IOCTB LEARN

REGULATORY REQUIREMENTS FOR CLINICAL RESEARCH MATERIALS

Presented by:

Innovation Office & Clinical Trials Branch

Health Products Regulation Group

Health Sciences Authority

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Outline

- Clinical Research Materials (CRM)
- Objectives of CRM Regulations
- CRM Notification
- Duties and Responsibilities of Local Manufacturers, Importers and Suppliers of CRM

Learning Objectives

1. Know what are Clinical Research Materials (CRM)
2. Understand the objectives of the CRM regulations
3. Know when CRM notification is applicable
4. Describe the duties and responsibilities of local manufacturers, importers and suppliers of CRM

DEFINITION: CLINICAL RESEARCH MATERIALS (CRM)

Regulatory Basis

Clinical research materials (CRM) are regulated under different subsidiary legislation of the Health Products Act.

CRM Product Type	Applicable Regulations (i.e., CRM Regulations)
• Therapeutic Product • Cell, Tissue and Gene Therapy Product	Health Products (Clinical Research Materials) Regulations
Medical Device	Relevant provisions under the Health Products (Medical Devices) Regulations

Clinical Research Materials (CRM)

Clinical Research Materials (CRM)

Registered or unregistered **therapeutic product (TP)**, **applicable* cell, tissue and gene therapy product (CTGTP)** or placebo

Registered or unregistered **Medical Device (MD)**

Manufactured, imported or supplied specifically for use in **any clinical research** in accordance with a research protocol

Regulated Clinical Trials

Clinical trials requiring a Clinical Trial Authorisation or Clinical Trial Notification

Clinical Research not regulated by HSA

- *Observational clinical trials of TP or Class 2 CTGTP*
- *Clinical research in which the TP is not the subject of investigation*
- *Medical device clinical trials*
- *Food and nutrition studies involving the use of MD*

* Refer to the next slide for the definition of applicable CTGTP CRM

Clinical Research Materials (CRM)

Applicable Cell, Tissue and Gene Therapy Product (CTGTP)

Cell, Tissue and Gene Therapy Products (CTGTPs) are risk-stratified into two classes as follows:

- 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.

Clinical Research Materials (CRM)

Applicable Cell, Tissue and Gene Therapy Product (CTGTP)

- An applicable CTGTP is either:
  - a Class 2 CTGTP; or
  - a Class 1 CTGTP for which no manufacturer, importer or wholesaler notifications have been made to HSA, to manufacture, import or to supply by wholesale the product, respectively.

- Class 1 CTGTPs for which manufacturer, importer or wholesaler notifications have been made are excluded from the definition of a CTGTP CRM.
  - Respective dealer notifications already enable the Class 1 CTGTP to be manufactured, imported or supplied, respectively, for use in clinical research.
  - Therefore, dealer licence exceptions provided for under CRM Regulations not needed.

OBJECTIVES OF THE CRM REGULATIONS

Key Objectives of CRM Regulations

- **Facilitate access to CRM**
- **Ensure CRM accountability and safeguard the supply chain**
  - CRM are supplied only for IRB-approved clinical research
  - CRM must be properly labelled
  - Detailed records must be kept of receipt, supply, use, and final disposal, including returned, unused, or expired CRM
  - For CRM that are cell, tissue, and gene therapy products, there must be complete traceability from manufacture or import through to end use and vice-versa
- **Ensure quality and safety of CRM**
  - Ensure appropriate quality of CRM
  - Safety reporting of unexpected serious adverse events related to the use of the CRM, product defects

CRM NOTIFICATION

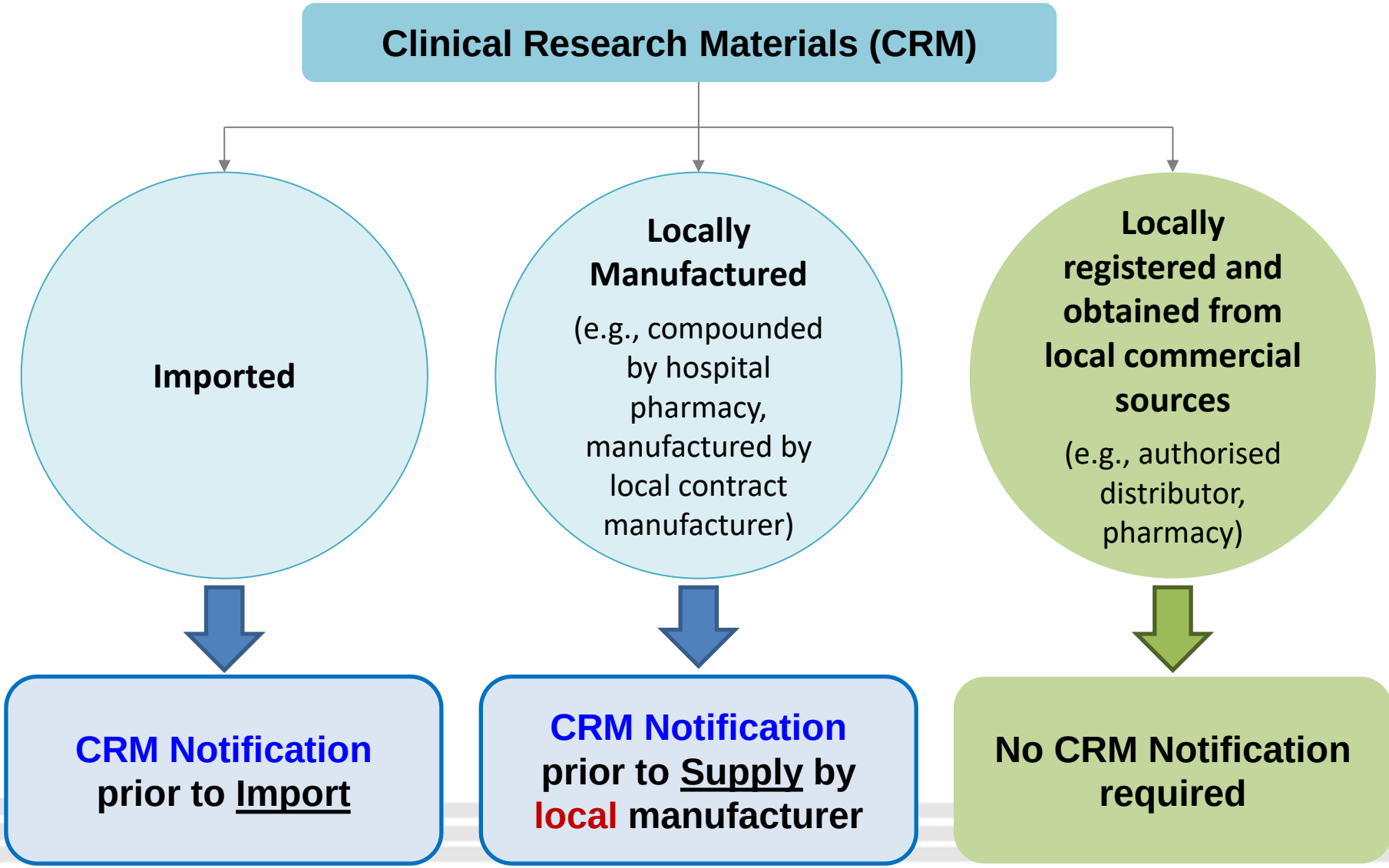
Facilitating Access to CRM

CRM Notification

Activity	Licence	CRM Notification*
Manufacture of CRM	Manufacturer's Licence Not required	**CRM Notification** required prior to supply of CRM by local manufacturer
Import of CRM	Importer's Licence Not required	**CRM Notification** required prior to import of CRM
Wholesale of CRM	Wholesaler's Licence Not required	-
Supply of CRM	Product Registration Not required	-

*Dealers of CRM are subject to prescribed duties and responsibilities.

When to Submit CRM Notification



CRM Notification vs Other Regulatory Routes

Examples of Use for Import

✅ Use CRM Notification (CRM-N)	🚫 Do Not Use CRM-N — Use Other Import Routes
Import of CRM for use in **local clinical research** (for HSA-regulated clinical trials and for clinical research conducted under the Human Biomedical Research governance framework)	Import-for-re-export of unregistered TP, CTGTP or MD for use in **overseas clinical trials**: → TP Importer's Licence (Restricted Activity) → CTGTP Importer's Licence → MD Special Access Route (SAR): Import for Re-export of unregistered medical devices
Import of unregistered medical device CRM (e.g., analytical test kits or reagents) for **analysis of clinical trial biological samples** (whether from local or overseas clinical trials) in **local central laboratories**	-

TP – Therapeutic Product CTGTP – Cell, Tissue and Gene Therapy Product
MD – Medical Device

CRM Notification Process

- CRM notification should be made through PRISM.
- The CRM notification process differs depending on whether the research is regulated by HSA:
  - For **regulated clinical trials**, the sponsor submits the CRM notification on behalf of the importer or the local manufacturer, using the same form as the clinical trial application. CRM notification submitted as part of this process is valid for the duration of the clinical trial.
  - For **clinical research that is not regulated by HSA**, the importer (if CRM is imported) or the local manufacturer (if CRM is locally manufactured), as applicable, submits the CRM notification. The CRM notification is valid for 1 year from the date of notification, which can be extended, if required.
- Upon successful submission of the CRM notification, an acknowledgement is generated and provided to the importer or local manufacturer, as applicable, and the sponsor.

Additional Regulatory Requirements

For Psychotropic Substances, Codeine Cough Preparations or Controlled Drugs

	Manufacturer's Licence	Importer's Licence	Wholesaler's Licence	Export Licence
Psychotropic Substances		✓		✓
Codeine Cough Preparations				✓
Controlled Drugs	✓	✓	✓	✓

Note: These licences are in addition to CRM Notification, where applicable.

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

Duties & Responsibilities of Dealers of CRM

Therapeutic Product & Cell, Tissue and Gene Therapy Product (CTGTP)

Duties and Obligations	Manufacturer	Importer	Supplier*	Sponsor
All CRM (including locally-registered products)				
Maintain records of receipt and supply	✓*	✓*	✓	✓*
Ensure compliance with labelling requirements	✓*	✓*	✓	✓*
Report unexpected serious adverse drug reaction (USADR)				✓
Establish & maintain a system of traceability (CTGTP CRM)	✓	✓	✓	✓*
Report CRM defects	✓	✓	✓	✓*
Notify HSA before recall of CRM	✓	✓	✓	✓*
Additional requirements for locally manufactured or imported CRM				
Ensure appropriate quality of CRM	✓	✓		
Maintain records of manufacture	✓			
CRM supply/use only for clinical research purpose	✓*	✓*	✓	✓*
Ensure CRM use only in IRB-approved research				✓
Ensure disposal/export of CRM after research/trial ends				✓
Maintain records of disposal/export of CRM				✓

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

Duties & Responsibilities of Dealers of CRM

Medical Device (MD)

Duties and Obligations	Manufacturer	Importer	Supplier*	Sponsor
All CRM (including locally-registered MD)				
Ensure appropriate quality of CRM	✓	✓		
Maintain records of manufacture	✓			
Maintain records of receipt and supply	✓*	✓*	✓	✓*
Ensure compliance with labelling requirements	✓	✓	✓	✓*
Report MD defects and adverse effects to HSA	✓	✓	✓	✓*
Maintain records of complaints	✓	✓	✓	✓*
Notify HSA concerning field safety corrective actions	✓	✓	✓	✓*
Notify HSA before recall of CRM	✓	✓	✓	✓*
Additional requirements for locally manufactured or imported MD CRM				
CRM supply/use only for clinical research purpose	✓*	✓*	✓	✓*
Ensure CRM use only in IRB-approved clinical research				✓
Ensure disposal/export of CRM after research/trial ends				✓
Maintain records of disposal/export of CRM				✓

*"Supplier" includes local manufacturer, importer, wholesaler, sponsor, investigator, where applicable, if the party is involved in the activity of supplying a MD as CRM.

Summary

- The CRM regulations apply to therapeutic products, CTGTPs, and medical devices used in clinical research.
- To facilitate access to CRM, the regulations provide exceptions from dealer licensing and product registration, conditional on CRM notification being submitted before import, or supply by local manufacturers.
- CRM dealers are expected to comply with specified responsibilities to ensure proper handling and accountability throughout the supply chain.
- This balanced framework facilitates timely access to clinical research materials while maintaining appropriate regulatory oversight.

References

- Health Products (Clinical Research Materials) Regulations
- Health Products (Medical Devices) Regulations
- HSA Regulatory Guidance (GN-IOCTB-03): Guidance on Clinical Research Materials

We welcome your enquiries and feedback!

HSA_CT@hsa.gov.sg

THANK YOU!