

Drug Master Files: An Elective Regulatory Submission to the US Food & Drug Administration

July 2019

By: Gayatri Baregoda

Author Bio:



Gayatri holds a Master's degree in Management from Mitcon Institute of Management, India and a Bachelor's in Pharmacy from Gujarat Technological University, India. She has been working in the pharmaceutical market data research industry since last 4 years.

A Drug Master File (DMF) is a confidential and comprehensive document submitted by the companies which are involved in the manufacturing of an Active Pharmaceutical Ingredient (API), Drug Product (DP) / finished form, and pharmaceutical packaging materials to the US Food & Drug Administration (FDA). This document contains information on facilities, processes, articles used in the production, processing, packaging, and storing of one or more human drugs. The key purpose of the submission of DMFs is to provide reference material to a party other than the DMF holder, without disclosing the confidential and proprietary information in the file (such as manufacturing / quality control procedure information).

Overview of DMFs

A DMF is a voluntary regulatory submission made by the manufacturer of an Active Pharmaceutical Ingredient (API), Drug Product (DP) and pharmaceutical packaging material. There are no legal or regulatory requirements to file a DMF and it is submitted at the will of the DMF holder to assist their customers. DMFs are never approved or dis-approved and, in fact, the FDA reviews the DMF only when an API manufacturer incorporates it as a reference to support its Investigational New Drug Application (IND), New Drug Application (NDA), an Abbreviated New Drug Application (ANDA), and Export Application. However, a DMF is not an alternative for an IND, NDA, ANDA, or Export Application and is used to only support these filings.

The status of a DMF is “active” when it is acceptable by the FDA from an administrative point of view and “inactive” when it has been closed either by the holder or by the FDA. The Holders update their list of DMFs through annual reports (which is not used to make any changes in the DMFs). If the DMF has not had an annual report submission in the last 36 months, the FDA sends “overdue notification letters” to the holder and if the holder does not respond within 90 days, the DMF can be closed by the FDA.

There are five types of DMFs, as listed below:

Type I: Production site, facilities, operating procedures and people

Type II: Drug substance, drug substance intermediate, and material used in their preparation, or drug product

Type III: Packaging material

Type IV: Excipient, colourant, flavour, essence, or material used in their preparation

Type V: FDA accepted reference information

The Type I DMF has been phased out, thus currently only four types of DMFs are actively submitted to the FDA. The Type II DMF is the most common one, followed by Type III.

Requirements for DMF Submission

There are certain requirements for the submission of each DMF, such as:

- Submission of transmittal letter - The original copy of the letter should be submitted, and it must contain the type of DMF and its subject.
- Administrative information in detail - The administrative information should include the name of the DMF holder, corporate headquarter, manufacturing facility, contact person information and agent details (if any).
- Information in the DMF must be in English - If the DMF is submitted in a language other than English then it must be accurately translated, and a certification of translation must be attached with the DMF.
- Any changes in the DMF must be reported as amendments and the holder should notify the authorised parties about the changes in the file.

All new DMFs submissions from May 5, 2018 onwards, other than Type III DMFs, must be done using an electronic Common Technical Document (eCTD), a standard format used for submitting applications, amendments, supplements, and reports to the US FDA. For Type III DMF, this requirement will go into effect from May 5, 2020. The eCTD submissions should be in FDA fillable forms and must include electronic signatures to enable automated processing of the submission.

Significance of Holding a DMF

A DMF helps the holder company in shortening the process length of INDs, NDAs, ANDAs or Export Applications by reducing the total number of review cycles; and increasing the chances of approval in the first cycle. In addition, a holder with a large number of DMFs is considered to be more reliable in terms of quality,

regulatory standpoint, and ability to meet current Good Manufacturing Practices (cGMP) requirements. Thus, holding a DMF strengthens the position of an API manufacturer over its competitors by building customer's trust thereby increasing the revenue potential across the globe (as international customers may consider a holder company's product more authentic). It can also help in penetrating the high-entry barrier of the US market.

However, possession of a DMF for API or DP does not confirm that the company is eligible to manufacture or supply that product in the US.

Considering the growing need from buyers on finding more reliable and certified API manufactures, IQVIA Chemical Intelligence (formerly known as Chemical Info Services) provides access to thousands of API manufacturing companies with DMFs, Veterinary Master Files (VMFs), and European EDQM Certificates of Suitability (CEPs) across the globe. This data is updated every quarter in IQVIA Chemical Intelligence.

Conclusion

The key objective of a DMF is to support regulatory requirements of a drug to help in proving its quality, safety and efficacy. This helps in obtaining the marketing authorisation grant, as it accelerates the entire process. With the implementation of eCTD format from May 2018, the DMF submission procedure has become simple and easy as any API or DP manufacturer across the world can submit a DMF to the FDA using the FDA's online platform.

IQVIA™ Chemical Intelligence (formerly known as Chemical Info Services) is a leading information provider to purchasers, sellers and researchers in the Pharmaceutical and Chemical industries worldwide. To find out more, please click [here](#).