Operational Facts of Master Files

A Model Master File (MMF) can be used to accommodate for portable, re-usable, generalizable, and sharable models with full model verification and validation (V&V) or settled with model V&V know hows, and should represent the best practice for a specific context of use in the regulatory setting.

MMFs can be viewed as a type of electronic Drug Master File[1] (DMF) submitted as an Electronic Common Technical Document[2] (eCTD). A single MMF Package (note, a MMF package may consist of multiple files as described in the sections below) with standardized data fields appropriate for regulatory submissions containing in silico methodologies and data can be submitted as a DMF.

The following operational aspects are reflected in the practice of drug master files including an MMF submission as a Type V DMF.

General Operational Facts:

- The information contained in the DMF may be used to support an Investigational New Drug Application (IND), a New Drug Application (NDA), an Abbreviated New Drug Application (ANDA), another DMF, or amendments and supplements to any of these.
- The submission of a DMF is not required by law or FDA regulation. A DMF is submitted solely at the discretion of the holder (i.e., owner).
- FDA neither independently reviews nor approves or disapproves a DMF. Technical contents of a DMF are reviewed only in connection with the review of an application.
- There are multiple types of DMFs.

For DMF holders:

- A DMF holder can authorize one or more applicants or sponsors to incorporate a DMF without having to disclose details to the applicants or sponsors. Only the FDA and the DMF holder (i.e., owner) have access to its proprietary content.
- A DMF holder can submit amendments to update a DMF at any time. An updated table of contents should be included with each submission.
- A DMF holder must notify each affected applicant or sponsor who they have shared their DMF or who has referenced its DMF of any pertinent change in the DMF to permit the sponsor/applicant to supplement or amend any affected application(s) as needed.
- Because of the proprietary information contained in the DMF, FDA deficiency on a DMF will be directed to the DMF holder and not to the authorized party.

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[1] https://www.fda.gov/drugs/forms-submission-requirements/drug-master-files-dmfs

[2] https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd

- Multiple DMFs for the same regulatory purpose can be developed and exist concurrently.

For authorized party (i.e., applicants, sponsors):

- An application may reference all or part of the contents of an existing DMF in support of the submission if the holder authorizes the incorporation in writing. The incorporation of a DMF must be accompanied by a copy of the DMF holder's letter of authorization.
- A sponsor or an applicant should apply the DMF within their regulatory application as applicable to the DMF type.
- The role of the DMF will be reassessed within each new application they support, even if it was referenced in a previous approved application.

List of DMFs:

- FDA performs an initial assessment of the completeness of a received DMF and publish a list of DMFs available to the public. The list of DMFs, which is updated quarterly, includes changes to the DMF activity status (A=active; I=inactive), DMF type, holder name and subject (title).