APPENDIX 11 *GUIDELINE ON DRUG MASTER FILE (DMF)*

This document provides guidance for the submission and processing of a Drug Master File (DMF) in support of a therapeutic product application.

1 INTRODUCTION

A DMF is a reference that provides information about specific processes or components used in the manufacturing, processing, and packaging of a drug. The DMF contains information of a proprietary nature that is not available to the drug product manufacturer or to the applicant of a product registration submission.

The DMF is generally divided into two parts – an open (or applicant's) part and a closed (or restricted) part. The open part contains most of the information found in Module 3.2.S (ICH CTD) or Part II.S (ACTD) – i.e. sections S.1**,** S.2.1 and S.3 to S.7. The closed part contains the confidential information in section 3.2.S.2 – i.e. sections S.2.2 to S.2.6.

2 DOCUMENTARY REQUIREMENTS

The documentary requirements for an application making reference to a DMF are as follows:

(a) From the Applicant:

- the open part of the DMF in PDF format, as part of the submitted dossier;
- a copy of the Letter of Access; and
- a copy of the acknowledgement email from HSA on the receipt of the Letter of Access.

(b) From the Drug Substance Manufacturer (also referred to as 'DMF Holder'):

- the completed Online DMF Submission Form (click here);
- a cover letter that makes reference to the Response ID obtained from the Online DMF Submission Form;
- the complete DMF – i.e. both the open and closed parts – in PDF format-; and
- a colour scanned copy of the Letter of Access.

All documents from the DMF Holder must be provided in softcopy in a CD/DVD. The original hardcopies are not required.

The Letter of Access authorises HSA to refer to the DMF in support of an application for a therapeutic product. Thus, the Letter of Access should state the following:

- the name of the therapeutic product(s) to be registered (product name, dosage form and product strength);
- the local applicant (name, address and email contact) responsible for product registration; and
- a declaration that the local applicant and HSA will be notified of any change in the drug substance specification, the manufacturing process or any other aspects that will likely affect the product's quality or safety.

A sample of the Letter of Access is provided in Appendix 11B for reference.

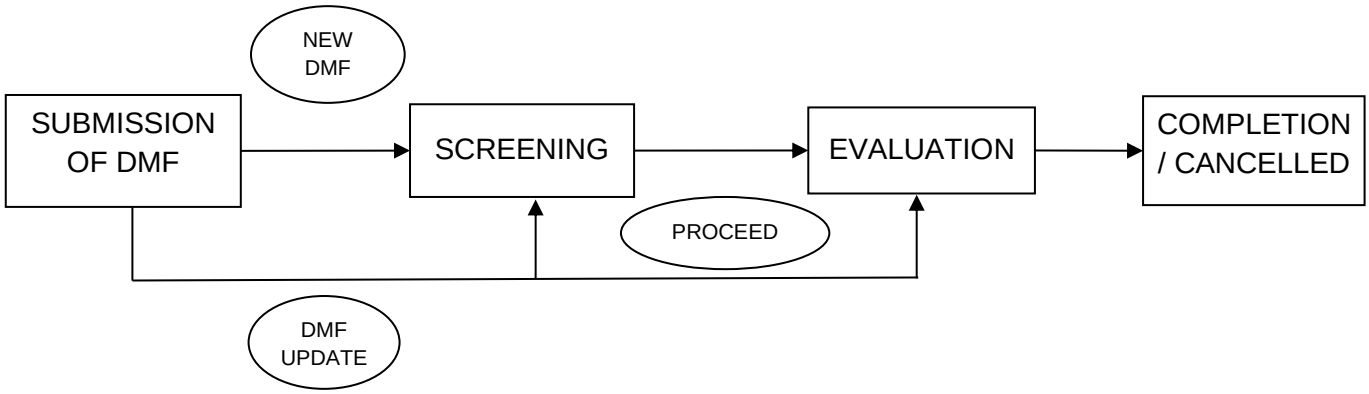
3 DMF SUBMISSION

The DMF Holder may submit the DMF directly to HSA to maintain confidentiality of the contents. The information contained in the closed part of the DMF will be regarded as confidential and will only be evaluated in support of the application(s) mentioned in the Letter of Access. The confidential information will not be disclosed to any third party without a written authorisation from the DMF Holder.

The DMF Holder must notify HSA of the submission using the Online DMF Submission Form [click here]. The Letter of Access and DMF must be submitted in softcopy via storage media such as CD/DVD ROMs. Upon receipt of the submission form and the softcopy files, HSA will assign a DMF number to the DMF and send an acknowledgement receipt via email. For future correspondence, the applicant and the DMF Holder should make reference to the assigned DMF number. If there are deficiencies within the closed part of the DMF, HSA will raise queries directly with the DMF Holder.

NOTE: A DMF number will only be assigned when the required documents are received in softcopy in a CD/DVD. Please **do not** submit hardcopy documents. The assignment of a DMF number does not constitute approval of the DMF – it is not approved or rejected.

4 LIFECYCLE FOR A DMF



At the screening stage, the DMF will be screened for completeness together with the NDA, GDA or MIV-1 application. Any screening queries on deficiencies in the open and/or closed part(s) will be sent to the DMF Holder. Screening queries on the open part will also be sent to the applicant together with the remaining screening queries of the product application for their information and necessary follow up with the DMF Holder, who will be providing the complete DMF response to HSA.

At the evaluation stage, the DMF will be evaluated together with the NDA, GDA or MIV-1 application. Any evaluation queries from the open and/or closed part(s) will be sent to the DMF Holder. Evaluation queries on the open part will also be sent to the applicant together with the remaining evaluation queries of the product application for their information and necessary follow up with the DMF Holder, who will be providing the complete DMF response to HSA.

If an application makes reference to an existing DMF version, the colour scanned copy of the original Letter of Access specific to the therapeutic product application should be provided by the DMF Holder. The Letter of Access may be submitted via the Online DMF Submission Form (click here). A copy of the same Letter of Access should be submitted by the applicant as part of the application dossier.

DMF Holders and applicants are responsible for maintaining and updating the DMF. When the DMF has been updated, the table of summary of changes (*Example 1*), the Online DMF Submission Form (click here) and the updated sections of the DMF in softcopy should be provided by the DMF Holder.

Example 1. Table of Summary of Changes

CTD section(s)	Current Version xx	Proposed Version xx	Rationale for revision
S2.1 Manufacturer	Manufacturer 1	Manufacturer 1 Manufacturer 2	Addition of manufacturer

If there are changes to the DMF that require post-approval variation(s) to be submitted for the drug substance or drug product, the DMF Holder must inform the product registrant(s) to file the necessary post-approval variation(s) (see Chapter F *Post-Approval Process*).

When the DMF is no longer relevant or required to support any therapeutic product, the DMF Holder may request for the DMF to be cancelled. Upon processing the request, HSA will notify the DMF Holder of the cancellation and the DMF is considered closed. Should the applicant wish to use the DMF again, it will be considered as a new DMF. The applicant and DMF Holder will be required to provide the relevant documents during the DMF submission process in support of the new product application.

REVISION HISTORY

Guidance Version (Publish Date)

TPB-GN-013-005 (Version 6; updated 30 June 2023)