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

This document provides guidance in the submission and processing of a Drug Master File (DMF) supporting a therapeutic product application or an application for a medical device containing a drug substance.

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.

If a drug substance is sourced from a manufacturer/company that is different from the drug product manufacturer/company, data on the manufacture, quality control and stability of the drug substance may be submitted in the form of a DMF. If the drug substance and drug product are manufactured by the same manufacturer/company, then either a DMF or a complete CTD S section can be submitted.

The DMF is 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; and
- a copy of the Letter of Access.
- a copy of email acknowledgement from HSA on the receipt of the Letter of Access.

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

- an electronically signed and completed DMF Submission Form in Appendix 11A;
- 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 the application for a drug product. Thus, the Letter of Access should state the following:

- the name of the drug 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.

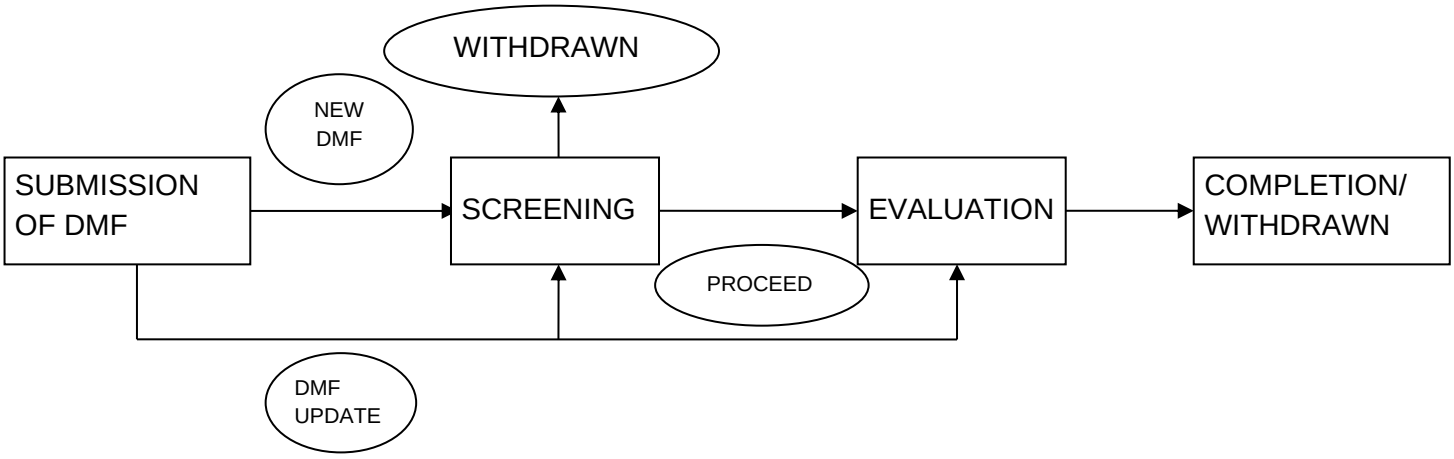
3 DMF SUBMISSION

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.

Upon receipt of the DMF Submission Form, Letter of Access and DMF from the DMF Holder in softcopy, 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. It is a separate document that is submitted in support of an application. When a DMF is no longer relevant or required to support the registration/continued registration of any therapeutic product/medical device, the DMF will be closed.

4 LIFECYCLE FOR A DMF



At the screening stage, the DMF will be screened for completeness together with the NDA, GDA, MIV-1 or medical device 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 response to HSA.

At the evaluation stage, following the acceptance of the therapeutic product/medical device application, the DMF will be evaluated together with the NDA, GDA, MIV-1 or medical device 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 response to HSA.

If a drug product/ medical device application makes reference to a currently listed DMF, the colour scanned copy of the original Letter of Access specific to the drug product/medical device application is to be provided by the DMF Holder. A copy of the same Letter of Access is to 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 DMF Submission Form 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 will result in a post-approval variation to the drug product, DMF holders must inform the product registrants to file a post-approval variation (see Chapter F *Post-Approval Process*).

When the DMF is no longer relevant or required to support the registration/continued registration of any therapeutic product and medical device, HSA will notify the DMF holder that 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)

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