RESPONSE TO FEEDBACK RECEIVED FROM THE PUBLIC CONSULTATION ON THE PROPOSED REGULATION FOR ACTIVE INGREDIENTS UNDER THE HEALTH PRODUCTS ACT

FREQUENTLY ASKED QUESTIONS

DEFINITION

1. What are Active Ingredients?

Under the Health Products Act 2007, Active Ingredients are defined as any substance or compound that is usable in the manufacture of a health product as a pharmacologically active constituent.

The scope of the Health Products (Active Ingredients) Regulations 2023 applies to active ingredients specified in The Schedule that are usable in the manufacture of the following health products:

- Therapeutic Products
- Cell, Tissue or Gene Therapy Products that are more than minimally manipulated cell or tissue
- Medical Devices

[1]Minimally manipulated refers to any processing of the cell or tissue stated below that does not alter the cell's biological characteristics or functions, or the tissue's structural properties. Refer to HSA | Regulatory overview of cell, tissue or gene therapy products.

Some examples of substances which are not considered Active Ingredients:

a) Multipotent stem cells which require further differentiation into pharmacologically active cells
b) Viral vectors used for *ex vivo* genetic modification of cells
c) Cell banks which require more than minimal manipulation before formulation into a CTGTP or used for production of a Therapeutic Product

TRANSITION APPROACH, APPLICATION PROCESS AND FEES

2. What is the transition approach for existing companies in the implementation of the Health Products (Active Ingredients) Regulations 2023? What are the fees for the new licences?

The Health Products (Active Ingredients) Regulations 2023, including the full list of fees is targeted for gazette and implementation in December 2023. To assist companies in the transition; existing importers, wholesalers and manufacturers of Active Ingredients will be given a 3-month grace period to apply for the required licences in PRISM following the implementation of the regulations.

Existing companies include companies that currently hold valid Form A Poisons Licences for dealing in Active Ingredients or hold valid GMP Certificates for manufacturing of Active Ingredients. HSA will share more information regarding the transition approach with affected industry stakeholders in due course.

LICENSING AND REGULATORY REQUIREMENTS

3. What are the licences, regulatory requirements and the applicable standards required for dealing in Active Ingredients?

Licences are required to import, wholesale or manufacture Active Ingredients that are specified in the Schedule to the Health Products (Active Ingredients) Regulations 2023.

A company holding a Manufacturer's Licence for Active Ingredient is required to comply with the current version of the PIC/S Guide to Good Manufacturing Practice for Medicinal Products – Part II (PE 009) which is published on the PIC/S website.

A company holding an Importer's Licence or Wholesaler's Licence dealing in Active Ingredients used for the manufacture of health products for local clinical use is required to comply with the current version of the HSA Guidance Notes on Good Distribution Practice (GUIDE-MQA-013) which is published on the HSA website.

Activities	Requirements
Manufacturing of Active Ingredients specified in the Schedule to the Health Products (Active Ingredients) Regulations 2023 and usable in the relevant health products.	• Manufacturer's Licence
Importing Active Ingredients supplied for manufacture of health products for local clinical use.	• Importer's Licence (Full Scope)
Importing Active Ingredients solely for export.	• Importer's Licence (Limited Scope) • A separate Wholesaler's Licence is not required for export of the Active Ingredients. • Supply of Active Ingredients for use in the local market is not allowed.
Importing Active Ingredients for non-clinical purposes such as scientific research ,reference standards, or other applications not involving use on or by humans.	• Importer's Licence (Limited Scope) • A separate Wholesaler's Licence is not required for supply.
Wholesaling Active Ingredients supplied for manufacture of health products for local clinical use.	• Wholesaler's Licence

4. With the issuance of the Active Ingredients Manufacturer's Licence / Importer's Licence, is the Form A Poisons Licence (FAPL) still required for importing Active Ingredients? When is a FAPL required?

With the implementation of the Health Products (Active Ingredients) Regulations 2023, a licensed manufacturer of Active Ingredients will no longer need to hold a FAPL and Active Ingredients Importer's Licence to import Active Ingredients used for manufacturing activities (e.g., quality control testing, re-processing, validation activities, etc) carried out in accordance with the scope of the Manufacturer's Licence. A single Active Ingredients Manufacturer's Licence would meet the regulatory requirements.

Similarly, a licensed Importer of Active Ingredients will not require a FAPL to import Active Ingredients.

The FAPL will remain applicable for companies dealing with products, such as veterinary products and test kits / reagents that contain Poisons. These products are not active ingredients as they are not usable in the manufacture of a health product as a pharmacologically active constituent.

5. What are the requirements for importing an Active Ingredient used for the manufacture of a health product used only in clinical research?

The importer is not required to hold an Active Ingredients Importer's licence for importing an AI used in the manufacture of a health product for clinical research. However, a notice to HSA is required prior to the import. HSA will provide more details on this notification on the HSA website.

6. What are the requirements for storage and wholesaling of Active Ingredients?

(i) Are third party warehouses used for storage of Active Ingredients required to be licensed?

Third party warehouses engaged by the licensed importers and wholesalers to provide services for storage and delivery of Active Ingredients are not required to be licenced. However, importers and wholesalers are responsible for ensuring that third party warehouses comply with regulatory requirements. All warehouses, including third party warehouses will be listed in the Active Ingredients. Importer's and wholesaler's licences are inspected by HSA to ensure compliance with regulatory requirements such as Good Distribution Practice standards, where applicable.

(ii) What does it mean in the legislative requirement that Active Ingredient must be stored in a place that is reserved solely for the storage of Active Ingredients?

Companies must ensure proper systems for storage of Active Ingredients. When Active Ingredients are stored together with other products (e.g. chemicals, etc) in the same warehouse, there should be measures to ensure that that the Active Ingredients are stored in a manner to allow proper traceability and to prevent mix-ups or cross contamination.

(iii) What is the rationale behind the requirement for Active Ingredients to be kept separate from foodstuffs and empty containers in which foodstuffs have been kept during transportation?

This requirement is to avoid any risks of cross contamination. This is also an existing requirement under the Poisons Rules.

(iv) What should companies ensure before supplying Active Ingredients by wholesale?

To ensure that Active Ingredients are supplied legitimately, the wholesaler must before the supply:

a) ensure that there is an order in writing, signed by the recipient, stating the recipient's name and address, trade, business or profession, and the name and total quantity of the active ingredient to be supplied;
b) be satisfied that the recipient carries on the trade, business or profession stated in the order mentioned in paragraph (a) and that such trade, business or profession is one in which the active ingredient is used.

The wholesaler must also ensure that proper records of supply are kept.

DUTIES OF LICENSEE

7. What are the requirements for Responsible Persons (RP) named in the Active Ingredients Importer's and/or Wholesaler's Licence?

The company (or licensee) must appoint competent personnel, known as the Responsible Person (RP), to be responsible for compliance to the duties and obligations for licences held. Where GDP standards are applied, the RP shall be responsible for implementing and maintaining an effective quality system.

In general, the RP should be a qualified pharmacist when dealing in Active Ingredients that are intended for manufacturing relevant health products for local clinical use. HSA will publish further details and guidelines on the duties of responsible persons named in the importer's Licence and Wholesaler's Licence on HSA's website.

8. Do Active Ingredients manufacturers need to inform HSA when recalling an Active Ingredient?

Active Ingredients manufacturers who intend to recall a defective or suspected to be defective Active Ingredient are required to notify HSA. HSA will share more details on when and how to notify HSA during a recall on the HSA website.