Clinical Research Material Notification (CRM-N) Pre-Submission Review for Device Development Project in SingHealth Medical Technology Office (MTO)

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Introduction

In 2016, the Health Sciences Authority (HSA) introduced the Clinical Research Material (CRM) regulations, which govern the import and supply of therapeutic or medicinal products and medical devices used on human subjects in regulated clinical trials and unregulated clinical research. CRM Notification (CRM-N) is a process of notifying HSA of the import or supply of CRM in situations of applicable exception to the requirement for the various dealers' licenses and product registration.

We have established a decision tool for the Principal Investigator(s) (PIs) involved in device development projects, in the determination of lead party responsible for the proper filing of CRM-N to HSA prior to commencement of clinical trial. The developed easy guide aims to empower PI(s) in the self-identification and assessment of lead party responsible for CRM-N filing so as to comply with HSA Medical Device Regulations.

Method

Following the EZ Guide: 4 simple steps

1 Determine if a CRM-N is required

Must a CRM Notification (CRM-N) Be Filed?

- I am conducting a regulated clinical trial *or* clinical research* not regulated by HSA
  **Clinical research: any research involving human subjects*
  - No → A CRM Notification does not need to be filed.
  - Yes ↓
- I am using Clinical Research Materials (CRM)* in my study or trial.
  **CRM: any registered or unregistered therapeutic product, licensed or unlicensed medicinal product, or placebo, that is manufactured, imported or supplied for the purpose of being used in clinical research (by way of administration to a subject) in accordance with the research protocol, or any registered or unregistered medical device whose planned use is for a clinical purpose in any clinical research.*
  - No → A CRM Notification does not need to be filed.
  - Yes ↓

A CRM Notification must be filed. (see next step)

References:
HSA GN-CTB-2-001C-001 CLINICAL TRIALS GUIDANCE: CLINICAL RESEARCH MATERIALS, 2 May 2017
SINGAPORE GUIDELINE FOR GOOD CLINICAL PRACTICE, Oct 2009

2 Determine who should file CRM-N

Who Must File the CRM-N for a Medical Device?

- Will the device to be used in a regulated clinical trial*?
  **Regulated trials: 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).*
  - Yes → **Local sponsor** needs to file the CRM-N on behalf of the importer or local manufacturer prior to import/supply. (see next step)
  - No ↓
- Is the device manufactured overseas and imported?
  - Yes → Is the CRM imported directly to the trial site in Singapore from overseas?
    - Yes → **Local sponsor** assumes the role of local importer and needs to file the CRM-N.
    - No → **Local importer** needs to file the CRM-N.
  - No ↓
- Is the device manufactured locally?
  - Yes → **Local manufacturer** needs to file the CRM-N.

3 Understand who takes the lead to file CRM-N

What is My Role?

- I am the sponsor* of the trial.
  **Sponsor: an individual, company, institution, or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial.*
  - Yes → You are the Lead Party for the CRM-N filing.
  - No ↓
- I am a Principal Investigator who contributed to the device design*.
  **I may be a contributor of the intellectual property on which the device is based.*
  - Yes → You are the Lead Party for the CRM-N filing.
  - No ↓
- The device was made according to a collaborator's or vendor's design specification*.
  **I did not contribute to the device design.*
  - Yes → The collaborator or vendor is the Lead Party for the CRM-N filing.

References:
HSA GN-CTB-2-001C-001 CLINICAL TRIALS GUIDANCE: CLINICAL RESEARCH MATERIALS, 2 May 2017
SINGAPORE GUIDELINE FOR GOOD CLINICAL PRACTICE, Oct 2009

4 Understand what to do next

What is the Next Step to File a CRM-N?

- I am the Lead Party responsible to file a CRM-N for a regulated clinical trial.
  - Yes → Contact your institutional clinical trials unit for help to file the CRM-N as part of your CTA/CTN/CTC application.
  - No ↓
- I am the Lead Party responsible to file a CRM-N for non-regulated clinical research.
  - Yes → Contact your institutional Research Office for help to file a standalone CRM-N through HSA's PRISM system.
  - No ↓
- My collaborator, vendor, importer or local manufacturer is the Lead Party responsible to file a CRM-N for non-regulated clinical research.
  - Yes → Contact the Lead Party to file a standalone CRM-N. Sponsors of non-HSA-regulated clinical research may be required to endorse the CRM-N that is to be submitted by the importer or local manufacturer. Contact your institutional RO for help.

A **CRM notification acknowledgement** will be generated and sent to sponsor, importer and manufacturer. It remains valid for 1 year for unregulated clinical research, or throughout duration of clinical trial i.e. until "last-patient-last-visit" LPLV for regulated clinical trials.

Result

We used the developed self-assessment matrix to evaluate the CRM-N needful on 3 internal projects prior to Institutional Review Board (IRB) submission. The developed guide was able to provide advice and support to PI(s) in the identification of the lead party for CRM-N compliance.

Conclusion

The identification and assessment of CRM-N leads in multi-parties device development and validation projects may indeed be complex. A well-defined, and transparent tool would be useful in ensuring timely application of CRM-N to HSA.