15 DECEMBER 2015

(A) PROPOSED HEALTH PRODUCTS ACT (AMENDMENT OF FIRST SCHEDULE) ORDER 2015

(B) PROPOSED HEALTH PRODUCTS (THERAPEUTIC PRODUCTS) REGULATIONS 2015

CONSULTATION PERIOD: 15 December 2015 to 15 January 2016

(A) PROPOSED HEALTH PRODUCTS ACT (AMENDMENT OF FIRST SCHEDULE) ORDER 2015

1. In order to bring the controls for pharmaceutical products under the HPA, amendment to the First Schedule of the Act will be necessary for this category of products to be specified and described in the Schedule, pursuant to Section 4 of the Act. With this, it is proposed that pharmaceutical products be introduced as a category of health products known as *"therapeutic products"*. This new category of health products will be specified in the first column of the Schedule, with the scope described in the second column of the Schedule.

2. The proposed description for *"therapeutic products"* is mapped against what is conventionally regarded as pharmaceuticals, i.e. chemical and biologic drugs. This is to ensure clarity in the types of products that would come under the regulatory regime for *"therapeutic products"*. Therefore, unlike *"medicinal product"* under the Medicines Act which is defined based solely on **purpose**, the proposed definition for *"therapeutic product"* includes an additional limb that describes the types of **active ingredients**.

3. The table below summarises the key differences between the scope of "medicinal product" compared to a "therapeutic product":

Purpose	Medicinal Product	Therapeutic Product
Treating or preventing disease	✓	✓
Diagnosing disease	✓	✓

Influencing, controlling or preventing contraception	✓	✓
Inducing anaesthesia	✓	✓
Preventing or interfering with the normal operation of a physiological function	✓	✓
Active Ingredient		
Chemicals & biologics	✗	✓

(B) PROPOSED HEALTH PRODUCTS (THERAPEUTIC PRODUCTS) REGULATIONS 2015

4. The key changes that will be introduced to the regulation of therapeutic product (TP) can broadly categorised into:

a) Changes to the licensing regime
b) Changes to post-marketing obligations

Proposed Changes to the Licensing Regime

5. HSA currently regulates the manufacture, import and supply of pharmaceuticals through product registration and the licensing of pharmaceuticals' dealers which includes manufacturers, importers and wholesalers.

6. The licensing regime under the HPA is designed as a modular system to control the same key control points (i.e. product approval, manufacturing, import and supply activities) and to amalgamate the licensing controls under a single medicines law. HSA has undertaken a thorough review of the existing framework in transferring the legislative controls from existing laws to the HPA. While there are fine-tuning to the licensing regime in moving over to the HPA, HSA will continue to work closely with the industry to minimise regulatory and business impact, so as to facilitate a smooth transition without compromising on public health and safety.

7. The key principle of the licensing regime under the HPA is an activity-based licensing regime for the registration, manufacture, import and wholesale of therapeutic products In Singapore. The level of licensing requirements and fees will

be calibrated according to the scale of activities and types of products dealt with by the company. Key proposed changes are as follows:

a) Activity-based licensing

As the HPA provides an activity-based licensing regime, Product Registrants (PRs) are required to hold Importer's Licence (IL) and/or Wholesalers' Licence (WL) if they are importing and/or wholesaling their own registered TPs. However, to facilitate the adoption of this new regulatory regime and ease the financial and regulatory impact, existing PRs who are required to hold new dealer licences will be given a 3-year grace period whereby IL and/or WL fees will be waived and time will be given to level up their compliance to GDP standard, as importers and/or wholesalers.

b) Stratified licence application fee based on types of products

IL and WL fees are stratified based on the types of therapeutic products (cold chain vs. non-cold chain) dealt with by the company. Importers and wholesalers of therapeutic products are required to comply with GDP standard and requirements to ensure that the quality of health products is maintained throughout the distribution chain. For example, companies that handle temperature sensitive therapeutic products (cold chain) are required to comply with cold chain requirements as specified in the GDP standard. The additional regulatory oversight and compliance requirements, as compared to non cold chain products, will have an impact on licensing fees to cover regulatory costs.

c) Bundling of licence application and reduction of bundled licence fees

To streamline administrative requirements, the application forms for IL and WL will be merged into a single application form. In addition, a single integrated audit will be conducted for both IL and WL as the same GDP requirements will be applied. Thus, there will be a reduction in the bundled licensing fee for companies who apply for both IL and WL at the same time due to the streamlined process. The Fee

Schedule is currently being reviewed and will be shared at a later stage.

d) Importer's Licence (IL) required for the import of TPs for specified purposes

Currently, companies importing TPs containing scheduled poisons for the following activities are required to hold a Form A Poisons Licence:

i. Import of unregistered TPs for patients' use;
ii. Import of TPs for Re-export;
iii. Import of TPs for supply to vessels/aircrafts;
iv. Import of TPs for non-clinical use in Singapore.

HSA's approval for each consignment is also required for import of unregistered TPs for patients' use while notification is required for import of TPs for re-export.

Under HPA, companies who import and supply TPs for the above activities will now be required to hold an IL so as to ensure proper record keeping and supply chain management to assure the quality of the TPs supplied.

Companies importing unregistered TPs for patients' use will be subject to GDP requirements as these TPs are intended for clinical use in Singapore. These companies will also be required to hold a WL for carrying out wholesale supply.

On the other hand, licensed healthcare institutions (HCIs), clinics and pharmacies that are importing and supplying unregistered TPs solely for their own patients' use will not be required to hold an IL or WL. The import and supply of these TPs by HCIs, clinics and retail pharmacies are meant for the use of respective patients under their care and is considered as part of their healthcare delivery service. There is no further distribution unlike in the case of a commercial trading company. Furthermore, the operations of HCIs, clinics and retail pharmacies are already separately licensed under the Private Hospital and Medical

Clinics Act (PHMCA) and Retail Pharmacy Licensing Regulations respectively. Hence, additional importer or wholesaler licensing would not be necessary.

HSA's approval of each consignment will continue to be required prior to importation of the TP by companies, HCIs, clinics or pharmacies. The introduction of a fee is currently being reviewed and will be shared at a later stage.

Companies importing TPs for re-export, supply to ships/aircrafts and for non-clinical use will not be subject to GDP audit requirements but are required to comply with the duties of importer and/or wholesaler as specified in the Health Products (TP) Regulations. These companies will need to hold an IL (with restricted scope of activities) and they may opt to apply for an annual IL or IL on a per consignment (single use) basis. The current requirement for notification of TPs imported for re-export will no longer be required.

e) <u>Form A Poisons Licence no longer required</u>

Form A Poisons Licence will no longer be required for the supply of TPs containing scheduled poisons. Poisons Act will however remain applicable to products (other than TPs) containing scheduled poisons such as Active Pharmaceutical Ingredients (APIs) and/or laboratory reagents etc.

Manufacturers will be exempted from holding a Form A Poisons Licence for the import of Active Pharmaceutical Ingredients (APIs) containing poisons which are used in the manufacture of their own TPs.

f) <u>Naming of Responsible Person(s) in IL & WL</u>

Under the Health Products (Therapeutic Product) Regulations, IL and WL holders will be required to name at least one Responsible Person (RP) in their respective IL & WL. The duties and responsibilities of the RP are stipulated in the draft TP Regulations. The RP named in an IL

or WL for the import or wholesale supply of pharmacy-only medicine or prescription-only medicine must be a registered pharmacist or such other persons as approved by HSA. It is already a current requirement that a Form A Poisons Licence holder for a company dealing in pharmacy-only medicines and prescription-only medicines must be a registered pharmacist or such other persons as approved by HSA. As the importer and wholesaler would no longer need to hold a Form A Poisons Licence upon the implementation of the TP Regulations, this requirement will be transferred to the naming of an RP in the IL and WL.

g) Compounding of Therapeutic Products in Hospitals and Clinics

Licensed hospitals and clinics may compound TPs without holding a Manufacturer's Licence subject to the prescribed conditions in the regulations. Compounding, in relation to a TP, means to formulate, mix, assemble, package or label the therapeutic product, with the intention of dispensing or administering the therapeutic product to a specific patient in accordance with the written instructions of a qualified practitioner. Proper temperature control for cold-chain products (temperature sensitive products) will also be required.

An expiry date in accordance to a specified reference publication (i.e. European Pharmacopoeia, British Pharmacopoeia, US Pharmacopoeia, or the National Formulary) must be stated when supplying a compounded TP. Stability studies must be conducted to support any variation of the shelf life beyond that specified in the reference publication. The records of these studies must be provided when requested by HSA.

Medical clinics compounding TPs must supply such TPs for their own patients only; and not for wholesale supply to other hospitals/medical clinics, unless approved by HSA. Hospitals may compound TPs and supply by wholesale to another hospital for specific patients' needs

without a wholesaler's licence. TPs prepared in this manner should not be further supplied to another 3rd party.

h) Compounding and manufacture of Therapeutic Products by Retail Pharmacies

Licensed retail pharmacies may compound TPs in accordance with valid prescriptions from qualified doctors and dentists, without holding a Manufacturer's Licence, subject to specified/prescribed (check) conditions in the regulations.

An expiry date in accordance to a specified reference publication (i.e. European Pharmacopoeia, British Pharmacopoeia, US Pharmacopoeia, or the National Formulary) must be stated when supplying a compounded TP. Stability studies must be conducted to support any variation of the shelf life beyond that specified in the reference publication. The records of these studies must be provided when requested by HSA.

Licensed retail pharmacies may also manufacture commercially unavailable TP for the purpose of supplying to vessels and aircrafts as required under the respective maritime and aviation legislation, subject to the prescribed conditions in the regulations.

i) Retail Sale of General Sale List (GSL) TPs via Vending Machines

The use of vending machines as an alternative supply channel for GSL pharmaceutical products will be allowed, subject to prescribed/specified (check) conditions to safeguard the interests of consumers:

i. The vending machine must be sufficiently equipped to ensure appropriate storage conditions for the medicines (temperature control, security).
ii. The medicines must be in appropriate consumer packs (i.e. adequate labelling and appropriate pack size).

iii. The name and contact information of the company (i.e. vending machine operator) must be prominently displayed on the vending machine.

Proposed Changes to Post-marketing Obligations

Duty to carry out risk management plan and submission of benefit-risk evaluation reports

8. HSA may require registrants to implement risk management activities to enhance the post-market surveillance and safety of therapeutic products in Singapore. This may be applicable to selected therapeutic products where safety concerns have been identified during product evaluation or post-approval, where additional pharmacovigilance or risk minimisation measures are necessary.

9. HSA may also require the registrants of certain registered therapeutic products to submit product benefit-risk evaluation reports (for example in the event where safety concerns are identified). When required, these reports should be submitted, at intervals of six months commencing from either the date of registration of the therapeutic product or its international birth date, for a period of two years; and thereafter, annually, for the next three years unless otherwise specified.

Duty to maintain records of defects and adverse effects

10. Every manufacturer, importer, or registrant of a therapeutic product must maintain a record of every event or occurrence that reveals any defect in the therapeutic product, or that concerns any adverse effect arising from the use of the therapeutic product. Such record will need to be produced for inspection by the HSA as and when required.

Duty to report defects and adverse effects

11. Every manufacturer, importer, supplier or registrant of a therapeutic product must upon becoming aware of:

a) Any defect in the therapeutic product, report the defect to HSA within 48 hours if the information relates to any defect that represents a serious threat to persons or public health; and within 15 days for all other defects, from the time the manufacturer, importer, supplier or registrant first receives notification of the defect.

b) Any event or occurrence that relates to a serious adverse reaction, report them to HSA immediately, but in any case no later than 15 days from the time the manufacturer, importer, supplier or registrant first becomes aware of the serious adverse reaction. This timeline is harmonised with international reporting timelines.

HEALTH SCIENCES AUTHORITY