Drug Master Files

Important Guidance Information

Important information about Master Files transferred from CBER

IMPORTANT ADDRESS INFORMATION

Please note that the current address for the Central Document Room for filing original DMFs and subsequent DMF documents is now:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville MD 20705-1266

This site contains lists of Drug Master Files (DMFs) as well as information concerning submission of DMFs. See below for information regarding the current DMF Guideline.

The list of DMFs is current as of October 2, 2006, through DMF 19875. Changes to the DMF activity status, DMF type, holder name, and subjects made since the last update of August 8, 2006 are included. The lists are updated quarterly.

For people who downloaded the previous list (through DMF 19616 August 8, 2006) and do not wish to download the entire updated lists the following lists are available:

1. New DMFs since the last list.

2. A list of changes in DMF activity status, DMF type, holder name, and subject.

The lists are available in Microsoft Excel and in ASCII (tab-delimited). Please note that only ACTIVE DMFs have been sorted into different types.

For the Excel files, the following lists are provided as different worksheets within one Excel file.

- All DMFs
- Active DMFs
- Active Type II DMFs
- Active Type III DMFs
- Active Type IV DMFs
- Active Type V DMFs

The following lists are still provided as separate files.

- New DMFs since the last list
- Changes

The types of DMFs are:

- Type I Manufacturing Site, Facilities, Operating Procedures, and Personnel (no longer applicable)
- Type II Drug Substance, Drug Substance Intermediate, and Material Used in Their Preparation, or Drug Product
- Type III Packaging Material
- Type IV Excipient, Colorant, Flavor, Essence, or Material Used in Their Preparation
- Type V FDA Accepted Reference Information

All files zipped (2.6 MB) (updated 11/13/2006)

Excel	ASCII
New	New
Changes	Changes
All	All
	All Active
	Type II Active
	Type III Active
	Type IV Active
	Type V Active

“A” = Active
“I” = Inactive
“N” = Not an assigned number
“P” = DMF Pending Filing Review

INACTIVATION AND RETIREMENT OF DMFs

There are two reasons for a DMF to be listed as inactive:

1. The holder requested that the DMF be retired, closed, inactivated., or withdrawn.
2. For DMFs filed before September 30, 2003:
    a. There have been no amendments or annual reports submitted since it was filed or
    b. There have been no amendments or annual reports submitted since September 30, 2003.

Note that the status “Inactive” in the list does not distinguish among these categories.

According to the regulations regarding DMFs (21 CFR 314.420(c)),:

“Any addition, change, or deletion of information in a drug master file (except the list required under paragraph (d) of this section) is required to be submitted in two copies and to describe by name, reference number, volume, and page number the information affected in the drug master file.”

As discussed in the "Guideline for Drug Master Files" (September 1989), DMF holders should update their DMFs annually (see below under Annual Reports).

FDA is in the process of sending “Overdue Notification Letters” (ONLs) to DMF holders that have not been updated, i.e., no amendments or annual reports in three years. If a DMF holder does not respond to this letter within 90 days, the DMF is retired and is unavailable for review.

Some DMFs may be listed as inactive which are, in fact, still active. Every effort will be made t correct any errors.

QUESTIONS OR COMMENTS ABOUT DMFs

Please address ALL comments or questions regarding DMFs to dmfquestion@cder.fda.gov. All inquiries MUST have an entry in the "Subject" field of the e-mail. Due to concerns about viruses and the amount of "spam" received by this account, e-mails with subject fields that are blank or contain meaningless text strings or contain only question marks will not be opened.

Other inquiries unrelated to DMFs should go to druginfo@fda.hhs.gov.

GUIDANCES

DMF Guideline The version posted on the web is the current version. No revision is planned fo the immediate future. Please address question regarding the DMF Guideline to dmfquestion@cder.fda.gov.

Note: FDA regulations require that all submissions to INDs and NDAs that are in a foreign language have “complete and accurate translations.” The same is true for DMFs. A “certified translation” is not required.

MORE INFORMATION ABOUT DMFs

See http://www.fda.gov/cder/Offices/ONDQA/presentations/shaw.pdf

TYPES OF DMFs

Type I DMFs

Type I DMFs are no longer accepted per a Final Rule published January 12, 2000 (65 FR 1776). See Type V DMFs below.

Holders of Type II, III, and IV DMFs should not place information regarding facilities, personne or operating procedures in these DMFs. Only the addresses of the DMF holder and manufacturing site and contact personnel should be submitted.

Type II DMFs

Type II DMFs may be submitted in the format for "Drug substance" in the "Guidance for

Industry M4Q: The CTD - Quality". Note that this is not required.

Module 1 should contain the following administrative information:

- Addresses of DMF holder and manufacturing and testing facilities
- Name and address of contact persons and/or agents
- Agent Appointment letters
- Letters of Authorization

Drug Substance:

See the current Guideline for Submitting Supporting Documentation in Drug Applications for the Manufacture of Drug Substances. The Draft Guidance for Industry: Drug Substance: Chemistry, Manufacturing, and Controls Information has been withdrawn.

Drug Product:

See the Guideline For Submitting Supporting Documentation In Drug Applications For The Manufacture Of Drug Products The Draft Guidance for Industry: Drug Product: Chemistry, Manufacturing, and Controls Information has been withdrawn

Type III DMFs

The applicable Guidance for Type III DMFs is the "Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics: CHEMISTRY, MANUFACTURING, AND CONTROLS DOCUMENTATION" and Questions and Answers.

Type V DMFs

The following types of DMFs may be filed as Type V DMFs without requesting prior clearance from FDA.

- Manufacturing Site, Facilities, Operating Procedures, and Personnel for sterile manufacturing plants. See Guidance for Industry for the Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products.
- Contract Facilities for the manufacture of biotech products. See Draft Guidance for Industry: Submitting Type V Drug Master Files to the Center for Biologics Evaluation and Research

ELECTRONIC DMFS

See Guidance for Industry: Providing Regulatory Submissions in Electronic Format — Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications To make sure you have the most recent versions of the specifications referenced in this guidance please check Electronic Common Technical Document (eCTD). Companies are encouraged to submit their DMFs in electronic form, including updating current paper DMFs.

All Letters of Authorization for electronic DMFs should specify that the DMF has been submitted in electronic format.

Companies that wish to submit an annual report or amendment in electronic format may do so.

However, once the DMF holder has made an electronic submission every subsequent submissior must be in electronic format. In such cases DMF holders are advised to resubmit the entire DMF in CTD format as an amendment. This allows the DMF to be reviewable in its entirety using the electronic DMF rather than mixing paper and electronic formats. If there are any changes in the technical content of the DMF as a result of the reformatting, e.g. addition of new information, th cover letter for the amendment should specify what areas of technical information have been changed.

AGENTS

There is no regulatory requirement for an agent for any DMF, foreign or domestic. An agent for DMF purposes is not the same as an agent for the purposes of the Drug Listing and Registration System. (DRLS) According to a Federal Register Notice, November 27, 2001 (Vol. 6, No. 228), effective May 24, 2002, all foreign drug establishments are required to register with the Food an Drug Administration (FDA). As published, foreign firms are required to register and identify a United States agent.

All "Agent Appointment Letters" for DMFs should be sent by the holder. FDA recommends that such letters include the phrase "appoint AGENT NAME as the agent for DMF" rather than "authorize AGENT NAME to act as the agent for DMF," since the latter can be confused with a "Letter of Authorization". An "Agent Appointment Letter" may be included in an original DMF.

FDA recommends that all letters appointing a new agent, notifying FDA of a change in the agent's name or rescinding the appointment of an agent be sent as separate amendments, rather than being included in an Annual Report or other amendment. If a company acting as an agent changes its name, FDA recommends that the DMF holder issue a new Agent Appointment Lette

HOLDER NAMES

When the company that owns a DMF (DMF holder) changes its name, whether through sale of the company or simply a change in the company's name, the DMF holder should notify FDA in a separate amendment, rather than including the information in an Annual Report or other amendment. See Section VII.E. in the Guideline for DMFs for further recommendations on the procedure for transferring ownership. A change in the name of a company for registration purposes under DRLS will not change the DMF holder name.

In general FDA expects the manufacturer to be the holder. If a manufacturer (Company A) of a MATERIAL wishes to have the DMF submitted by another company (Company B) and Company B wishes to act as the holder, the DMF must include statements from both companies that Company B takes full responsibility for all the information in the DMF and for all the processes and testing performed by the manufacturer. The title of the DMF which will appear on the list of DMFs will be "MATERIAL manufactured by COMPANY A in LOCATION OF COMPANY A for COMPANY B."

ANNUAL REPORTS

According to the DMF Guideline, Annual Reports are **NOT** to be used to report changes in the DMF. Note that Annual Reports to DMFs are not REQUIRED by law or regulation.

> "Section VII.C.
>
> The holder should provide an annual report on the anniversary date of the original submission. This report should contain the required list as described in B.1. and should also **identify all changes and additional information incorporated into the DMF sinc**

the previous annual report on the subject matter of the DMF."

"VII. B.1.

A DMF is required to contain a complete list of persons authorized to incorporate information in the DMF by reference [21 CFR 314.420(d)]. The holder should update the list in the annual update. The updated list should contain the holder's name, DMF number and the date of the update. The update should identify by name (or code) the information that each person is authorized to incorporate and give the location of that information by date, volume, and page number."

BIOLOGICS MASTER FILES

Master Files submitted in support of products regulated by the Center for Biologics Evaluation and Research (CBER) should be submitted as BB-MFs. See the CBER web site for the products regulated by CBER.

NEW

As a result of the transfer for the review responsibility for a number of products from CBER to CDER, a number of Master Files held as BB-MFs have been transferred to CDER and are now DMFs. These DMF numbers are in the range of 18584 to 18686. Some of thee DMFs that were i the process of being transferred were retired by their holders. These are listed as "N = NOT AN ASSIGNED NUMBER."

BINDERS

See "FDA IND, NDA, ANDA, or Drug Master File Binders

Back to Top Back to Drug Information

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