15 DECEMBER 2015

INTRODUCTION OF NEW REGULATIONS FOR CONTROLS ON CLINICAL RESEARCH MATERIALS FOR USE IN CLINICAL RESEARCH INCLUDING REGULATED CLINICAL TRIALS

(A) PROPOSED HEALTH PRODUCTS (THERAPEUTIC PRODUCTS AS CLINICAL RESEARCH MATERIALS) REGULATIONS 2015

(B) PROPOSED HEALTH PRODUCTS (MEDICAL DEVICES) (AMENDMENT) REGULATIONS 2015

CONSULTATION PERIOD: 15 December 2015 to 15 January 2016

INTRODUCTION

Current System for Approval of Clinical Trial Materials

1. For clinical trials on medicinal products that are currently regulated by HSA, Clinical Trial Certificates (CTC) are issued upon approval of the clinical trials. For the importation of these medicinal products for the purposes of the clinical research, Clinical Trial Material (CTM) import approvals are also issued by HSA to the sponsors of the trial.

2. For clinical research on medical devices that are currently not regulated by HSA, Clinical Trial Material – Medical Devices (CTM-MD) import approvals are issued to the sponsors of such trials to facilitate the importation and supply of medical devices for the purposes of the clinical research.

Proposed System for Approval of Clinical Research Materials

3. Upon the transfer of controls of pharmaceutical products to the Health Products Act, the legislative approach for the import and supply of medicinal

products, therapeutic products and medical devices for use in clinical research, including regulated clinical trials, will be streamlined and simplified. To simplify the approach, a unified term called the **Clinical Research Materials (CRM)** will be used to define these types of products for clinical research.

4. CRM refers to any medicinal products, therapeutic products or medical device, whether registered or not, that is intended to be administered or used for a clinical purpose in accordance with the research protocol in any clinical research involving human subjects. CRM may be imported (overseas source), locally manufactured or procured from commercial sources (local source).

5. The purpose of the new regulations for the controls on **Clinical Research Materials (CRM)** is to provide a simplified and harmonised regulatory approach to the handling of medicinal products and therapeutic products as CRMs under the Medicines Act and Health Products Act[1] respectively. The Health Products (Medical Devices) Regulations will also be amended to harmonise the regulatory control for the use of medical devices as CRM.

6. Access to CRM for importation and supply for use in local clinical research will be facilitated via a notification system, which will replace the current import permit issuance system. For CRM that is imported, or supplied by a local manufacturer, a CRM notification is required prior to the import, or supply by the local manufacturer, respectively. To further streamline the regulatory process and reduce the regulatory impact on stakeholders, the CRM notifications for trials regulated by HSA may be made as part of the clinical trial application/notification to HSA (i.e. there is no need for a separate notification process).

7. Duties and obligations are imposed on the local manufacturers, importers, suppliers (including sponsors) of CRM to ensure:

a. Restriction of supply of CRM to IRB-approved clinical research only;

[1] *Upon the transfer of clinical trials regulations of therapeutic products to the HPA, a CRM that is a therapeutic product or medical device would be regulated under the Health Products Act, whereas a CRM that is a medicinal product (e.g., cell- and tissue-based products and gene therapy products, complementary health products investigated for therapeutic purpose) would continue to be regulated under the Medicines Act.*

b. Proper record keeping to assure traceability, accountability and appropriate handling of CRM;
c. Quality of the CRM; and
d. Proper reporting and management relating to safety and defects of CRM.

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

8. All local importers and manufacturers are responsible for ensuring that the imported or locally manufactured CRM is of appropriate quality standards (i.e. conforms with applicable standards of strength, quality, purity, safety and/or performance for that product) to minimise risks to research subjects arising from the use of the product.

9. In addition, the following duties and obligations will apply to the following parties:

<u>Manufacturers</u>

a. Keep records of the manufacture, assembly and testing of CRM;
b. Keep records of supply of CRM; and
c. Ensure appropriate labelling of supplied CRM

<u>Importers</u>

a. Keep records of receipt and supply of imported CRM; and
b. Ensure appropriate labelling of supplied CRM

<u>Suppliers</u>

a. Keep records of receipt and supply of CRM; and
b. Ensure appropriate labelling of supplied CRM

<u>Sponsors</u>

a. As suppliers, keep records of receipt and supply of CRM;

b. As suppliers, ensure appropriate labelling of supplied CRM;
c. Ensure disposal or export of unused locally manufactured or imported CRM after completion or termination of research;
d. Keep records of disposal or export of unused CRM; and
e. Notify HSA of any serious, unexpected adverse drug reactions (USADR[2]), or device defects and adverse effects[3], occurring in a subject within specified timelines.

Any person who intends to recall any CRM are required to notify HSA of the recall within specified timelines.[4]

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[2] For events that result in death and are life-threatening, the timeline is to notify HSA within 7 days and for other USADRs, the timeline is within 15 days.

[3] For defects or effects representing serious threat to public health, the timeline is within 48 hours. If it leads to death or serious deterioration to patient's health, the timeline is within 10 days. If a recurrence could lead to death or serious deterioration to patient's health, the timeline is within 30 days.

[4] For recall of CRM, the timeline is within 24 hours of recall.