U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Drug Master Files (DMFs)

This site contains lists of Drug Master Files (DMFs) as well as information concerning submission of DMFs to the FDA's Center for Drug Evaluation and Research (CDER). The list is updated quarterly, although there may be delays of up to a month. See below for information regarding the current **Guideline for Drug Master Files (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073164.htm)** (September 1989) (DMF Guidance).

IMPORTANT NEW INFORMATION
The FDA has published a Final Guidance "Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM333969.pdf)[45] (May 15, 2015) regarding electronic submissions. See Electronic DMFs below.

- **Download DMF Files**

QUESTIONS OR COMMENTS ABOUT DMFs

- Please address ALL comments or questions regarding DMFs to **dmfquestion@cder.fda.gov (mailto:dmfquestion@cder.fda.gov)** except for inquiries specifically related to DMFs filed under GDUFA. Questions related to DMFs submitted under GDUFA should be sent to **AskGDUFA. (mailto:AskGDUFA@fda.hhs.gov)**
- All inquiries MUST have an entry in the "Subject" field of the e-mail that indicates what the e-mail is about and how it relates to DMFs.
- 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.
- If the inquiry concerns a specific DMF, the DMF number should be in the subject field of the message.
- Other inquiries unrelated to DMFs should be sent to **druginfo@fda.hhs.gov (mailto:druginfo@fda.hhs.gov)**. Note that inquiries regarding the reporting category for a change in a DMF should be sent to the druginfo address.

DMF LISTS

The current list contains DMFs **RECEIVED** by March 31, 2015 for which acknowledgment letters were sent before April 8, 2015, as well as DMFs that have received a pre-assigned number but have not been submitted yet.

The list of DMFs is current as of March 31, 2015, through DMF 29221. Changes to the DMF activity status, DMF type, holder name, and subject made since the last update of December 31, 2014 are included.

The list is available in **Microsoft Excel and in ASCII (tab-delimited) (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm#dmffiles)**.

TYPES OF DMFs

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

STATUS OF DMFS

- "A" = Active. This means that the DMF was found acceptable for filing, administratively, and has not been closed.
- "I" = Inactive. This means a DMF that has been closed, either by the holder or by the FDA.
- "P" = DMF Received, Pending Administrative Filing review.
- "N" = DMF has a pre-assigned number but the DMF has not been submitted or the DMF has been cancelled. A DMF can be cancelled for a number of reasons, e.g., the holder withdrew the DMF during the administrative review or the DMF was transferred to another Center.

Note that the Administrative Filing review is not related to the "Initial Completeness Assessment," which is performed for Type II DMFs submitted to support ANDAs ONLY. **See GDUFA below (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm#GDUFA)**

The status conveys no information about whether a DMF has been reviewed for technical content or whether it has undergone a Completeness Assessment.

Overdue Notification Letters: DMFs must be current at the time of review. According to the regulations regarding DMFs (**21 CFR 314.420(c) (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.420)**):

> "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."

The DMF Guidance recommends that DMF holders update their DMFs annually (see below under **Annual Reports).**

In order to ensure that DMFs are current, FDA sends "Overdue Notification Letters" (ONLs) to DMF holders for DMFs that have not had an Annual Report submitted in the past three years. If a DMF holder does not respond with the submission of an Annual report to this letter within 90 days, the DMF may be closed by the FDA.

Reactivating a Inactive (Closed) DMF

An Inactive DMF can be returned to ACTIVE status only by submission of a REACTIVATION, which should contain a complete resubmission of the DMF, updated to meet current Guidances. The cover letter must specify that the submission is a "REACTIVATION."

GUIDANCES

Guideline for Drug Master Files (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073164.htm) (DMF guidance) The version posted on the web is the current version. Note that the address for submitting DMF documentation to the FDA in the Guidance has been superseded by the **Beltsville address** below. Please address questions regarding the DMF Guidance to **dmfquestion@cder.fda.gov (mailto:dmfquestion@cder.fda.gov)**.

MORE INFORMATION ABOUT DMFs

See Slides from **FDA Small Business Office Webinar Nov. 14, 2011 (/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM279666.pdf) and CDER's Small Business Assistance Office Webinar entitled "Drug Master Files (DMFs) under Generic Drug User Fee Amendments (GDUFA)" (http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM339118.pdf) on February 11, 2013.**

The recommendations in the DMF Guidance are, in general, still applicable. However the information below provides additional information or clarification of the recommendations in the Guidance. This information provided below falls into four categories:

Category 1: Recommendations which are no longer applicable due to changes in regulations or guidances.
Category 2: Additional clarification of recommendations in the Guidance.
Category 3: New information for aspects of DMF filing that was not in effect when the Guidance was written.
Category 4: Information related to the Generics Drug User Fee Act (GDUFA)

Address for Filing Original DMFs and All Subsequent DMF Documents (Category 3)

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

All submissions to an existing DMF that is in paper must be submitted in two copies in paper to the address above. Submissions via e-mail are not accepted.

This address should be used when submitting electronic DMFs via disc. **See Electronic DMFs.**

Paper DMFs may be submitted printed on two sides.

Review of DMFs (Category 3)

Administrative Review

The FDA does not send a notification to the submitter when any submission, including a DMF, is received by the document room. After receipt, the DMF undergoes an administrative review to determine whether it is administratively complete. This administrative review may take 2-3 weeks. If the DMF is acceptable from an administrative point of view, an Acknowledgement Letter will be issued, notifying the holder of the DMF number. At this point the DMF is "ACTIVE." If it is not acceptable from an administrative point of view, the holder will be notified of what deficiencies need to be corrected and the DMF remains "PENDING."

DMFs are subject to a complete review for technical information only under the following circumstances:

1. The DMF is ACTIVE.

2. The DMF holder submits a Letter of Authorization (LOA) in two copies (if a paper submission) to the DMF. If the DMF is electronic, the LOA should be submitted in Section 1.4.1. This LOA should contain the DMF number.

3. The holder sends a copy of the LOA to the authorized party (customer).

4. The customer submits an application to the FDA that contains a copy of the LOA. The copy of the LOA should be submitted in Section 1.4.2.

Complete Assessment

Type II DMFs to support ANDAs under GDUFA are subject to an initial "Completeness Assessment" under the conditions specified in the Draft Initial CA Guidance.

GDUFA (Category 4)

The Generics Drug User Fee Act (GDUFA) section of the **Food and Drug Administration Safety and Innovation Act" (S.3187) (http://www.gpo.gov/fdsys/pkg/BILLS-112s3187enr/pdf/BILLS-112s3187enr.pdf)** includes provisions for fees for DMFs, an initial completeness assessment , and communications with DMF holders. GDUFA applies only to Type II DMFs for drug substances (Active Pharmaceutical Ingredients (APIs)) used to support Abbreviated New Drug Applications (ANDAs). See definition of API below. It does NOT apply to any of the following DMFs:

- Type III, IV or V DMFs
- Any of the following Type II DMFs:
  - used to support only NDAs or INDs
  - API intermediates
  - material used in the preparation of APIs drug product manufacturing intermediates
  - drug products.

See also Slide 48 in CDER's Small Business Assistance Office Webinar entitled **"Drug Master Files (DMFs) under Generic Drug User Fee Amendments (GDUFA)" (http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM339118.pdf)**

See also the following Web sites:

- **GDUFA Web Site (http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/default.htm)**
- **Draft Guidance for Industry: Generic Drug User Fee Amendments of 2012: Questions and Answers (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM316671.pdf)**
- **Draft Guidance for Industry: Self-Identification of Generic Drug Facilities, Sites, and Organizations (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM316672.pdf)**
- **Q&A for DMFs under GDUFA (http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm319567.htm)**
- **Draft Guidance for Industry Initial Completeness Assessments for Type II API DMFs Under GDUFA (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM321884.pdf)**

The list of DMFs that have passed the Completeness Assessment and are available for reference by ANDAs under GDUFA is available at **http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM332875.xls (http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM332875.pdf17)**.

Currently, the list is updated weekly.

DMFs that have passed the Administrative review (have an active status) and have had the user fee paid are place in the queue for a Completeness Assessment. It is not necessary for there to be an LOA for the DMF to undergo a Completeness Assessment review. The time frame for the Completeness Assessment depends on workload and may take a number of weeks.

Pre-assignment of DMF Numbers (Category 3)

To request a DMF Pre-Assigned Number, see "**Requesting a Pre-Assigned Application number (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm114027.htm)**." Companies wishing to obtain a pre-assigned DMF number for a **Type V DMF** should obtain clearance to file a Type V DMF with the exception of DMFs for information regarding manufacturing site, facilities, operating procedures, and personnel for sterile manufacturing plants or for biotechnology products, which do not require clearance. In those two cases the request for a pre-assigned number should specify what the DMF covers e.g., Biotechnology Product Manufacturing Facility.

Format and Content of the Chemistry, Manufacturing, and Controls Section of an Application (Category 1)

The "Guideline for the Format and Content of the Chemistry, Manufacturing, and Controls Section of an Application" cited in the DMF Guidance has been withdrawn. DMFs should be submitted following the format recommended in the "**Guidance for Industry M4Q: The CTD - Quality (http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073280.pdf)**" (CTD-Q) and the "**Draft Guidance for Industry Submitting Marketing Applications According to the ICH-CTD Format —General Considerations (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073308.pdf)**" (CTD Guidance).

A Manual of Policies and Procedures (MAPP 5015.10) covering reviewer responsibilities for review of applications submitted using the **Question-based Review (QbR) format (/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM423752.pdf)** has been issued. All Type II DMFs for Drug Substances and Drug Products are recommended to be submitted using the QbR format, although this is not required.

- **Conversion to CTD**

Companies may convert an existing DMF in non-CTD format to CTD format. In such cases DMF holders are advised to submit an amendment containing all sections specified in the CTD format that are applicable to the material covered by the DMF. Each section should be complete and contain up-to-date information. For drug substances and excipients all sections of 3.2.S in Module 3 should be submitted. For drug products all sections of 3.2.P in Module 3 should be submitted. If there are any changes in the technical content of the DMF as a result of the reformatting, e.g. addition of new information, the cover letter for the new submission should specify what areas of technical information have been changed.

Type III DMFs may be submitted in CTD format, treating the finished product as if it were a drug product. e.g. the Materials of construction would be in P.1, the finished packaging material release specification would be in P.5.

DMFs that cover multiple items e.g. Type III DMFs for components of container-closure systems or Type IV DMFs for flavors, can be submitted in CTD format. The technical information can be in Module 3, following the outline in the Drug Product Section. The different sections within 3.2.P. can be populated as appropriate. Each product e.g. different flavors, would have a different name e.g. 3.2.P.[Flavor 1], 3.2.P.[Flavor 2]. Information that is common to different products e.g. analytical procedures can be accessed by reference (or links in the case of an **Electronic DMF) from the relevant section for that product e.g. 3.2.P.5.1 [Flavor 1] for specifications. (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm#EDMF)**

DMFs in CTD format should follow the recommendations in the Appendix "Granularity" the **ICH Harmonised Tripartite Guideline: Organisation Of The Common Technical Document For The Registration Of Pharmaceuticals For Human Use: M4 (http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/M4_R3_Organisation/M4_R3__organisation.pdf)**. This supersedes the recommendation in the DMF Guidance.

For conversion of a paper DMF to electronic CTD format, see **Electronic DMF.**

It is not necessary to submit all Modules i.e. it is not necessary to submit Module 4 and 5. However, all Sections within Module 3 S or P - should be submitted.

DMF holders submitting DMFs for Sterile Manufacturing can consult the Manual of Policies and Procedures 5040.1: **Product Quality Microbiology Information in the Common Technical Document - Quality (CTD-Q) (http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/ucm079570.pdf)**

Products manufactured at separate facilities do not need to be filed as separate sections unless the manufacturing processes are different. Note that the **Draft Initial CA (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM321884.pdf)** contains recommendations regarding the submission of DMFs for multiple processes.

Module 1 should contain the following information
Section 1.2: Cover Letter, **Statement of Commitment** and Generic Drug User Fee Cover Sheet (3794), where applicable

According to the **DMF Guidance (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073164.htm)** (Section IV.B.1.c), the Statement of Commitment is:

“A signed statement by the holder certifying that the DMF is current and that the DMF holder will comply with the statements made in it.“

- Section 1.3: Administrative Information
  - **1.3.1 Contact/sponsor/Applicant information**
    - **1.3.1.1 Change of address or corporate name**
      Can be used to supply addresses of DMF holder and manufacturing and testing facilities
    - **1.3.1.2 Change in contact/agent**
      Can be used to supply the name and address of contact persons and/or agents, including Agent Appointment Letter.
- Section 1.4: Reference Section
  - **1.4.1 - Letter of Authorization (LOA)**
    Submission by the owner of information, giving authorization for the information to be used by Authorized Party. An Agent Appointment Letter is NOT an LOA and should not be called “Letter of Authorization” and should not be submitted in Section 1.4.1.
  - **1.4.2 - Statement of Right of Reference**
    This section should be completed in an application (IND, NDA, ANDA, or DMF) submitted by the Authorized Party that references a DMF. It should contain a copy of the Letter of Authorization from the holder giving the Authorized Party permission to reference the DMF. If a DMF holder references other DMFs a list of those DMFs can be provided in this section, similar to Section 30 on **Form 356h (http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM082348.pdf)**used for NDAs and ANDAs. This is not the same as the list of authorized parties to be provided in 1.4.3.
  - **1.4.3 - List of authorized persons to incorporate by reference**
    This list should be submitted in DMF annual reports.
- Section 1.12.14 Environmental Analysis: See **Environmental Assessment**
- Section 1.14: A copy of the label, where applicable.

The language in the following sentence in the DMF Guidance, Section VII.B.1, has given rise to some confusion on the part of DMF holders.

“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)].”

It does NOT mean a list of individuals within the DMF holder’s company who are authorized to submit information to the DMF.

The language in the CFR is more explicit:

> “The drug master file is required to contain a complete list of each person currently authorized to incorporate by reference any information in the file, identifying by name, reference number, volume, and page number the information that each person is authorized to incorporate.”

English Translations of DMF in a Foreign Language (Category2)

FDA regulations (21 CFR.1(a)(1)) state:

“If any part of the application is in a foreign language, an accurate and complete English translation shall be appended to such part.”

The same is true for DMFs.

Debarment Certification for DMF Holders (Category 3)

According to the **Draft Guidance for Industry: Submitting Debarment Certification Statements (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM080584.pdf)**, DMF Holders are included in the category of “Persons whose services were used in any capacity in connection with the application” required under Section 306(k)(1) of the Food Drug and Cosmetic Act. DMF holders may include a Debarment Certification statement in their DMF.

TYPES OF DMFs

Type I DMFs (Category 1)

Type I DMFs are no longer accepted per a Final Rule published January 12, 2000 (**65 FR 1776 (http://frwebgate3.access.gpo.gov/cgi-bin/waisgate.cgi?WAISdocID=12883518412+2+0+0&WAISaction=retrieve)**). See **Type V DMFs** below.

Holders of Type II, III, and IV DMFs do not need to place information regarding facilities, personnel or general operating procedures in these DMFs. Only the addresses of the DMF holder and manufacturing site and contact personnel should be submitted. See **Administrative** Information in a DMF.

Type II DMFs (Category 1)

For Type II DMFs filed in CTD-Q format, Module 2 (QOS) is expected.

- Drug Substance

  Type II DMFs for drug substances may be submitted in the format for "Drug substance" in the "**Guidance for Industry M4Q: The CTD - Quality (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073280.pdf)**".(Category 3) Drug Substance.

  It is not necessary to include a Methods Validation Package (3.2.R.3). Methods Validation information should be submitted in Section 3.2.S.4.3.

  See also the ICH Guidance “**Q11 Development and Manufacture of Drug Substances**

(http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM261078.pdf)"

Guidance for Industry: ANDAs: Stability Testing of Drug Substances and Products: Questions and Answers (http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/guidances/ucm320719.htm)
DRAFT GUIDANCE

Note that **GDUFA** includes requirements for Type II DMFs for Active Pharmaceutical Ingredients (APIs).

Drug Product:

Type II DMFs for drug products may be submitted in the format for "Drug product" in the "**Guidance for Industry M4Q: The CTD - Quality (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073280.pdf)**".(Category 3) Drug Product.

It is not necessary to include a Methods Validation Package (3.2.R.3). Methods Validation information should be submitted in Section 3.2.P.5.3.

Separate DMFs should be submitted for drug substances and drug products.

Active Pharmaceutical Ingredient (API) (Category 4)

The term 'active pharmaceutical ingredient' means (SEC.744A(2) in GDUFA):

(A) a substance, or a mixture when the substance is unstable or cannot be transported on its own, intended—

(i) to be used as a component of a drug; and
(ii) to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the human body; or

(B) a substance intended for final crystallization, purification, or salt formation, or any combination of those activities, to become a substance or mixture described in subparagraph (A)"

Type III DMFs (Category 1)

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" (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070551.pdf)** and **Questions and Answers (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070553.pdf)**. (Category 3)

A Manual of Policies and Procedures covering reviewer responsibilities for review of Type III DMFs has been implemented. MAPP 5015.5 **CMC Reviews of Type III DMFs for Packaging Materials (http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/UCM205259.pdf)** This MAPP instructs reviewers to look for information regarding many packaging materials in the application (IND, NDA, or ANDA) for the drug product that utilizes the packaging material before reviewing the DMF. Much of the information needed for review can be provided directly to the applicant for inclusion in the application, thereby avoiding the need to review the DMF.

Type III DMFs may be submitted in CTD format. Single components and materials of construction may be submitted as if they were drug substances e.g., the preparation of the item should be in S.2. An assembled container closure systems may be treated as if it were a drug product e.g. the Materials of construction would be in P.1, the finished packaging material release specification would be in P.5.

Type IV DMFs (Category 3)

See relevant section in the DMF Guidance (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073164.htm) If toxicology studies are submitted in the same DMF (in paper) as the CMC information, they should be in a separate volume or volumes, although it is preferable for holders to submit such information as a separate **Type V DMF** . Toxicology studies in an electronic DMF for an excipient should be submitted in the appropriate module. See also the "**Guidance for Industry: Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients" (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079250.pdf)**

Note that, in keeping with the recommendation in the DMF Guidance, components of flavor mixtures should include a CFR citation, where applicable, in addition to any other reference, e.g. GRAS or FEMA references.

Type V DMFs (Category 3)

As specified in **21 CFR 314.420(a) (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.420)**(5), DMF holders wishing to submit a Type V DMF must obtain clearance from the FDA, with two exceptions (see below). Prospective Type V DMF holders should send their request to **dmfquestion@cder.fda.gov (mailto:dmfquestion@cder.fda.gov)**, including the following:

1. An explanation of the necessity for filing the information in a Type V DMF.

2. The rationale for not submitting the information in an IND, NDA, or ANDA.

3. The clinical division that will be reviewing the information, if applicable.

Exceptions to requirement for obtain clearance to file a Type V DMF

> Information regarding 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 (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072171.pdf)**. The Subject field should specify what the DMF covers i.e., Sterile Processing Facility.
>
> Information regarding manufacturing site, facilities, operating procedures, and personnel for biotechnology products. The Subject field should specify what the DMF covers i.e., Biotechnology Product Manufacturing Facility.

Administrative Information in a DMF (Category 3)

The elements of the administrative information that should be in a DMF are:

- The name and address of the holder
- The name and address of manufacturing facility
- For the contact person:
  - Name
  - Mailing Address
  - Telephone number
  - Fax number
  - E-mail address
- The name and address of the agent (if applicable)
- For the contact person at the agent (if applicable):

- Name
- Mailing Address
- Telephone number
- Fax number
- E-mail address

- **Statement of Commitment**

The appointment of an Agent is optional. See discussion below under "**Agents**".

Submission of Amendments, Annual Reports, and Letters of Authorization (Category 3)

To facilitate processing of documents that are submitted to an existing DMF, please list the Submission Type and the Category/Subcategory of the Amendment (Supporting Document) in bold type in the header on the transmittal letter. See list below. More than one Submission Type/Category/Subcategory can be used but all should be listed.

Example: If updated stability data is submitted at the same time as an Annual Report, the heading of the Cover Letter should state:

> Annual Report
> Original: Quality/Stability

FDA's database is structured as follows:

Application:

> Submission
>
> > Amendment (called "Supporting Document") in the database

Amendments (Supporting Documents) are named by a Category and Subcategory

For the Application Type "Drug Master File" the Submission Types are:

- Original: Information containing changes to technical information are filed in the "Original" submission. Note that a new DMF does not need a "Category" designation by the holder. See **Categories and Subcategories** below.
- Annual Report: There is only one Category with two Subcategories:
  - Annual Report
  - Amendment
- Letter of Authorization: There is only one Category with two Subcategories:
  - Letter of Authorization
  - Withdrawal of Authorization
- General Information (Reactivation, Closure Request, Administrative Information)
  - Categories of Amendments (Supporting Documents) in General Information
    - Category: Closure Request
    - Category: **Reactivation** (Used only when a DMF has been **Closed (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm#closedbyh)**.)
    - Category: Administrative

Subcategories under Administrative Category

- change in the holder name
- change in holder address
- change in ownership of the DMF (either internal name change, or change in ownership)
- change in the agent name or address.
- change in the contact person at the holder or agent.
- change in the subject of the DMF.
- change in the type of DMF
- response to an Administrative Filing Letter

Note that a change in manufacturing address does NOT require a "Change in Subject amendment."

- Categories of Amendments (Supporting Documents) in Original Submission:

Category: Quality **Subcategories under Quality Category (with corresponding CTD Sections, where applicable). Changes to a Subsection not specifically listed below should be reported as the next level up e.g. changes in Control of Materials (S.2.3) should be reported as Manufacture Information S.2. Subcategory**	**Applicable Section in modules 2 and 3**
New item: Additional item e.g. flavor added to a multi-item DMF	
Controls Information (specifications)	S.4 and P.5
Dissolution Data (Usually applies to drug product only)	P.5
Facility Information (changes in manufacturing and or testing sites)	S.2.1 and P.3.1
Formulation Information (Usually applies to drug product only)	P.1 and related sections
Lot Release (batch analysis)	S.4.4 and P.5.4
Manufacture Information	S.2 and P.3
Microbiology Information	
New Strength (Usually applies to drug product only)	P.1 and related sections
Quality (Not covered by other subcategories)	
Packaging Information (Applies to packaging of the material that is the subject of the DMF e.g. plastic bags for packaging a bulk drug substance in a Type II DMF)	S.6 and P.7
Stability Information	S.7 and P.8
Response to Information Request	
Response to Deficiency Letter	

Category: Non-clinical

- Non-clinical
- Carcinogenicity Information

A response to an **Overdue Notice Letter** (ONL) to retain activity of a DMF should be identified as an Annual Report and contain the information listed below for an **Annual Report**. Additional administrative and technical information may be included as **amendments**. Responses to **ONL**s will not be sufficient to keep the DMF in active status if they meet ANY of the following conditions:

- The submission is not labeled as Annual Report.
  or
- The submission state that an update will be submitted in the future
  or
- The submission does not contain the information specified below under an **Annual Report**s

FDA does not acknowledge, whether via e-mail or letter, any submission after the original DMF.

Submissions that cover multiple DMFs should have a copy submitted for each DMF.

When a change is made to one part of a DMF the entire DMF does not need to be resubmitted. For DMFs in CTD format, the entire changed "Document" (Section) should be submitted e.g. a change in the material used in the synthesis should be included in a resubmission of Section S.2.3.

All submissions should be paginated within the submission. Pages that replace an already-numbered page from a previous submission should also contain the page number in the current submission (e.g. a page replacing Page 10 in the original submission may be page 14 in the new submission). For DMFs in CTD format, only the pages within the changed "Document" (Section) are subject to re-numbering.

No pages are ever physically replaced in a DMF.

REPORTING CHANGES TO A DMF (Category 2)

As stated in **21 CFR 314.420(c) (http://www.gpo.gov/fdsys/pkg/CFR-2008-title21-vol5/xml/CFR-2008-title21-vol5-sec314-420.xml)**

> *"If the drug master file holder adds, changes, or deletes any information in the file, the holder shall notify in writing, each person authorized to reference that information. 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."*

The notification of the change should also include the date for the "information affected in the drug master file." Paragraph (d) in the regulation refers to the list of authorized persons.

There are no reporting categories for DMFs. All changes must be reported as amendments. The DMF holder should notify customers of the nature of the changes, providing as much detail as is consistent with the confidentiality agreement between the DMF holder and each customer, so that the customer can determine how to report the changes in their approved NDA or ANDA. See **21 CFR 314.70 (http://edocket.access.gpo.gov/cfr_2009/aprqtr/21cfr314.70.htm)** and related Guidances.

Also **Guidance for Industry: Changes to an Approved NDA or ANDA (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm077097.pdf)** and the **Q&A (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm122871.pdf)**
CMC Postapproval Manufacturing Changes Reportable in Annual Reports (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM217043.pdf) (Draft Guidance)

ELECTRONIC DMFs (Category 3)

The FDA has published a ***Final Guidance: "Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications"*** **(http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM333969.pdf.)** (5/ regarding electronic submissions. See the Guidance for further information regarding requirements for electronic DMF submissions.

All electronic submissions must have an application number. For a new DMF, the holder must request a **pre-assigned (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm#preassign)** number in order to populate the US Regional.xml. The ECTD format provides the backbone for the submission and a guide as to where to place information. It is not necessary to submit modules that are not applicable to the subject of the DMF e.g. it is not necessary to submit Module 4 and 5 for a Type II DMF for a drug substance. All Sections within Modules 1, 2 and 3 should be submitted. DMF holders are encouraged to submit all subsequent submissions electronically after the initial electronic submission. See also **Electronic Common Technical Document (eCTD). (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm)** Electronic signatures are accepted for electronic DMFs.

Electronic DMFs may be submitted either through the Gateway or by sending a disc (one copy) to the Central Document Room at the **address (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm#address)** provided above.

CONVERSION OF PAPER DMFS TO ELECTRONIC DMFS (Category 3)

If a DMF currently in paper format is being converted to electronic format, it is not necessary to request a pre-assigned number or a new number. The previously assigned number in 6-digit format should be used e.g. 1234 becomes 001234. The first submission in electronic format should be given the sequence number “0000.”

The use of mixed formats (paper and electronic) can delay the review of a DMF but it is important for FDA to be able to readily access the historical record in the DMF. Therefore DMF holders are encouraged to do the following when a DMF is converted from paper to electronic format:

- Use the same DMF number, rather than submitting a new electronic DMF covering the same information.
- Submit complete Modules 1, 2, and 3, incorporating any revisions since the most recent paper submission. It is not necessary to resubmit the previous individual paper submissions in electronic format, although this is highly encouraged.
- In section 1.11 provide a list of amendments that had been submitted in paper after the original submission, including the dates of the amendment and a brief summary of the changes they covered.
- Submit all subsequent submissions, including Letters of Authorization, in electronic format.

LETTERS OF AUTHORIZATION (Category 2)

All Letters of Authorization (LOAs) should be submitted in two copies to the DMF, if the DMF is in paper format. If the DMF is electronic, the LOA should be submitted in Section 1.4.1. A copy of the LOA must then be sent by the DMF holder to the Authorized Party (company or individual authorized to incorporate the DMF by reference). Failure to submit the LOA to the DMF may result in a delay in review of the DMF. LOAs should specify the name of the specific item being referenced and the date of the submission of information about that item. The LOA should not be called a “Letter of Access.”

An LOA should be submitted even if the DMF holder is the same company as the authorized party.

LOAs should NOT be submitted with original paper DMFs (unless the DMF has received a pre-assigned number) because the LOA should contain the DMF number. Therefore DMF holders should wait before submitting an LOA until they have received an acknowledgment letter containing the DMF number.

It is not necessary to reissue LOAs if there have been no changes in the holder, authorized party, subject of the DMF or item referenced.

If the holder changes names, whether this represents a change in ownership or not, new LOAs should be submitted to the DMF and copies sent to the authorized party. If the authorized party changes its name, the new authorized party should request a new LOA from the DMF holder. Failure to do so may result in a delay in review of the DMF.

If there has been a name change, it is not necessary to submit a Withdrawal of Authorization Letter for the holder or authorized party's previous name.

If a company has a Master File submitted to another Center in the FDA, e.g. a Biologics Master File (**MF**) submitted to the Center for Biologics Evaluation and Research, the Letter of Authorization should be submitted to the Master File in that other Center rather than CDER.

- **LOA Template (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263200.doc)**

Note: The "Subject" field in the Letter Templates refers to the Subject of the DMF, not the Item within the DMF being referenced. The Item name should be included in the body of the letter.

AGENTS (Category 2)

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) (http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/DrugRegistrationandListing/ucm084014.htm)**. Holders should not include the name of the agent for Registration purposes in the DMF unless the same person of company is the agent for both the DMF and DRLS. Also note that in the US, the process of "Registration" applies ONLY to "registering" an establishment with the FDA.

- **National Drug Code Directory (NDC) (/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072339.pdf)**
- **Electronic Submissions Gateway (ssLINK/UCM177328)**

All "Agent Appointment Letters" for DMFs should be signed 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."

Agents for DMF purposes are not required to be located in the United States, although this is recommended.

An "Agent Appointment Letter" may be included in an original DMF.

If possible, the word "Agent" should be used for the legal entity (whether a company or an individual) who is authorized to act on behalf of the DMF holder. The word "Representative" or "Contact Person" should be used for an individual who is employed by the Agent or Holder as the contact point for FDA.

If a company acting as an Agent changes its name, FDA recommends that the DMF holder issue a new Agent Appointment Letter.

A different agent can be appointed for different DMFs submitted by the same holder.

- **Agent Appointment Template (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263204.doc)**

HOLDER NAMES (Category 2)

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 (file:///\\cdsnas\cmccc\DMFCOM\LIST\Templates%20for%20holders\Change%20in%20Holder%20Name%20Letter%202011-07-13.doc)**, the DMF holder must notify FDA. See Section VII.E. in the **DMF Guidance (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073164.htm)**for further recommendations on the procedure for transferring ownership. A change in the name of a company for registration purposes under **DRLS (http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/DrugRegistrationandListing/ucm084014.htm)** will not change the DMF holder name.

When a DMF is transferred from one company to another, the original holder should submit an administrative amendment stating that they are **TRANSFERRING (file:///\\cdsnas\cmccc\DMFCOM\LIST\Templates%20for%20holders\HolderTransfer%20Letter%202011-07-13.doc)** the DMF to the new holder. The new holder should then submit an administrative amendment stating that they are **ACCEPTING (file:///\\cdsnas\cmccc\DMFCOM\LIST\Templates%20for%20holders\New%20Holder%20Acceptance%20Letter%202011-07-13.doc)** the DMF from the former holder.

If the holder changes names, whether this represents a change in ownership or not, new LOAs should be submitted to the DMF and copies sent to the authorized party.

If the authorized party changes its name the new authorized party should request a new LOA from the DMF holder. Failure to do so may result in a delay in review of the DMF.

It is not necessary to submit a Withdrawal of Authorization Letter for the holder or authorized party's previous name.

A DMF holder is expected to retain a complete reference copy that is identical to, and maintained in the same chronological order as, their submissions to FDA (See Section IV.D.1 in the **DMF Guidance (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073164.htm)**). Therefore the old owner of the DMF is expected to transfer that copy to the new owner of the DMF.

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 should 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.

If Company B changes its name to Company C, whether through an internal name change or a through sale of the company, the new holder should notify the FDA of the name change. This submission should contain a statement that the new holder of the DMF takes full responsibility for all the information in the DMF and for all the processes and testing performed by the manufacturer.

ANNUAL REPORTS (Category 2)

According to the **DMF Guidance (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073164.htm)**, Annual Reports are **NOT** to be used to report changes in the DMF. However, as described **above**, an Annual Report can be submitted at the same time as other information.

The Annual Report should contain (for **Cover Letter** see Templates below):

1. An administrative page containing the Administrative Information specified above (Administrative Information in a DMF)

AND 2. One of the following

- Date(s) of the amendment(s) reporting changes since the last Annual Report or the original DMF filing date, whichever is most recent.

  Or

- A statement that no amendments have been submitted since the last Annual Report or the original DMF filing date, whichever is most recent.

AND 3. One of the following:

- A complete list of all parties authorized to make reference to the DMF, identifying by name, reference number, volume, date, and page number the information that each person is authorized to incorporate by reference and the date of the LOA.

  Or

- A statement that there are no Authorized Parties.

AND 4. List of all parties whose authorization has been withdrawn

Note that the DMF Guidance uses the terms “Annual Update” and “Annual Report” interchangeably. All submissions of Annual Reports should be labeled “Annual Report.” The term “Annual Update” should not be used.

Note that the Annual Report should contain a COMPLETE list of Authorized Parties, even if the list of Authorized Parties is unchanged.

BIOLOGICS MASTER FILES (Category 3)

Master Files submitted in support of products regulated by the Center for Biologics Evaluation and Research (CBER) should be submitted as **MFs (http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm079467.htm)**. See the **CBER web site (http://www.fda.gov/BiologicsBloodVaccines/default.htm)** for the products regulated by CBER.

BINDERS (Category 2)

See ”**FDA IND, NDA, ANDA, or Drug Master File Binders (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm)**

The “binders” are actually covers. These may be ordered from the U.S. Government Printing Office (GPO) Web site: **http://bookstore.gpo.gov/ (http://bookstore.gpo.gov/)** or by calling 202-512-1800 to speak with a GPO customer service representative. The binders may be obtained from another supplier, provided they meet the requirements specified on the GPO Web site.

The direct links for online ordering are

- **Blue Binder (http://bookstore.gpo.gov/actions/GetPublication.do?stocknumber=017-012-00405-9)**
- **Red Binder (http://bookstore.gpo.gov/actions/GetPublication.do?stocknumber=017-012-00404-1)**

One copy of the DMF should use the blue cover and one should use the red cover.

Fasteners must be obtained separately. Use 2 Piece Prong Fasteners, 8 1/2" Center to Center, 3 1/2" Capacity. Binders should be used for all subsequent submissions to FDA that are more than 10 pages.

If a DMF is submitted using any other kind of binder, it should be a loose-leaf type of binder so that the pages can be removed and placed in FDA-approved binders. DMFs should not be submitted as “bound” books.

FEES (Category 4)

GDUFA requires DMF fees for Type II DMFs for drug substances (Active Pharmaceutical Ingredients (APIs)) used to support Abbreviated New Drug Applications (ANDAs). See definition of API above.

Since GDUFA does not apply to any other type of DMF or to Type II DMFs used to support NDA or INDs, there are no fees for these types of DMFs.

FORMS (Category 2)

Certain forms are required for submission of NDAs and INDs. However there are no forms required or available for DMFs, except for the forms discussed above under **Binders** and the **Generic (http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322629.htm)** Drug User Fee Cover Sheet. The latter applies only to Type II DMF submitted to support ANDAs under GDUFA.

CONFIDENTIALITY OF DMFs (Category 2)

The public availability of the contents of DMFs is covered in 21 CFR 314.430(e). There are no “open” or “closed” parts of DMFs filed with the FDA. The decision as to how much information DMF holders share with their customers is a business decision between the parties involved and is not covered by FDA regulations or Guidances. All requests for information about DMFs beyond that provided in the tables below must be made through the **CDER Freedom of Information Web site (http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/ucm113237.htm)**.

FILING DMFs AND PATENT EXPIRATION AND EXCLUSIVITY ISSUES (Category 2)

DMFs may be filed at any time. The Patent Expiration date and the Exclusivity Expiration dates listed in the **Orange Book (http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm)** have no impact on DMF filing. The submission of Abbreviated New Drug Applications (ANDAs) that reference DMFs is subject to the regulations regarding filing of ANDAs.

ENVIRONMENTAL ASSESSMENTS (Category 2)

Since DMFs are neither approved nor disapproved, there is no need to file an Environmental Assessment. However the DMF should contain a commitment by the firm that its facilities will be operated in compliance with applicable environmental laws.

REORGANIZATION OF A DMF (Category 1)

The advice in the Guidance does not apply. It is not necessary to consult with FDA before reorganizing a DMF.

REQUEST FOR CLOSURE OF A DMF BY THE HOLDER (Category 2).

It is not necessary to include a statement that "the holder's obligations as detailed in Section VII have been fulfilled," as recommended in the DMF Guidance. It is sufficient to include a statement that all of the parties authorized to reference the DMF have been notified that the DMF is being closed.

LETTER TEMPLATES AND COVER LETTERS (Category 2)

Note that a “Transmittal Letter” and a “Cover Letter” are the same thing.

- **Cover Letter for Original DMFs (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263264.doc)**
- **Cover Letter for Subsequent Amendments and Annual Reports (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263266.doc)** (Not applicable to Holder Transfer, New Holder Acceptance, Holder Name Change, Letter of Authorization, and Closure Requests)
- **Cover Letter for Reactivation of a Closed Drug Master File (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263321.doc)**

The following submissions do not require a Cover Letter:

- **Holder Transfer (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263217.doc)**
- **New Holder Acceptance (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263219.doc)**
- **Holder Name Change (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263214.doc)**
- **Letter of Authorization (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263200.doc)**
- **Closure Request (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263209.doc)**
- **Withdrawal of Authorization (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM275811.doc)**

Drug Master File Lists

- **1Q2015 - All - Excel (XLS - 5.3MB) (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM370722.xls)**
- **1Q2015 - All - Text (TXT - 2.9MB) (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM370723.txt)**

Drug Master File Letters

- **Change in Holder Name letter (DOC - 33KB) (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263214.doc)**
- **Holder Transfer Letter (DOC - 32KB)**

(/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263217.doc)

- New Holder Acceptance Letter (DOC - 34KB) (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263219.doc)
- Letters of Authorization Template (DOC - 37KB) (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263200.doc)
- Request for Closure Letter (DOC - 32KB) (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263209.doc)
- Agent Appointment Template (DOC - 34KB) (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263204.doc)
- Cover Letter for Original Drug Master Files (DOC - 31KB) (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263264.doc)
- Cover Letter for Subsequent Amendments and Annual Reports (DOC - 53KB) (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263266.doc)
- Cover Letter for Reactivation of a Closed Drug Master File (DOC - 35KB) (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM263321.doc)
- Withdrawal of Authorization (DOC - 34KB) (/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/UCM275811.doc)

More in Development & Approval Process (Drugs) (/Drugs/DevelopmentApprovalProcess/default.htm)

Forms & Submission Requirements (/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/default.htm)

Drug Master Files (DMFs) (/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm)

FDA IND, NDA, ANDA, or Drug Master File Binders (/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm)