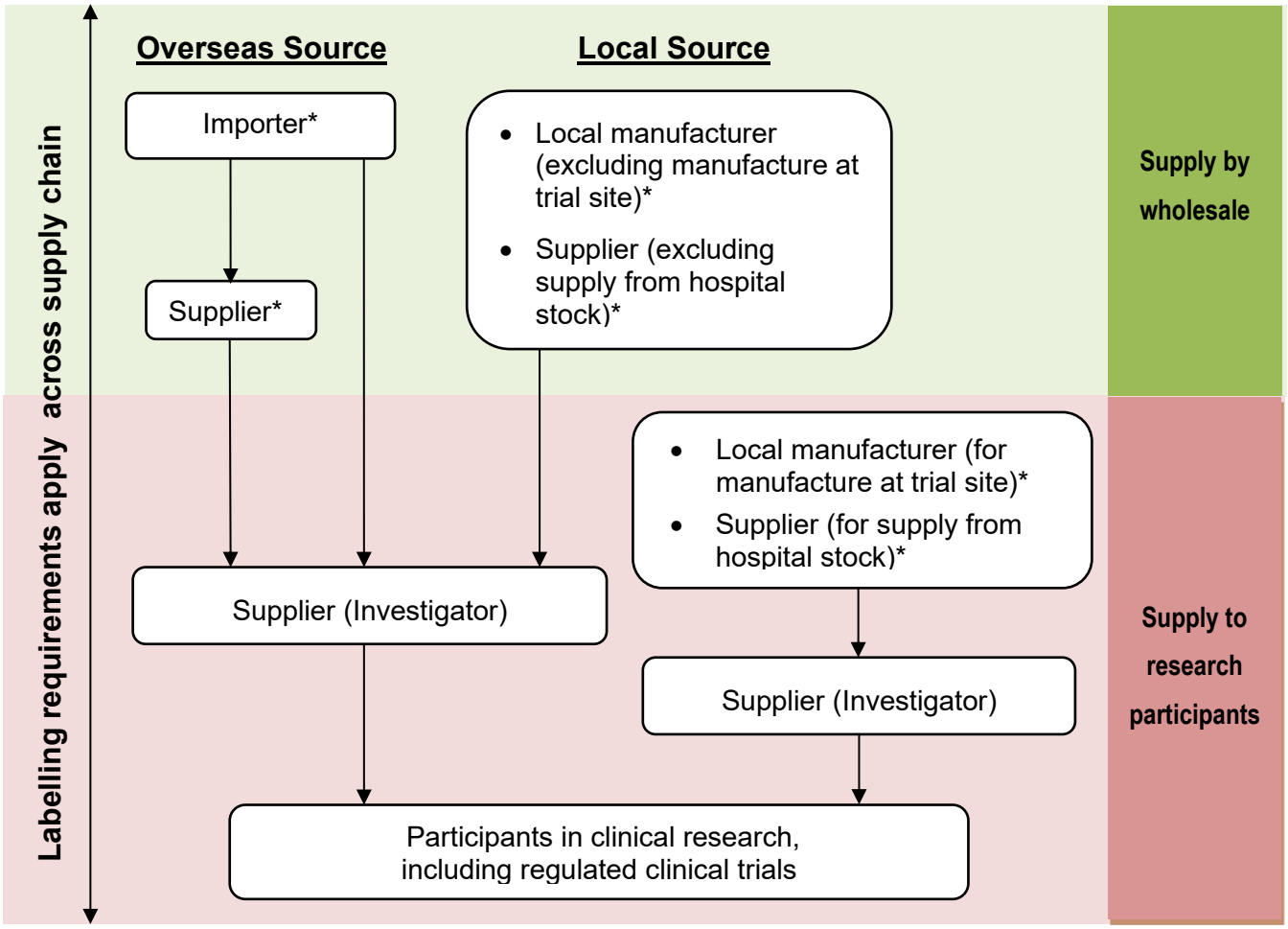
The CRM regulations provide controls to safeguard the supply chain relating to CRM that are imported, locally manufactured or supplied for use in clinical research.

Parties involved in supply chain management (Figure 8) have a responsibility to ensure supply chain integrity and prevent the inadvertent or deliberate release of unregistered CRM into the market for use other than in clinical research.

Proper record keeping enables proper evaluation to be made of the accountability and product tracking of the CRM.

Proper labelling of CRM also enables proper identification and storage of the product throughout the supply chain, and ensures that clinical research participants receive the correct product and use it appropriately.

Figure 8. The Product Supply Chain



** The local sponsor can be any of these parties.*

5.1. Duties and obligations of local manufacturers, importers and suppliers of CRM other than medical device CRM

Table 4 summarises the duties of local manufacturers, importers and suppliers of CRM other than MD CRM. It also points readers to other HSA Guidance documents that elaborate on the particular duty, or to the relevant section in this CRM Guidance.

It is to be noted that Table 4 serves only as a guide, based on the typical scope of roles of the different parties involved in supply chain management. It remains the responsibility of each party to comply with the requirements based on the actual activities the company is engaged in.

Table 4: Duties and obligations of parties involved in supplying CRM other than medical device CRM

Duties and Obligations	Parties			
	Local Manufacturer	Importer	Supplier	Sponsor
All CRM (including locally-registered products)				
Maintain records of receipt and supply *(Ref: Section 5.1.1)*	✓*	✓*	✓	✓*
Ensure compliance with labelling requirements *(Ref: Guidance on Labelling of Investigational and Auxiliary Products in Clinical Trials)***	✓*	✓*	✓	✓*
Report unexpected serious adverse drug reaction (USADR) to HSA *(Ref: Guidance on Expedited Safety Reporting Requirements for Clinical Trials)***				✓
Establish and maintain a system of traceability (only for CRM that is a CTGTP)	✓	✓	✓	✓*
Report CRM defects *(Ref: Guidance on Product Defect Reporting and Recall Procedures for Therapeutic Products and Cell, Tissue and Gene Therapy Products)*	✓	✓	✓	✓*
Notify HSA 24 hours before recall of CRM *(Ref: Guidance on Product Defect Reporting and Recall Procedures for Therapeutic Products and Cell, Tissue and Gene Therapy Products)*	✓	✓	✓	✓*
Additional requirements for locally manufactured or imported CRM				
Ensure the CRM (TP/MP) is of the correct identity and conforms with the applicable standards of strength, quality and purity for the material	✓	✓		
Maintain records of manufacture, assembly and testing	✓			
Ensure CRM supply/use only for clinical research purpose	✓*	✓*	✓	✓*
Ensure CRM use only in IRB-approved clinical research				✓
Ensure disposal/export of CRM within 6 months after research completion/ termination				✓
Maintain records of disposal/export of CRM				✓

* Responsibility as “Supplier”. (Supplier includes local manufacturer, importer, wholesaler, sponsor, investigator, where applicable, if the party is involved in the activity of supplying a TP/CTGTP/MP as CRM)

** This Guidance also applies to TP, CTGTP and MP used in other clinical research.

5.1.1. Record keeping in relation to CRM other than medical device CRM

This section applies to:

Any supplier of CRM other than medical device CRM, including

- **Importers**
- **Local manufacturers**
- **Wholesaler (e.g., distributor)**
- **Sponsor**
- **Investigator or other healthcare professional (e.g., pharmacist) supplying CRM**

5.1.1.1. Records of Manufacture of Locally Manufactured CRM (other than medical device CRM)

(a) Who is required to keep records of manufacture of the locally manufactured CRM (other than MD CRM)?

A manufacturer of any CRM must keep records of the manufacture, assembly and testing of the material, and, in the case of a CRM that is a CTGTP, records of traceability.

(b) For how long should records of manufacture of the locally manufactured CRM (other than MD CRM) be kept?

All records relating to any manufacture, assembly and testing of CRM (other than MD CRM) should be kept for the following duration:

- for registered and unregistered investigational CRM and unregistered auxiliary CRM:
  - 5 years after the completion or discontinuation of the last clinical trial in which the batch was used.
- for registered auxiliary CRM, the longer of the following periods:
  - one year after the expiry date of the material; or
  - 5 years after the date of such manufacture, assembly and testing; and

- for traceability records relating to CTGTP CRM:
    - 30 years after expiry date of the product or any other shorter period that HSA allows in a particular case.

5.1.1.2. Records of Receipt & Supply of CRM (other than MD CRM)

(a) Who is required to keep records of receipt and supply of CRM (other than MD CRM)?

Any person who supplies CRM is required to records of receipt and/or supply, as applicable. The keeping of such records is important to enable proper accountability of the CRM.

(b) What should be the format of records of receipt and supply of CRM (other than MD CRM)?

The records of receipt and supply need not follow any specific format. However, they should include the following elements:-

- the proprietary name (i.e., brand name) or other description of the CRM
- the identification number of the CRM (e.g., control number, lot number or batch number)
- details of each receipt or supply, including
    - the date on which the CRM was received or supplied
    - the quantity of CRM received or supplied, and
    - the name and address of the person from whom the CRM was received, or to whom the CRM will be supplied.

The records must be kept up-to-date at all times, and be available for inspection by HSA upon request.

(c) For how long should records of receipt and supply of CRM (other than MD CRM) be kept?

The record-keeping duration for regulated clinical trials is aligned to the clinical trial regulations. Therefore, if the records relate to CRM that is

supplied for use in a regulated clinical trial, records of receipt and supply must be kept until the following time-point, whichever is latest:

- when there is no more pending or planned application for registration of the TP, CTGTP or MP that was tested in the clinical trial or research
- 2 years after the last of such registrations has been granted
- 2 years after HSA was informed of the termination of a clinical trial
- 6 years after the completion of a clinical trial (i.e., 6 years after "Last-Patient-Last-Visit),
- if the clinical trial involves an applicable CTGTP and in the case of a record that relates to the traceability of the product, 30 years after the expiry date of that product or any other shorter period that HSA allows in a particular case;
- any other period as directed by HSA

If the CRM is supplied for use in other clinical research, records of receipt and supply must be kept for the following period, as applicable:

- If the CRM is not a CTGTP:
  - 2 years after the supply;
- If the CRM is a CTGTP and;
  - the records do not relate to traceability:
    - 2 years after the supply; or
  - the records relate to traceability:
    - 30 years after the expiry date of the CTGTP, or any other shorter period that HSA allows in a particular case;

(d) Why are there additional records for Pharmacy-Only (P) and Prescription-Only Medicines (POM) supplied as CRM? What are these additional requirements?

These record-keeping requirements for P and POM medicines are aligned with the requirements in the Health Products (Therapeutic Products) Regulations.

Other than the general record-keeping requirements for the supply of CRM as described in the section above, there are additional record-keeping requirements if the clinical research material is a Pharmacy-Only (P) Medicine or a Prescription-only medicine (POM) that is supplied directly to the trial participant, such as in a retail pharmacy setting.

These additional records must be made on the day of supply or if not reasonably practicable, the next day.

Pharmacy-Only Medicine

The person (e.g., pharmacist) supplying a P-Medicine as CRM to a trial participant must keep records of the following:

- name, NRIC number or other identification document number (e.g., FIN number) and contact details of the trial participant
- strength of the CRM supplied
- dosage, frequency and purpose of the treatment for which the supply was made

Prescription-Only Medicine (POM)

The person supplying a POM as CRM to a trial participant must keep records of the following:

- name, NRIC number or other identification document number (e.g., FIN number) and contact details of the trial participant
- the name and address of the doctor or dentist who signed the prescription (if the POM-CRM is supplied by a qualified pharmacist or a person under the pharmacist's supervision)

5.1.1.3. Records of Putting to Some Other Use, Disposal or Export of Imported/Locally Manufactured CRM (other than MD CRM)

The sponsor is responsible for ensuring that any unused CRM (including expired CRM or those which can no longer be used for research) that was imported or locally manufactured is disposed of (e.g., sent for destruction) or exported within 6 months of the conclusion or termination of the clinical research.

Alternatively, if the sponsor deems that any unused CRM is fit to be put to some other use other than in clinical research (e.g., for laboratory research or channeled to normal clinical practice), the sponsor must obtain permission from HSA before using the material for that other purpose.

Permission may be sought in writing by sending an email to HSA_CT@hsa.gov.sg.

If permission is granted for the unused CRM to be used for that other purpose, the material will no longer be considered to be a CRM. Depending on the proposed use, it may be subject to other applicable laws. For example, if an unused TP CRM is to be channeled for use in normal clinical practice, it will be subject to the laws of the Health Products (Therapeutic Products) Regulations when it ceases to be a CRM and is used as a TP.

(a) Who is required to keep records of putting to some other use, disposal or export of imported/locally manufactured CRM (other than MD CRM)?

Sponsors are required to keep records relating to all CRM that are put to some other use, disposed of or exported.

(b) What should be the format of records of putting to some other use, disposal or export of imported/locally manufactured CRM (other than MD CRM)?

The records need not follow any specific format. However, they should include the following:-

- the proprietary name (i.e., brand name) or other description of the CRM
- the identification number of the CRM (e.g., the control number, lot number or batch number)
- details of the disposal, export or putting to some other use, including
- the date on which the CRM was disposed, exported or put to some other use,
- the quantity of CRM disposed, exported or put to some other use, and
- the name and address of the person responsible for the disposal, export or putting to some other use of the CRM

(c) For how long should records of putting to some other use, disposal or export of imported/locally manufactured CRM (other than MD CRM) be kept?

If the records relate to CRM that is supplied for use in a regulated clinical trial, records of putting to some other use, disposal or export must be kept until the following time-point, whichever is latest:

- when there is no more pending or planned application for registration of the TP, CTGTP or MP that was tested in the clinical trial or research
- 2 years after the last of such registrations has been granted
- 2 years after HSA was informed of the termination of a clinical trial
- 6 years after the completion of a clinical trial (i.e., 6 years after “Last-Patient-Last-Visit),
    - if the clinical trial involves an applicable CTGTP and in the case of a record that relates to the traceability of the product, 30 years after the expiry date of that product or any other shorter period that HSA allows in a particular case;
- any other period as directed by HSA

If the CRM is supplied for use in other clinical research, records of putting to some other use, disposal or export must be kept for the following period, as applicable:

- If the CRM is not a CTGTP: 2 years after the putting to some other use, disposal or export, as the case may be;
- If the CRM is a CTGTP and;
    - the records do not relate to traceability: 2 years after the putting to some other use, disposal or export, as the case may be; or
    - the records relate to traceability: 30 years after the expiry date of the CTGTP, or any other shorter period that HSA allows in a particular case;

5.2. Duties and obligations of local manufacturers, importers and suppliers of medical device as CRM

Table 5 summarises the duties and obligations of local manufacturers, importers and suppliers of MD for clinical research, based on the existing Health Products (Medical Devices) Regulations and the Health Products (Medical Devices) (Amendment) Regulations 2016. The new CRM requirements, as laid out in the Amendment Regulations are marked “new”. The existing requirements are however incorporated in the same table for ease of reference and to facilitate awareness of the full list of responsibilities as a local manufacturer, importer or supplier of medical devices for clinical research.

Table 5 also points readers to other HSA Guidance documents that elaborate on the particular duty, or to the relevant section in this CRM Guidance.

Please note that Table 5 serves only as a guide, based on the typical scope of roles of the different parties involved in supply chain management. It remains the responsibility of each party to comply with the requirements based on the actual activities the company is engaged in.

Table 5: Duties and obligations of parties involved in supplying medical device for clinical research purposes

Duties and Obligations	Parties			
	Local Manufacturer	Importer	Supplier*	Sponsor
All CRM (including locally-registered products)				
Ensure the CRM (MD) complies with "Safety and Performance Requirements for Medical Devices" in the First Schedule of the Health Products (Medical Devices) Regulations *(Ref: GN-16: Guidance on Essential Principles for Safety and Performance of Medical Devices)*	✓	✓		
Maintain records of manufacture, assembly and testing	✓			
Maintain records of receipt and supply *(Ref: Section 5.2.1.1 and GN-06: Guidance on Distribution Records for Medical Devices)*	✓*	✓*	✓	✓*
Ensure compliance with labelling requirements *(Ref: GN-23: Guidance on Labelling for Medical Devices)*	✓	✓	✓	✓*
Report MD defects and adverse effects to HSA *(Ref: GN-05: Guidance on Reporting of Adverse Events for Medical Devices)*	✓	✓	✓	✓*
Maintain records of complaints *(Ref: GN-07: Guidance on Complaint Handling of Medical Devices)*	✓	✓	✓	✓*
Notify HSA concerning recall *(Ref: GN-04: Guidance on Medical Device Recall)*	✓	✓	✓	✓*
Notify HSA concerning field safety corrective actions (FSCAs) *(Ref: GN-10: Guidance on Medical Devices Field Safety Corrective Action)*	✓	✓	✓	✓*
Additional requirements for locally manufactured or imported CRM				
Ensure CRM supply/use only for clinical research purpose	✓*	✓*	✓	✓*
Ensure CRM use only in IRB-approved clinical research				✓

Duties and Obligations	Parties			
	Local Manufacturer	Importer	Supplier*	Sponsor
Ensure disposal/export of CRM within 6 months of research completion/termination				✓
Maintain records of disposal/export *(Ref: Section 5.2.1.2)*				✓

* Responsibility as "Supplier". (Supplier includes local manufacturer, importer, wholesaler, sponsor, investigator, where applicable, if the party is involved in the activity of supplying a MD for clinical research).

5.2.1. Record keeping in relation to medical device (MD) as CRM

5.2.1.1. Records of Receipt & Supply of MD as CRM

(a) Who is required to keep records of receipt and supply of MD as CRM?

Any person who supplies MD as CRM (including manufacturers, importers, wholesalers, sponsors) is required to records of receipt and/or supply, as applicable.

The keeping of such records is important to enable proper accountability and traceability of the CRM.

(b) What should be the format of records of receipt and supply of MD as CRM?

The records of receipt and supply need not follow any specific format. However, they should include the following elements:-

- the proprietary name (i.e., brand name) or other description of the CRM
- the identification number or mark of the CRM (e.g., control number, lot number, batch number, serial number)
- details of each receipt or supply, including
    - the date on which the CRM was received or supplied
    - the quantity of CRM received or supplied, and
    - the name and address of the person from whom the CRM was received, or to whom the CRM will be supplied.

The records must be kept up-to-date at all times, and be available for inspection by HSA upon request.

(c) For how long should records of receipt and supply of MD as CRM be kept?

If the records relate to an unregistered MD CRM that is supplied for use in a regulated clinical trial, records of receipt and supply must be kept until the following time-point, whichever is latest:

- when there is no more pending or planned application for registration of the TP or MP that was tested in the clinical trial or research
- 2 years after the last of such registrations has been granted
- 2 years after HSA was informed of the termination of a clinical trial
- 6 years after the completion of a clinical trial (i.e., 6 years after "Last-Patient-Last-Visit), or
- any other period as directed by HSA

If the MD CRM (whether registered or unregistered) is supplied for use in other clinical research, or if the MD CRM is a registered MD, records of receipt and supply must be kept for either

- the projected useful life of the medical device, or
- 2 years after the date on which the medical device was supplied, whichever is the longer period

5.2.1.2. Records of Disposal of Imported/Locally Manufactured MD as CRM

The sponsor is responsible for ensuring that any unused MD CRM that was imported or locally manufactured is disposed of (e.g., sent for destruction) or exported within 6 months of the conclusion or termination of the clinical research.

Alternatively, if the sponsor deems that any unused CRM is fit to be put to some other use other than in clinical research, the sponsor must obtain permission from HSA before using the material for that other purpose.

Permission may be sought in writing by sending an email to HSA_CT@hsa.gov.sg.

If permission is granted for the unused MD CRM to be used for that purpose, the MD will no longer be considered to be a CRM. However, it continues to be subject to applicable laws relating to medical devices, including the Health Products (Medical Devices) Regulations.

(a) Who is required to keep records of disposal of imported/locally manufactured MD CRM?

Sponsors are required to keep records relating to all CRM that are put to some other use, disposed of or exported.

(b) What should be the format of records of disposal of imported/locally manufactured MD CRM?

The records need not follow any specific format, but should include the following:-

- the proprietary name (i.e., brand name) or other description of the MD CRM
- the identification number or mark of the CRM (e.g., the control number, lot number, batch number, serial number)
- details of the disposal, export or putting to some other use, including
- the date on which the CRM was disposed, exported or put to some other use,
- the quantity of CRM disposed, exported or put to some other use, and
- the name and address of the person responsible for the disposal, export or putting to some other use of the CRM

(c) For how long should records of disposal of imported/locally manufactured MD CRM be kept?

If the records relate to an unregistered MD CRM that is supplied for use in a regulated clinical trial, records of disposal must be kept until the following time-point, whichever is latest:

- when there is no more pending or planned application for registration of the TP or MP that was tested in the clinical trial or research
- 2 years after the last of such registrations has been granted
- 2 years after HSA was informed of the termination of a clinical trial
- 6 years after the completion of a clinical trial (i.e., 6 years after “Last-Patient-Last-Visit), or
- any other period as directed by HSA

If the MD CRM (whether registered or unregistered) is supplied for use in other clinical research, or if the MD CRM is a registered MD, records of disposal must be kept for 2 years after the time when the medical device is put to some other use, disposed of or exported.

6. CRM NON-COMPLIANCES

CRM non-compliances may include the following:

(i) CRM notification that was not submitted prior to the import or prior to the supply of locally manufactured CRM for clinical trial/research use, in the case where an exception from dealers' licence was required for these activities;

(ii) Import of CRM or supply of locally manufactured CRM with an expired CRM Notification;

(iii) Import of CRM or supply of locally manufactured CRM in excess of the quantity declared in the CRM Notification; or

(iv) Failure to comply with duties and obligations of importers, local manufacturers or suppliers that may have a significant impact on trial/research participant safety (e.g., failure to report a USADR or use in a research study that has not been approved by the IRB).

(a) Who should notify CRM non-compliances to HSA?

Suppliers of CRM (e.g. importer, local manufacturer, wholesaler, sponsor, or investigator) should notify CRM non-compliances to HSA.

(b) When should CRM non-compliances be notified to HSA?

CRM non-compliances should be notified to HSA as soon as possible and no later than 15 calendar days from the supplier's awareness of the non-compliance.

(c) How should CRM non-compliances be notified to HSA?

CRM non-compliances should be notified to HSA by completing the CRM Non-Compliance Form available on the HSA website. The submitter will receive a copy of the completed CRM Non-Compliance Form via email after submission.

Separate forms should be submitted for individual protocols. In the event the CRM non-compliance involves multiple protocols, you may, in place of separate forms for separate protocols, submit a tabular summary of all the fields of the CRM Non-Compliance Form for the affected protocols to HSA_CT@hsa.gov.sg.

The submitter should ensure that the completed CRM Non-Compliance Form and relevant correspondences are filed.

7. REFERENCES

(i) Health Products (Clinical Trials) Regulations

(ii) Health Products (Clinical Research Material) Regulations

(iii) Medicines (Clinical Trials) Regulations

(iv) Medicines (Medicinal Products as Clinical Research Material) Regulations

(v) Health Products (Medical Device) Regulations

(vi) Guidance on Determination of Whether a Clinical Trial Requires a Clinical Trial Authorisation (CTA), Clinical Trial Notification (CTN) or a Clinical Trial Certificate (CTC)

(vii) Guidance on Labelling of Investigational and Auxiliary Products in Clinical Trials

(viii) Guidance on Expedited Safety Reporting Requirements for Clinical Trials

(ix) Guidance on Product Defect Reporting and Recall Procedures for Therapeutic Products and Cell, Tissue and Gene Therapy Products

(x) GN-16: Guidance on Essential Principles for Safety and Performance of Medical Devices

(xi) GN-06: Guidance on Distribution Records for Medical Devices

(xii) GN-23: Guidance on Labelling for Medical Devices

(xiii) GN-05: Guidance on Reporting of Adverse Events for Medical Devices.

(xiv) GN-07: Guidance on Complaint Handling of Medical Devices

(xv) GN-04: Guidance on Medical Device Recall

(xvi) GN-10: Guidance on Medical Devices Field Safety Corrective Action

HEALTH SCIENCES AUTHORITY

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