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 dossier that contains detailed information about specific processes or components used in the manufacturing, processing, and packaging of a drug. It may be submitted to support a therapeutic product registration application as an alternative to the following sections of the CTD:

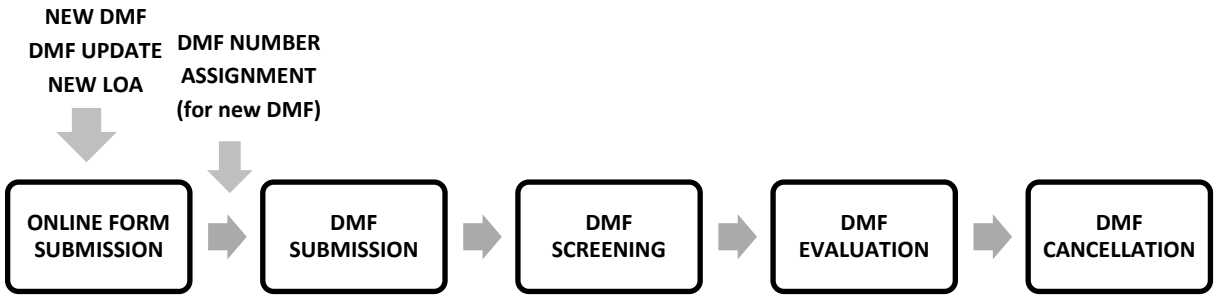
- Drug substance dossier (Module 3.2.S in ICH CTD or Part II.S in ACTD).
- Drug product intermediate dossier (Module 3.2.P in ICH CTD or Part II.P in ACTD).

The DMF is reviewed only in conjunction with the specific product registration application it supports. HSA does not issue standalone approval for DMF.

A DMF is generally divided into two parts – an Open (or Applicant) Part and a Closed (or Restricted) Part. For drug substances, the Open Part, which is shared with drug product manufacturers and/ or applicants, 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 through S.7. The Closed Part contains proprietary information typically provided in section S.2 – i.e. sections S.2.2 through S.2.6.

To maintain confidentiality of the DMF contents, the DMF Holder may submit the DMF directly to HSA. Information in the Closed Part is regarded as confidential and is not disclosed to the drug product manufacturer or the applicant submitting the product registration application.

2 DMF LIFECYLE AND PROCESS



The regulatory submission process begins when the DMF Holder submits the online *Notification of DMF Submission Form (Link) ("notification form")* to notify HSA of a planned DMF submission. The DMF Holder and applicant (where applicable) will be informed of the assigned DMF number (where applicable) and any subsequent steps within 20 working days. Both the DMF Holder and applicant must reference the assigned DMF number when submitting the DMF and in all subsequent correspondence with HSA.

The DMF Holder may then proceed with the DMF submission. Upon receipt of the complete DMF dossier, HSA will inform the DMF Holder and applicant (where applicable). Thereafter, the applicant may proceed to submit the product application. Following which the DMF will be screened for completeness. Any deficiencies in the Closed Part will be raised directly to the DMF Holder, while queries on the Open Part will be issued to both the DMF Holder and the applicant. The same process for queries applies during the evaluation stage after the application is accepted for evaluation.

Throughout the DMF lifecycle, the DMF Holder must notify HSA of any changes to the DMF through submitting a new notification form accompanied by a Table of Summary of Changes. When the DMF is used to support additional product applications, the DMF Holder must submit a new notification form together with the new Letter of Access.

Both DMF Holders and applicants are responsible for maintaining and updating the DMF and registered dossier. DMF Holders must promptly notify product registrants of any changes that may impact product quality or safety, and registrants must then file appropriate post-approval variations (see Chapter F *Post-Approval Process*). When a DMF is no longer required to support any products, the DMF Holder may submit a request to cancel the DMF. Upon processing the request, HSA will notify the DMF Holder and close the DMF.

3 DMF SUBMISSION REQUIREMENTS

The DMF Holder and the Applicant must coordinate their submission when referencing a DMF in a therapeutic product application following the process in Section 2. The detailed submission requirements for the DMF Holder and Applicant are provided in Section 3.1 and Section 3.2, respectively.

3.1 DMF Holder

3.1.1 Initial Notification

The DMF Holder must submit the online *Notification of DMF Submission Form* (click here) to notify HSA when submitting any of the following:

- New DMF
- New Letter of Access
- DMF update

The submission must include the Letter of Access and the Table of Summary of Changes, where applicable.

Letter of Access

The Letter of Access authorises HSA to reference the DMF in support of a therapeutic product application. The Letter of Access will remain valid throughout the DMF's lifecycle and is applicable across all DMF versions. The Letter of Access must specify 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 of commitment to notify both the local applicant and HSA of changes that will likely affect the product's quality or safety.

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

Table of Summary of Changes

DMF updates must be accompanied by a Table of Summary of Changes documenting the changes. For reference, an example is shown below:

CTD section(s)	Current Version xx	Proposed Version xx	Rationale
S.7. Stability	Retest period: 24 months	Retest period: 36 months	Update of retest period

3.1.2 DMF Submission

The DMF Holder is to submit:

- the complete DMF (both open and closed parts) in machine-readable PDF format; and
- a cover letter stating the Response ID of the *Notification of DMF Submission Form* and assigned DMF number.

All documents must be provided in softcopy, either via CD/DVD or through a cloud-based file exchange software (EasiShare). Guidance on submission via EasiShare is provided in the document titled "Key Points to Note when Preparing Documents for Therapeutic Product Application Dossier Submission via EasiShare" (click here).

3.2 Applicant

The Applicant must submit the open part of the DMF in machine-readable PDF format as part of the dossier, and a copy of the Letter of Access. The open part version must match the version submitted by the DMF Holder.

REVISION HISTORY

Guidance Version (Publish Date)

TPB-GN-013-007 (uploaded 30 July 2025)