APPENDIX 16 *GUIDELINE ON THE SUBMISSION OF RISK MANAGEMENT PLAN DOCUMENTS*

This document is intended to provide guidance on the submission of risk management plan (RMP) documents in support of NDA, GDA and MAV applications.

1 SUBMISSION REQUIREMENTS FOR DIFFERENT APPLICATION TYPES

All NDA-1 and biosimilar product applications must have an accompanying RMP submitted.

For other application types such as NDA-2 or 3, major variation application (MAV) or generic drug application (GDA), RMP documents may be requested by HSA on a case-by-case basis:

- For NDA-2, the request for RMPs may be in response to a new safety concern arising from a new route of administration.
- For MAV, the request may arise as a result of a new safety concern associated with a new indication that may require additional pharmacovigilance (PV) activities and/or risk minimisation activities (RMAs).
- For GDA, a RMP may be required if the innovator or reference product has safety concerns that have been identified to require additional local PV activities and/or RMAs.

2 DOCUMENTARY REQUIREMENTS

The required RMP documents should be attached in PRISM, Section 7 (Supporting Attachments) under *Other Supporting Documents*. The submission of the documents in hardcopy is not required.

2.1 NDA-1 and Biosimilar Product Applications

RMP documents required in support of NDA-1 and biosimilar product applications should be provided as part of the application dossier at the point of application submission.

The RMP documents should include the following:

a) Singapore-Specific Annex (SSA);
b) Latest version of the approved EU-RMP and/or US REMS (where available); and
c) Proposed local RMP materials (e.g. draft educational materials, if any).

During HSA's review of the application, if an updated version of the EU-RMP and/or US REMS becomes available, it should be submitted to HSA. Submission of the updated EU-RMP and/or US REMS should be made as soon as possible upon receipt of the updated documents to facilitate the timely review of the application. The relevant updates to the EU-RMP and/or US REMS should be highlighted in a cover letter. It is not necessary to submit updated versions of the EU-RMP and/or US REMS after the product applications have been approved, unless otherwise requested by HSA.

Please refer to Chapter E on Biosimilar Product Application Submission for further details on the vigilance requirements for biosimilar product applications.

2.1.1 Singapore-Specific Annex (SSA)

The SSA serves as documentation of the RMP to be implemented for the therapeutic product in Singapore.

A SSA template is provided at Appendix 16A.

The SSA template includes the following sections:

- Product information (product name and active ingredients);
- Safety concerns (important identified and important potential risks);
- Description of the proposed local PV activities;
- Description of the proposed local RMAs; and

- Additional information (if applicable).

For more details on the RMP requirements, please refer to the *Guidance for Industry – Post-marketing Vigilance Requirements for Therapeutic Products and Cell, Tissue and Gene Therapy Products.*

2.2 Other Application Types (NDA-2/3, GDA, MAV)

For other application types, routine submission of RMP documents at the point of application submission is not required. However, if deemed necessary, the company will be informed about the RMP documents that are required in support of the application during the evaluation process.

3 TIMELINES FOR SUBMISSION

3.1 NDA-1 and Biosimilar Product Applications

RMP documents required in support of NDA-1 and biosimilar product applications should be provided as part of the application dossier at the point of application submission.

For applications submitted via the full or abridged route, if the applicant is unable to submit the complete RMP documents before the acceptance of the application, a letter of commitment to provide these documents within 40 working days from the date of application acceptance will be required. If the documents are not received within the 40 working days, an Input Request (with corresponding stop-clock imposed) will be sent to the applicant for the submission of the RMP documents. For applications submitted via the verification route, the complete set of RMP documents has to be submitted prior to the acceptance of the application.

3.2 Other Application Types (NDA-2/3, GDA, MAV)

RMP documents requested by HSA in support of NDA-2/3, GDA, or MAV applications should be submitted within the timeline specified in the Input Request.

4 FINALISATION OF RMP DOCUMENTS

RMP documents will be reviewed together with the application dossier and the final local risk management activities to be implemented in Singapore will be discussed during the evaluation process.

All local RMP materials to be implemented in Singapore will have to be finalised before approval of the product application.

5 POST-APPROVAL UPDATES/AMENDMENTS

Post-approval revisions affecting the clinical use and/or safety content of the approved local RMP materials (e.g. educational materials) should be submitted for review and approval by HSA prior to distribution to the healthcare professionals. However, for revisions that do not affect the clinical use and/or safety content of the local RMP materials (e.g. editorial changes, administrative changes, corrections of typographical errors, and changes in address), a notification of the soft copy of the revised materials to HSA will be sufficient (i.e. approval from HSA is not needed). The revised materials may be distributed following the notification to HSA.

Post-approval revisions to the local RMP materials should be submitted using the online form.

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