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Review Article

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Drug Master File- A Review

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Abstract

Drug master file "DMF" is a record that contains information on the practices, infrastructure, or resources utilized in or even during the production, processing, packaging, and storage of one or more human medicines. The chemistry, production and control of a drug component are contained in a DMF. When two or businesses collaborate to develop or produce a drug product, a DMF is submitted. The filing of DMF enables business for safeguard the intellectual property of its partner with adhering to legal specifications for the disclosure of processing information. Chemistry, stability, purity, production, packaging, impurity profile and cGMP status of a drug formulation available as detail in DMF. No single chemical entity will be marketed without researchers, especially medical researchers and specialists who labored for ensuring that they will win regulatory authority clearance; DMF need to submit to the Food and Drug Administration having two parts and five types as discussed in this review article.

Keywords: Drug Master File (DMF), Food and Drug Administration (FDA), Drug Regulatory Affairs, DMF Filing.

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1. Introduction

1.1.Definition of DMF

A DMF, or drug master file, is a written report submitted to the Food and Drug Administration that contains sensitive information on the practises, infrastructure, or resources utilised in or even during the production, processing, packaging, and storage of one or more human medicines. (1,2)

The Pharmaceutical company creates DMF and submits it exclusively based on its discretion to the relevant regulatory body in the target drug market. When two or more businesses collaborate on the research and production of a medication formulation or product, a DMF is often required to be filed. The DMF filing enables a business to safeguard its intellectual property alongside its partner while adhering to legal specifications for the disclosure of processing information. (3,4)

Detailed information regarding the active pharmaceutical ingredient (API), a completed drug formulation, or dose form is used to create DMF. In the US and Europe, it is referred to as the European Drug Master File (ASMF) and the US-Drug Master File (US-DMF), respectively. DMF include accurate and thorough information about chemistry, stability, purity, production, packaging, impurity profile, and cGMP status of any human dosage form containing a drug. (5,6)

DMF refers to the submission of data to the FDA for examination in support of a third party's submission. The data often relates to the Chemical, Manufacturing, and Controls (CMC) of a drug product component. Information on drug products or other non-CMC information may be included in a DMF. (Or) A DMF submission to the Food and the Drug Administration (FDA) may be used to offer private, in-depth details regarding the establishments, procedures, or items utilised in the production, processing, packing, and storage of one or more human drugs. (7,8)

1.2 Parts of DMF

DMFs typically consist of two parts: (9,10)

(1) Part of the applicant: The licence holder must evaluate this non-confidential information for marketing purposes.

(2) Restricted Part: This only has to be given to authorities and contains private information about the manufacturing process.

1.3 Types of DMF (1,7,9)

1.3.1 Type I DMF:

The manufacturing site, facilities, operational procedures, and employees are all covered by the type I DMF. The writer of this sort of DMF may give the FDA information so that it can carry out site investigations outside of the US. The layout and capacities of the equipment, as well as the manufacturing site, should all be fully described. A physical address, total area, and a map of the site must be provided by the holder. An illustration of the main production and processing regions can be used to demonstrate the operating layout. (1,7,9,11)

Table 1. Types of DMF

Sr.no	DMF types	Information
1	Type I	Data related to manufacturing units such as the name of manufacturing sites, facilities, operating procedures and professionals
2	Type II	Data related to the drug such as drug substances and intermediates, the materials involved in the manufacturing etc.
3	Type III	Data regarding the packaging material
4	Type IV	Data about the excipients, colorants, flavors, etc.
5	Type V	Reference information accepted by the FDA

1.3.2 Type II DMF:

Information about drug substances, drug substance intermediates, and materials utilised in the manufacture of a API or a drug formulations are included in Type II DMFs. The most typical DMF to be submitted is Type II, and it allows for the inclusion of dose from medications made under contract for another business that would file ANDA. (1,7,9)

1.3.3 Type III DMF:

An FDA-required document known as a Drug Master File (DMF) can be used to give private specific information on the facilities, procedures, or equipment utilised in the manufacture, processing, packaging, and storage of one or more human pharmaceuticals. Neither the FDA regulations nor the legislation necessitate the submission of a DMF. A DMF is only ever filed if the holder so chooses. An export application, an investigational new drug application (IND), a new drug application (NDA), an abbreviated new drug application (ANDA), an alternate DMF, or updates and amendments to these may all be supported by the information in the DMF. (1,7,9)

An export application, an IND, an NDA, or an ANDA are NOT substitutes for a DMF. It is neither approved nor disapproved. Only. The primary goal of a DMF is to protect the holder's proprietary information, such as a manufacturing technique, from disclosure. Additionally, it enables FDA reviewers to examine data to help applications submitted by one or more applicants. DMFs often cover Chemistry, Manufacturing, and Controls (CMC) of a drug product's ingredient, such as the active pharmaceutical ingredient, an excipient, or a packaging material. A DMF may contain information about drug products or non-CMC information. (7,12)

1.3.4 Type IV DMF:

Preparation Materials like Excipient, Colorant, Taste, and Essence fall within the category of Type IV DMF. These additives must be documented in terms of their specifications, testing procedures, and production process. Toxicological information regarding these materials must also be submitted in the same DMF.

New additives for which CMC and safety information is not readily available in the relevant rules or in the USP-NF must submit a DMF. A non-clinical safety of new excipient's assessments may be given in module 4 of the Type IV DMF or module 4 of a different Type V DMF. The safety data about the potential for infectious agent contamination of excipients obtained from animals have to provide and have to inform immediately to the appropriate parties. (9,11)

1.3.5 Type V DMF:

Type V DMF can be used to transmit information (such as data from non-clinical and clinical studies, shared system REMS, contract manufacturing facilities, sterilising procedures, and medical devices) that is not covered by Type II and Type IV. Device master files could include comprehensive details about certain manufacturing processes, techniques, or parts utilised for creation, medical device processing, or packaging. They might also include details about medical gadgets that have been finished. (1,6,13)

Table 2. The comparative study of DMFs between the US, EU, and India (11-15)

S.no	Parameters	US	EU	India
1.	Regulatory Authority	Food and Drug Administration (FDA)	CEP: European Directorate for Quality of Medicines and Healthcare (EDQM) ASMF: European Medicines Agency (EMA)	Central Drug and Standard Control Organization (CDSCO)
2.	Use of DMF in Support of Application	IND, NDA, ANDA	MAA	MAA
3.	Mandatory	No	No	No

4.	Information Provided	Drug Substance Intermediate, Drug Products, Flavours Etc.	Active Substance	API, Drug Products, Flavours, Colorants, etc.
5.	Fees for Assessment	Only for ANDA	No Fee	No Fee
6.	Submission in CTD Format	Required	Required	Required in Indian CTD format.
7.	Forms for DMF Filling	Not Applicable Except Type I DMF, Form FDA 3794	Not Applicable	Not Applicable
8.	Language	English	English	English
9.	Submission of DMF	eCTD format	eCTD format	eCTD format
10.	DMF Number Assigned by Reviewers	Yes	No	No
11.	Approved/Disapproved by Regulatory Authority	Not Approved and Only Accepted in Support of Applications	Only Accepted	Only Accepted
12.	Deficiency Letter	Applicable	Applicable	Applicable
13.	Changes and Approved	Applicable	Applicable	Applicable
14.	Appointment of In-Country Care Taker	Applicable	Applicable	Applicable
15.	Letter of Authorization	Applicable	Applicable	Applicable
16.	Closure or Withdrawal	Applicable	Applicable	Applicable
17.	Reactivation	Applicable	Applicable	Applicable

2. Mechanism of DMF Filing (1,7,9)

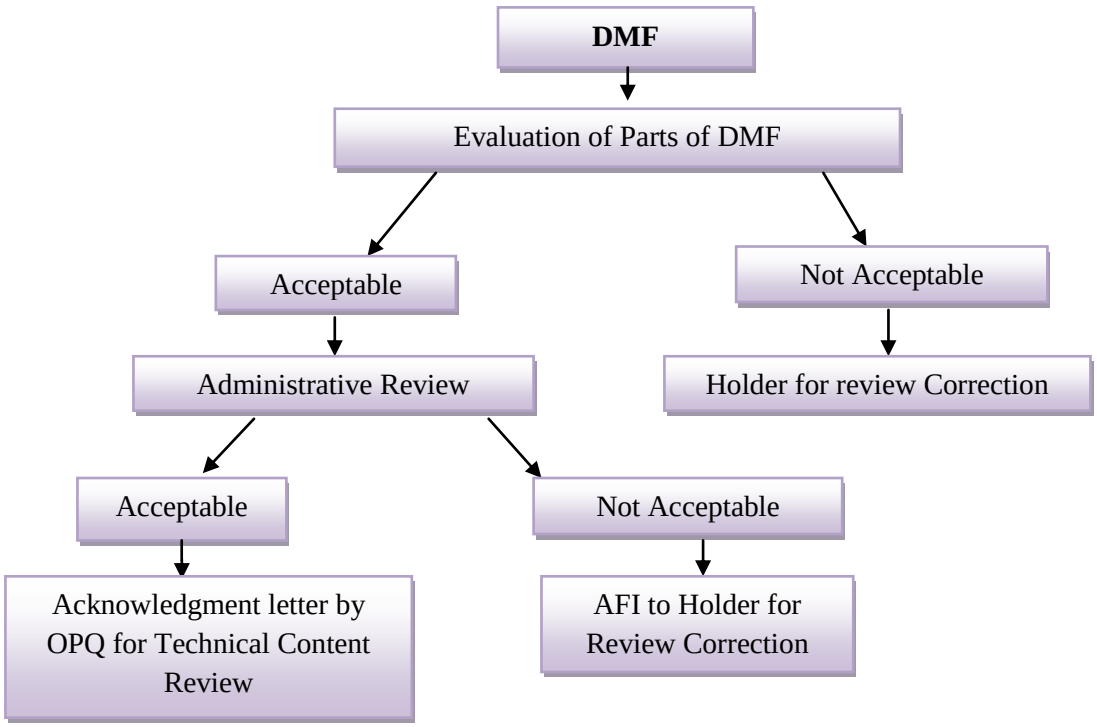

Figure 1. Flowchart for Mechanism of Drug Master File (1,7,9)

3. Conclusion

The drug master file contains complete & correct information about active pharmaceutical ingredient or finished drug dosage form and CMC data i.e., chemistry, manufacture, stability, purity, impurity profile, packaging of any drug product or excipient. The main purpose of DMF is to support regulatory requirements of a medicinal product to prove its quality, safety and efficacy and this helps in obtaining a market authorization grant.

Now from 2016, most of the countries will use the eCTD format for DMF submission.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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