

Cross-comparison to Other Drug Master Files and Lessons Learned

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Model Master Files: Advancing Modeling Simulation in Generic Drug
Development and Regulatory Submissions - March 13, 2025

Disclaimer



This presentation reflects the views of the author and should not be construed to represent FDA's views or policies.

Everyone deserves
confidence in their *next* dose
of medicine.

Pharmaceutical quality
assures the
availability,
safety,
and efficacy
of *every* dose.

Overview

- What are Drug Master Files (DMFs)?
- Example Timeline for a DMF
- Operational Considerations

Drug Master Files (DMFs)



- Allow parties to reference material without disclosing DMF contents to those parties.
- Are not required by statute or regulation.
- Are neither approved nor disapproved.

Types of Drug Master Files (DMFs)



- **Type II:** Drug substance, drug substance intermediate, and materials 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 *including MMFs*

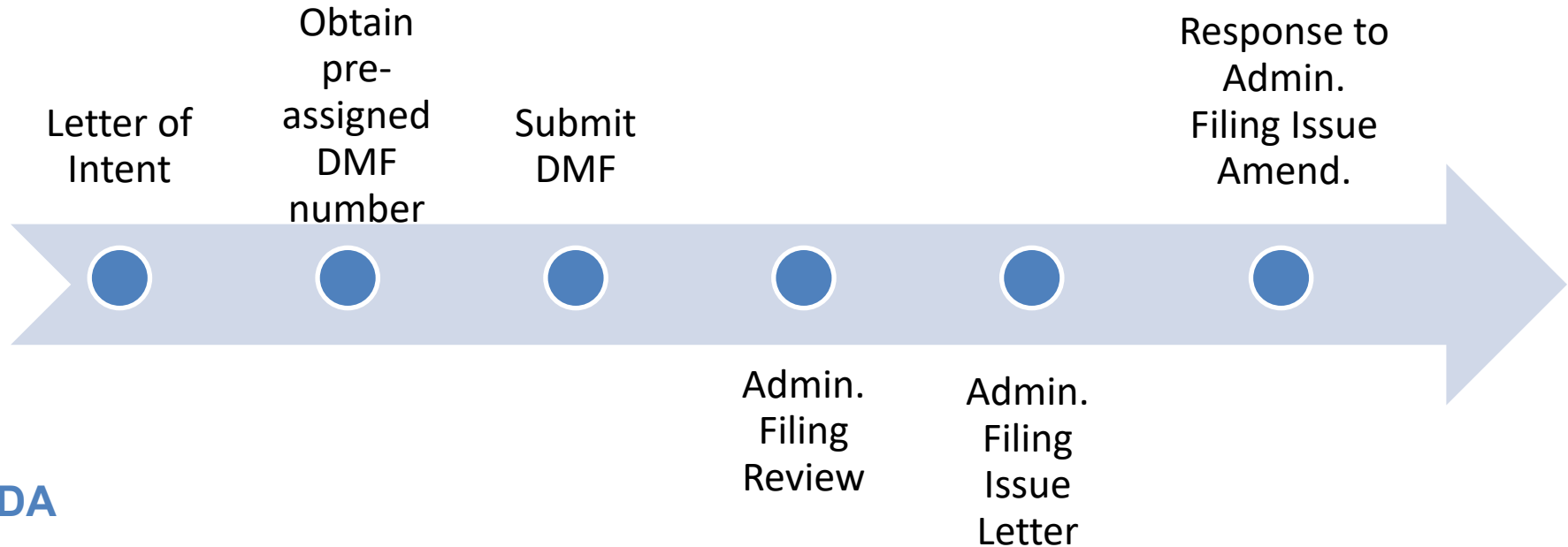


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DMF Timeline

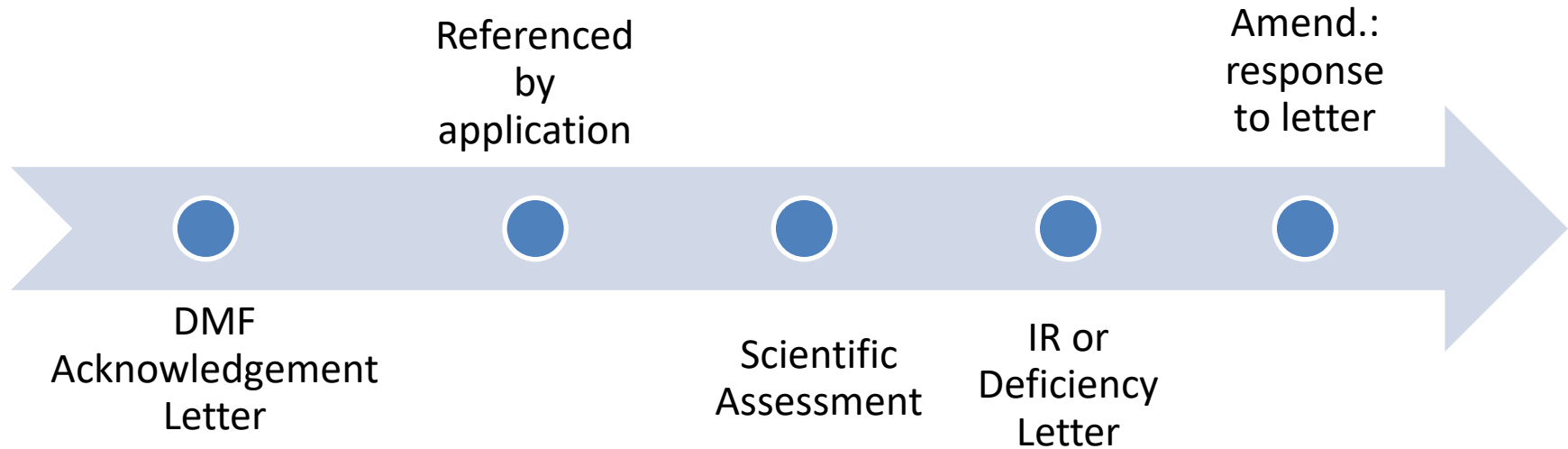
DMF Holder



FDA

DMF Timeline

DMF Holder



FDA

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Letter of Intent & Preassign number



- Letter of intent
 - DMFQuestion@fda.hhs.gov *See Eleftheria Tsakalozou's presentation for more details*
- Obtain [Pre-assigned Number](#)
 - cderappnumrequest@fda.hhs.gov
 - Name of holder, holder address, US Contact info
 - Subject of Master File

DMF submission

Formatting:

- eCTD format
- [ICH M4](#)
- [DMF Guidance](#)

Tips:

- Include [Form 3938](#)
- Include “MMF” in cover letter

[Managing Electronic DMF Submissions](#) – Jonathan Resnick

[Administrative Aspects of Managing a DMF](#) – Vathsala Selvam

Acknowledgement of DMF



- Once received, the holder will receive:
 - Administrative Filing Issue Letter, if applicable
 - Acknowledgement Letter if there are no filing issues

Quarterly list of Active DMFs

List of Drug Master Files (DMFs)



The list of DMFs, which is updated quarterly, contains DMFs RECEIVED by December 31, 2024, for which acknowledgment letters were sent before January 13, 2025.

The list is current through DMF 041157. Changes to the DMF activity status (A=active ; I=inactive), DMF type, holder name and subject (title) made since the last update of September 30, 2024, are included.

- [4Q2024 Excel](#) (XLS - 1.93 MB)

<https://www.fda.gov/drugs/drug-master-files-dmfs/list-drug-master-files-dmfs>

Letters of Authorization (LOA)



- Grants permission for a third party or self to reference a DMF and for FDA to review the DMF

DMF Draft Guidance: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/drug-master-files-guidance-industry>



Flexibility in Referencing

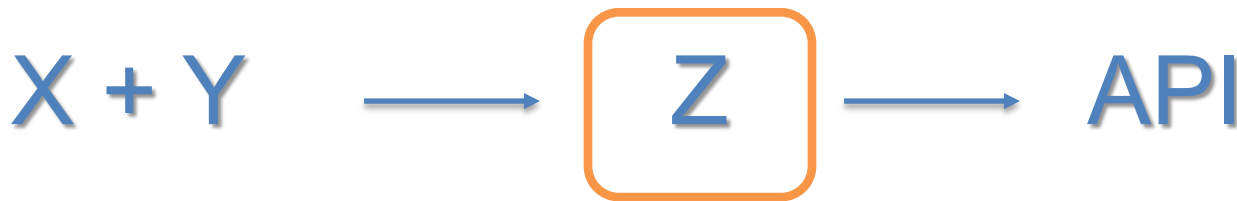


Flexibility in Partial Referencing



A DMF may be referenced in part. For example:

- One flavoring in a type IV DMF with many flavorings
- Single component in a type III DMF with multiple components
- Intermediate in a type II DMF for an API



What information can FDA share?

- With the DMF Holder
 - Status, admin, and technical information of their DMF
 - *Cannot share confidential application status information (e.g., Goal Dates)*
 - *Cannot share application technical or scientific information*
- With the Applicant
 - Public Information (e.g., Quarterly Inventory DMF list)
 - Status Information of referenced DMF (e.g., adequate or inadequate)
 - *Cannot share confidential administrative or review information of referenced DMF*

DMFs are not Approved

- DMF is either:
 - Adequate to support application
 - Inadequate to support application



Amendments (Changes) to DMF



- Administrative Amendments
- Quality Amendments
 - Technical Updates
 - Summary of Changes
 - Assessment of changes
 - 21 CFR 314.420(c)

Type II DMF A

- Change 1
- Change 2
- Change 3

Assessment of
changes DMF A

Resources

- [FDA Drug Master Files](#) (and references therein)
- [DMF Draft Guidance For Industry](#)
- [ICH M4](#)
- [Federal Register Notice on MMFs](#)
- [Guideline for Drug Master Files \(DMF\)](#)

Summary

- Model Master Files can be submitted via existing FDA pathways for DMFs
- DMFs are confidential submissions to the FDA
- DMFs offer holders flexibility and a streamlined method for making changes

Acknowledgements

- Claude Theophin
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