Letter of Authorization:
Drug Master File Letter of Authorization Guidance and Template

ICTR Navigators
September 30, 2013
Version 2.0

The Johns Hopkins Institute for Clinical and Translational Research
ICTR—Where Science and People Connect
CTSA

JOHNS HOPKINS MEDICINE

1.0 Table of Contents

2.0 Abbreviations

ANDA	Abbreviated New Drug Application
BB-DMF	Biologics Product Master File
BLA	Biologic License Application
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CFR	Code of Federal Regulations
CMC	Chemistry, Manufacturing, and Controls
DMF	Drug Master File
FDA	U.S. Food and Drug Administration
IND	Investigational New Drug
NDA	New Drug Application
PMA	Pre-Market Application

3.0 Definitions

Agent or representative means any person who is appointed by a DMF holder to serve as the contact for the holder.

Authorized Party is the *Sponsor-Investigator* or ***Applicant*** whose application references the DMF

Holder means a person who **owns the DMF** being referenced.

Letter of authorization means a written statement by the holder or designated agent or representative permitting FDA to refer to information in a DMF in support of another person's submission without direct disclosure.

Sponsor-Investigator is someone who is both 1) responsible for initiating the studies conducted with the investigational drug product and 2) who conducts the studies. The sponsor-investigator holds the IND.

4.0 FDA Websites

A list of several FDA websites is provided below containing useful information for investigators seeking to reference a drug master file in their IND applications.

FDA Guideline for Drug Master Files

- http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073164.htm

(NOTE: While this guidance is current, additional information or clarification of the recommendations in the Guidance may be found at the following link below (**FDA Drug Master Files (DMFs)**). Also note that the address in the Guidance is now superseded by the Beltsville address*:*

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)

FDA Drug Master Files (DMFs)

- http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm

FDA CDER Drug Master File (DMF) List:

- http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm

NOTE: The current list contains DMFs **RECEIVED** by June 30, 2013. However the submitted date is listed for each DMF.

The list of DMFs is current as of June 30, 2013, through DMF 27250. Changes to the DMF activity status, DMF type, holder name, and subject made since the last update of March 31, 2013 are included.

5.0 Regulatory References

The enclosed information is intended to provide basic information about drug master files, as well as FDA suggested content and a template for a Letter of Authorization to a Drug (or Biologic Product) Master File. The contents of this document are based on the FDA regulations governing investigational drugs (21CFR312), new drug marketing (21 CFR 314), public information (21 CFR 20), and FDA guidance documents.

6.0 Drug Master Files

6.1 Drug Master Files

Per the FDA Guideline for Drug Master Files (DMF) (September 1989), "a Drug Master File (DMF) is a submission to the FDA that may be used to provide confidential detailed information about facilities, human drugs. **The submission of a DMF is not required by law or FDA regulation. A DMF is submitted solely at the discretion of the holder**. 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, an Export Application, or amendments and supplements to any of these."

DMFs:

- Are generally created to allow a party other than the holder of the DMF to reference material without disclosing to that party the contents of the file.
- do not take the place of other applications such as INDs, NDAs, ANDAs, or BLAs
- are not formally approved or disapproved by the FDA
- are only accessed by FDA reviewers when referenced in another application (e.g. another DMF, an IND, NDA, ANDA, or BLA)

6.2 Types of DMFs

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

6.3 Status of DMFs

"A"- Active; this means that the DMF was found acceptable for filing, administratively, and has not been closed.

"C"- Complete; this means that the DMF has undergone a successful Completeness Assessment

"I"- Inactive; this means a DMF that has been closed, either by the holder or by the FDA.

"P"- DMF Pending Administrative Filing review

"N"- Not an assigned number; this can occur for a number of reasons, e.g., the holder withdrew the DMF during the administrative review or the DMF was transferred to another Center.

7.0 Letters of Authorization (LOA)

7.1 Letters of Authorization

In the US, the Letter of Authorization is very commonly referred to as a "*Right of Reference*" letter. In the EU, an LOA may be referred to as a "*Letter of Access."* **Neither of these terms should be used in formal correspondence with FDA.**

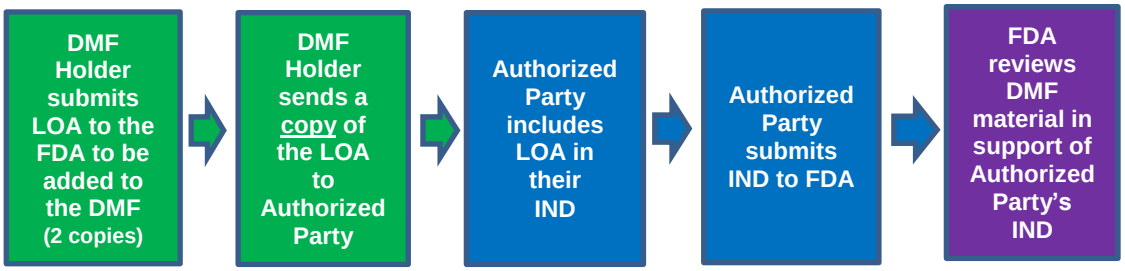
A Letter of Authorization grants the Authorized Party (i.e. the IND Sponsor-Investigator) the right to incorporate the information contained within the DMF into their IND or other application by reference as opposed to direct disclosure. The Letter of Authorization also grants FDA reviewers permission to review the proprietary information within the DMF.

7.2 LOA Contents

No cover or transmittal letter is necessary. As per the enclosed letter template provided in Section____ of this guidance, LOAs should specify the item being referenced by its code name, page number within the DMF and, most importantly, DATE OF THE SUBMISSION as it appears on the cover letter of that submission (not an internal document date) (Volume number is not useful)

Note: The "Subject" field in the Letter Template to follow refers to the subject of the DMF as listed in the FDA DMF listings, not to the Item within the DMF being referenced. The Item name should be included in the body of the letter.

7.3 LOA Process



7.4 Points to Consider

- Submission of an LOA permits FDA reviewers to access the DMF in support of an IND or other application. **A LOA does NOT permit the Authorized Party to examine the contents of the DMF. The FDA does not have open and closed parts of DMFs.**
- Failure by the DMF Holder to submit the LOA to the DMF **may result in a delay in review of the DMF in support of the Authorized Party's submission**.

- Because of the proprietary information contained in the DMF, **FDA deficiency and GMP compliance issues will be directed to the DMF Holder and NOT to the Authorized Party**. As such, **the Authorized Party will potentially not be privy to the review issues related to the DMF contents which affect the status of their IND or other application**.

7.5 When a New LOA is Needed

- When the Authorized Party changes its name, the DMF Holder should issue a new LOA to the DMF and send a copy to the Authorized Party
- When the DMF Holder changes their name the DMF holder should issue a new LOA and send a copy to all Authorized Parties.

8.0 Number of Copies to be submitted

DMF Holder
All Letters of Authorization should be submitted by the DMF Holder in two copies to the DMF, if the DMF is in paper format. 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). Submissions via e-mail are not accepted.

Authorized Party
The Authorized party (e.g. sponsor-investigator) should include a copy of the DMF Letter of Authorization in the IND application.

9.0 FDA Mailing Address

FDA Address for **DMF Holder** filing the of Letter of Authorization

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

NOTE: If a Biologics Product Master File (BB-MF), the LOA should be **sent by the MF Holder** to this address as per CBER SOPP 8110:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center, HFM-99, Suite 200N
1401Rockville Pike
Rockville, MD 20852-1448

10.0 Website Address Hyperlinks

All hyperlinks to websites included in this document are operational as of the date of this version. If any non-functional hyperlinks are identified, please contact the ICTR Research Navigator via the contact information below so that the links may be updated.

11.0 Questions and Additional Information Contacts

For questions relating to any of the information presented or use of the template, please contact the ICTR Research Navigators at ICTR_Navigators@jhmi.edu or via telephone at 410-614-5383.

Investigators may also direct comments or questions regarding DMFs to dmfquestion@cder.fda.gov.

All inquiries to dmfquestions@CDER.fda.gov 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. If the inquiry concerns a specific DMF, the DMF number should be in the subject field of the message.

12.0 LOA Template

Please see the LOA template on the following page.

[Place on DMF Holder letterhead]

Date: *[Insert date that the authorization is issued]*

DMF#: *[Enter number]*

Holder: *[Enter the Name of DMF Holder]*

Subject Name: *[Enter the Subject of the DMF as it appears on the DMF listing at FDA website]*

Letter of Authorization for: *[Enter the name of the Item being referenced*]*

Dear Sir or Madam:

This letter authorizes the U.S. Food and Drug Administration (FDA) to make reference to **[Insert Holder's name]** DMF No. **[Insert DMF number**] in connection with any New Drug Application, Abbreviated New Drug Application, Investigational New Drug Application, or supplements thereto involving the use of **[Insert product name]** submitted by:

[Insert Authorized Party's name in bold font]
[Insert Authorized Party's address in bold font]

DMF No. **[Insert DMF number]** was filed initially on **[Insert date]**. Information on this product is located in our initial submission in Section **[Insert Section number]** at pages **[Insert page numbers]** and in Amendment **[Insert number and/or date]** at pages **[Insert page numbers]**.

[Insert Holder's name] states that DMF No. **[Insert DMF number]** is current and **[Insert Holder's name]** will comply with the statements made within it. **[Insert Holder's name]** will notify FDA through an amendment to DMF No. **[Insert DMF number]** of any addition, change, or deletion of information in the DMF. **[Insert Holder's name]** will also notify in writing **[Insert Authorized Party's name]** that an addition, change, or deletion of information has been made to the DMF.

The information contained in this letter does not reflect any substantive change with regard to the chemical composition, quality control procedures, or manufacturing methodology for the product, and is intended to assist FDA in its review of applications filed with respect to new drugs in accordance with Section 341.420 of the New Drug Regulations.

Following the required procedure, we are submitting a duplicate of this letter of authorization, as well as an additional copy of this letter for your use in acknowledging receipt. Thank you for your assistance with this matter.

Sincerely,

Signature of Responsible Official
Name of Responsible Official

Responsible Official's Title
Responsible Official's Company i.e. Holder or Agent
Responsible Official's Telephone number
Responsible Official's Fax number
Responsible Official's e-mail address