Best Practices for Securing Timely Approvals of ANDAs :

Drug Master Files (DMFs)

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GRx+Biosims 2024

October 21, 2024


Everyone deserves
confidence in their *next* dose
of medicine.
Pharmaceutical quality
assures the
availability,
safety,
and efficacy
of *every* dose.

Keys to Securing Timely Approvals

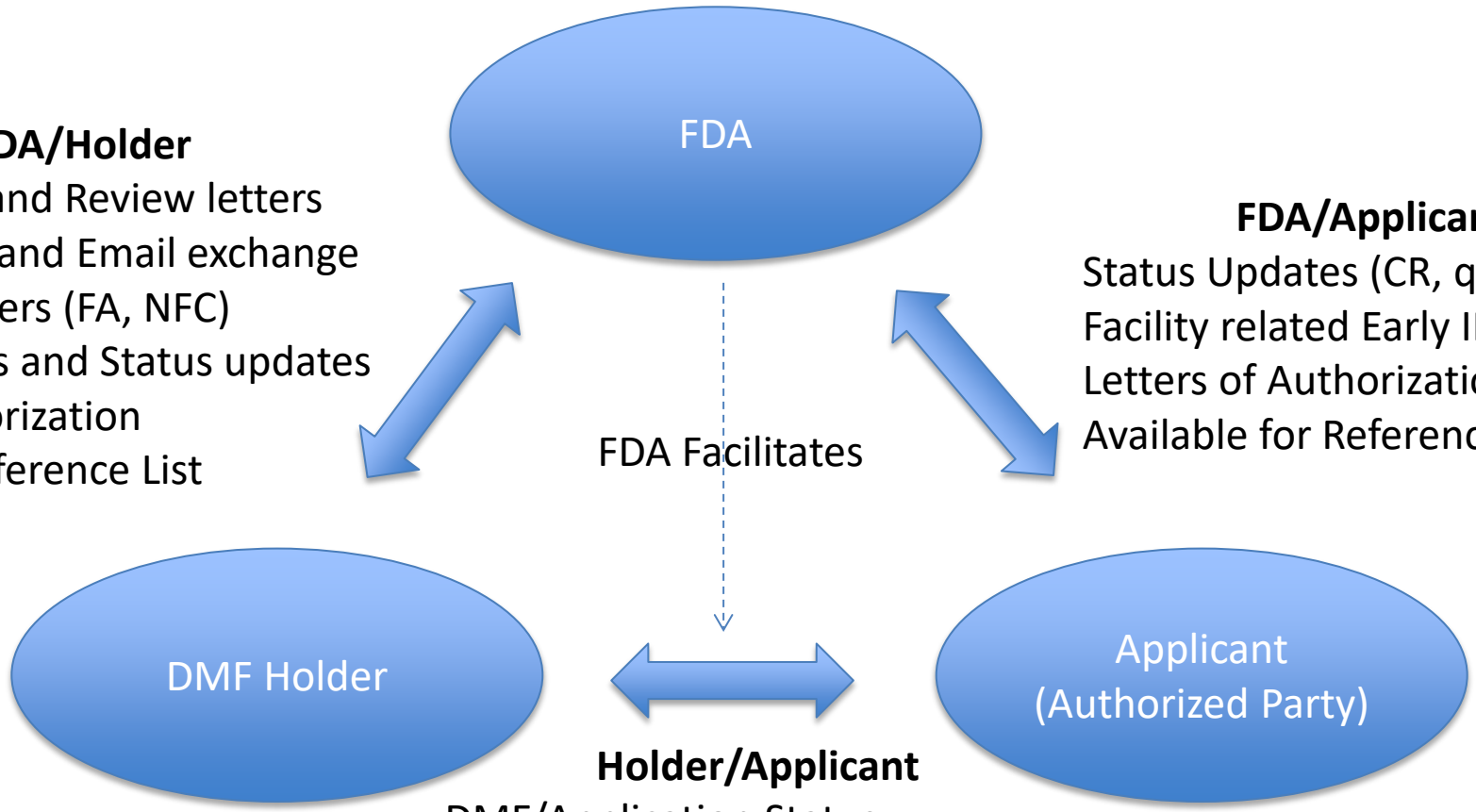
- Submit the DMF and pay GDUFA fee at least six months prior to ANDA submission.
- Follow the Completeness Assessment guidance before submitting a DMF to the agency.
- **FDA form 3938 is highly recommended with each DMF submission.**
- Effective communication between the industry and FDA.
- Effective commutation between the DMF holder and applicant(s) (authorized party).

Keys to Securing Timely Approvals

- Submit the responses to GDUFA Incomplete Comments and responses to DMF deficiency letter in a timely manner.
- Obtain a secure email address for faster communications.
- When applicable, use the GDUFA III prior assessment pathway to submit the DMF 6 months prior to ANDA submission:
  - For example, request prior assessment for a PAS to add a new API source for a drug product that could help mitigate or resolve a drug shortage, or for a drug product that could help address a public health emergency

Communication Pathways

FDA/Holder
Administrative and Review letters
Teleconference and Email exchange
Information letters (FA, NFC)
Informal queries and Status updates
Letters of Authorization
Available for Reference List



FDA/Applicant
Status Updates (CR, queries)
Facility related Early IRs
Letters of Authorization
Available for Reference List

Holder/Applicant
DMF/Application Status
Letters of Authorization
Action Timelines
Submission Timelines
Change Notifications

What information can FDA share?

- With the DMF Holder
  - Public Information (e.g., Available for Reference list, Quarterly DMF Inventory list)
  - Status Information of their DMF (e.g., adequate or inadequate)
  - Confidential Administrative Information, fee, or Completeness Assessment
  - Confidential Review Information or technical DMF information
  - *Cannot share confidential application status information (e.g., Goal Dates)*
  - *Cannot share application technical or scientific information*
- With the Applicant
  - Public Information (e.g., Available for Reference list, Quarterly Inventory DMF list)
  - Status Information
  - *Cannot share confidential administrative or review information of the referenced DMF*

Formal and Informal Communication

- Formal Communication
  - Review letters (e.g., CR, IR, AC, DMF Incomplete)
  - Informational letters (e.g., FA, NFC, General Advice)
  - Formally granted teleconferences
  - Formally granted email exchanges
  - Controlled Correspondence

- Informal Communication
  - Communication outside of formal communication channels
  - Responses to email queries

Teleconferences

- FDA will grant teleconferences when requested to clarify **1st Cycle** DMF deficiency letters ***only***.
- DMF holders must request such teleconferences in writing within **30 days of CR letter receipt** for specific issues to be addressed.
- Follow the instructions in the CR letter when submitting the teleconference request.

Email Exchange

- Introduced in GDUFA II and is the preferred communication pathway by industry regarding deficiencies (>90%).
- Submit the request within 30 days of receiving the CR letter.
- We will respond to Email Exchange requests generated from any cycle (i.e., not limited to first cycle).
- Eligible for one follow up exchange after receiving the initial response.
- Follow the instructions in the CR letter when submitting the Email Exchange request.

Whom should I contact with my specific questions?

DMFOGD@FDA.HHS.GOV :

- Status updates
- Response notifications as instructed in our letter templates
- Questions about No Further Comments and First Adequate letters
- Email Exchange Requests and Teleconference Requests
- Queries about Completeness Assessments the “Available for Reference” list
- Any time you just can’t figure out where to send the query and its somehow related to a DMF or API

Whom should I contact with my specific questions? Cont.

dmfquestion@fda.hhs.gov:

- General queries about DMFs
- Administrative queries about DMFs
- Questions about FDA forms and letter templates for DMFs
- General questions based on information on the FDA DMF webpage
- Questions about submitting Type V DMFs
- Questions about Type III and IV DMFs

CDER-OPQ-Inquiries@fda.hhs.gov:

- Technical or policy questions related to API review. Please include "DMF Inquiry, Type XX DMF: ….." in the subject.

CDERCollections@fda.hhs.gov:

- User fee related questions

Effective Communication Between Applicants and DMF holders

- Helps avoid unnecessary delays to approvals (i.e., goal date extensions)
  - Poorly timed unsolicited amendments to primary DMFs **AND** secondary DMFs continue to adversely impact application timelines.
- FDA role is to facilitate Applicant/DMF Holder communication by providing relevant information to both parties
- Actual communication is up to YOU!
- From the FDA perspective poor communication is often a barrier for first cycle approvals

Communication Between Applicants and DMF holders – Facilities

- Accurate facility information is critical for a timely application review
  - Facility evaluations and inspections require planning.
  - DMF related facilities discovered late in a review process adversely impact approval actions.
- FDA uses the TCIR process (only for original ANDAs) to help avoid adverse consequences of hidden facilities, but this is an industry responsibility.
- Applicants need to have visibility on all facilities that impact their application
  - Manufacturing and routine release and stability sites.
  - Clarity provided in LOAs when there are facilities in the DMF not being used for a particular application.
  - Manufacturing sites include intermediates
  - FDA cannot share DMF related facility information with an applicant if the facility is not included in their application.

Helpful Links

- Email Addresses:
  - DMFOGD@fda.hhs.gov
  - dmfquestion@fda.hhs.gov
  - CDER-OPQ-Inquiries@fda.hhs.gov
  - CDERCollections@fda.hhs.gov
  - esub@fda.hhs.gov
  - SecureEmail@fda.hhs.gov.
- FDA Guidance:
  - DMF Guidance (draft): https://www.fda.gov/regulatory-information/search-fda-guidance-documents/drug-master-files-guidance-industry
  - ANDA Submissions — Amendments to Abbreviated New Drug Applications Under GDUFA: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/anda-submissions-amendments-abbreviated-new-drug-applications-under-gdufa

Helpful Links

- Effective Communication Strategies For Drug Master Files (DMFs): https://www.youtube.com/watch?v=lzwgxSGmlPI
- Administrative Aspects of Managing a DMF: https://www.youtube.com/watch?v=anqYUy77bpQ
- FDA Form 3938 DMF: https://www.youtube.com/watch?v=OyHk9G4omOo
- SBIA DMF Workshop, November 2022 (GDUFA III Enhancements): https://sbiaevents.com/dmf2022/
- GDUFA III Impact on DMF Assessment, SBIA Generic Drug Forum 2023: https://sbiaevents.com/gdf2023/