



## NEW INITIATIVES FOR REGISTRATION OF THERAPEUTIC PRODUCTS

Dear Industry Stakeholders,

As part of HSA's ongoing initiative to streamline the regulatory controls for health products, the Therapeutic Products Branch, Health Products Regulation Group is pleased to share the following new initiatives.

### Highlights of New Initiatives

#### 1. Introduction of MIV-2 'Do-and-Tell' Approach

A new "Do-and-Tell" option will be introduced for a list of specified post-approval minor variations (MIV-2) to allow companies to implement minor administrative changes without prior approval from HSA. This option aims to enable timely implementation of changes by companies as well as enhance regulatory efficiency. Companies may bundle all changes effected and notify HSA via a single MIV-2 application within 6 months of implementation. Please refer to the attached **Quick Guide** for more information.

Appendices 13 and 14 of the Guidance on Therapeutic Product Registration of Singapore will be updated to include the list of Do-and-Tell MIV-2. The updated versions of the appendices will be published on 15 Jan 2019. With this initiative, we hope to reduce the regulatory submission burden and allow greater flexibility for companies in terms of submission planning.

#### 2. Re-categorisation of Post-approval Variations (MAV-1 and MIV)

##### a) Amendment to definition of Major Variation (MAV-1) – Exclusion of concomitant administration of vaccines

The inclusion of clinical information on concomitant administration of vaccines in the product label will be re-categorised from MAV-1 to MIV-1. This is part of HSA's on-going efforts to refine our regulatory approach, taking into consideration that such updates relating to the potential interference (or the lack of) between co-administered vaccines do not entail an extension of use of the product. With this, the definition of MAV-1 will be amended to exclude variations related to concomitant vaccines administration.

##### b) Re-categorisation of MIV-1 to MIV-2

The following MIV-1s will be re-categorised to MIV-2s as part of a risk-based approach to simplify the regulatory filing for safety/administrative changes:

- Alignment of the Package Insert/Patient Information Leaflet of generic drugs with the corresponding current labels of the Singapore Reference Product
- Addition or amendment of information on "Instructions for Use" for products with special delivery system/device (e.g. transdermal patches, inhalers, prefilled syringes, etc)

- Addition or amendment to the Drug interactions and overdose sections that result in strengthening of safety information or restriction of use.

### 3. Revision of Guidance on Therapeutic Product Registration in Singapore and Related Appendices

#### a) Revision of site-specific stability data requirement

For the registration of multiple primary packagers, the stability data requirement has been streamlined to remove primary packager site-specific data, provided that the same container closure system is used for all sites. This applies to new drug applications, generic drug applications, and post-approval variations.

The stability data requirements for drug product will be further aligned for both chemical and biological therapeutic products. Please refer to the revised Chapter C ('Stability Data of Drug Product') of the Guidance for more information.

#### b) Revision of Appendix 13 (Guideline on Minor Variation Applications for Chemical Therapeutics Products)

The checklists for MIV-1 and MIV-2 applications will be updated, the highlights are as below:

- Addition or replacement of alternative site for primary packaging for a non-sterile product may be submitted as a MIV-2 application (new checklist).
- Addition of a new checklist for "*Change of Specification of Drug Product*". This change was previously included under "*Change of Specification of Drug Substance (where CEP is not available)*".
- Requirement for a MIV-1 submission for the deletion of a specification parameter which may have a significant effect on the quality of the drug substance or drug product, vis-a-vis MIV-2 submission for the deletion of a non-significant specification.
- No variation application is required for changes in the supplier of the primary packaging material, provided that the type of primary packaging material and specification remain unchanged.
- Addition of two MIV-2 Checklists – "*Submission of CEP for an approved drug substance manufacturer*", and "*Change of Specification of starting material*".
- Deletion of "*Change in Name and/or address of Product Registrant*". This change should be submitted via [Transfer@PRISM](mailto:Transfer@PRISM) instead.
- Other changes to streamline submission requirements ( e.g., checklist B8, C6, C12, C16, C22) as well as to strengthen certain checklists (e.g., checklist B5, B7, B15, C27), and clarification of conditions and/or documentation requirements.

Please note the checklist numbering will change with the above revisions. Applicant should ensure that the appropriate application type is selected during submission of MIV-1/2s applications in PRISM.

#### c) Creation of e-forms for Appendix 1 (Patent Declaration Forms) and 11A (DMF Submission Form)

The existing forms in Word format will be converted to an electronic pdf format as part of HSA's drive to digitalise business processes. With the digitised forms, it is no longer necessary to print, sign and scan the hardcopy forms.

**The above initiatives will take effect for applications submitted from 15 Jan 2019. The revised guidance documents will be published on the [HSA website](#) by this date.**

For enquiries, please [click here](#)

**Therapeutic Products Branch  
Medicinal Products Pre-Market Cluster  
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