SBIA-DMF Drug Substance Workshop

March 3 & 4, 2021 (Virtual)

Timeline for DMF Risk-based Assessment and Improvement of the First Cycle Approval Rate

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Virtual

PURPOSE

This poster explains the mechanism and timeline for processing risk-based DMF assessment within Agency.
A late DMF CR response or amendment submission may result the extension of goal date and delay the action date for the corresponding application.

OBJECTIVE(S)

1. **Introduce the timeline of DMF risk-based assessment**
2. **Understand the workflow of DMF review assignments**
3. **Provide the strategy to improving first cycle approval**

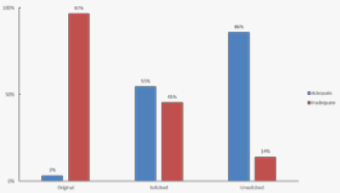
METHOD:

The first part of this study includes 2790 DMF assessments completed in FY 2019. The completion rate and the adequacy rate were compared by submission type.

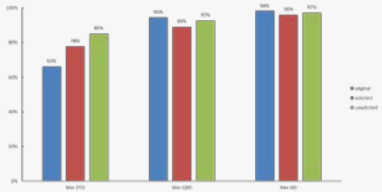
The second part of the study focuses on the outcome of total 1462 original DMFs which were referenced by ANDA applications. Among 1462 original DMFs, we issued 1448 complete response letters. 1332 DMF holder submitted their response. The duration of the first CR response is discussed.

RESULT

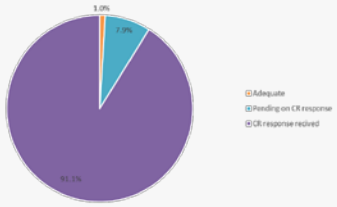
Adequacy Rate by DMF Submission Status (FY2019)



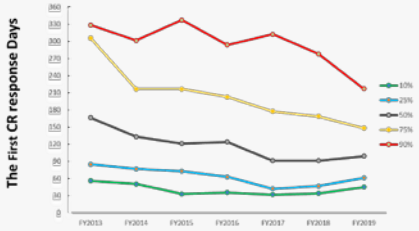
DMF Completion Rate by Internal Due Date (FY 2019)



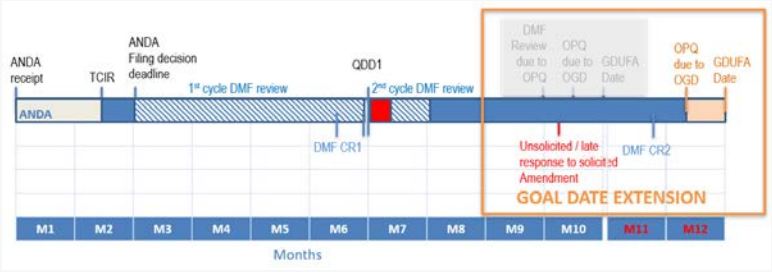
Outcomes of First Cycle Original DMFs Supporting ANDA Applications (FY 2013 –FY 2019)



The Distribution of the First CR letter Response (FY 2013-FY 2019, 1332 DMF CR response)



Late CR Response/Amendment Results Goal date Extension



CONCLUSION(S)

- **In FY 2019, 85% of unsolicited DMF submissions were found adequate, 55% of solicited DMF amendments were found adequate, and only 3% original DMF were found adequate.**
- **In FY 2019, 98% Original DMFs, 96% of solicited DMFs, and 97% of unsolicited DMFs met the GDUFA goal dates.**
- **Multiple internal due dates ensure the completion of DMF assessment by GDUFA goal date.**
- **In the last six years, the Agency issued 1462 CR letters for original DMF submission. Less than 10% DMF CR response were submitted within 30 days. The average first CR response time has dropped from 190 days (FY 2013) to 114 days (FY 2019), a decrease of about 40%.**
- **Late submission of CR response or amendment doesn't allow the second cycle DMF review, which decreases the first cycle approval rate.**
- **Submit CR response promptly and communicate with Applicants effectively will allow the second cycle DMF review and improve the DMF adequacy rate**

Timeline for DMF Risk-based Assessment and Improvement of the First Cycle Approval Rate

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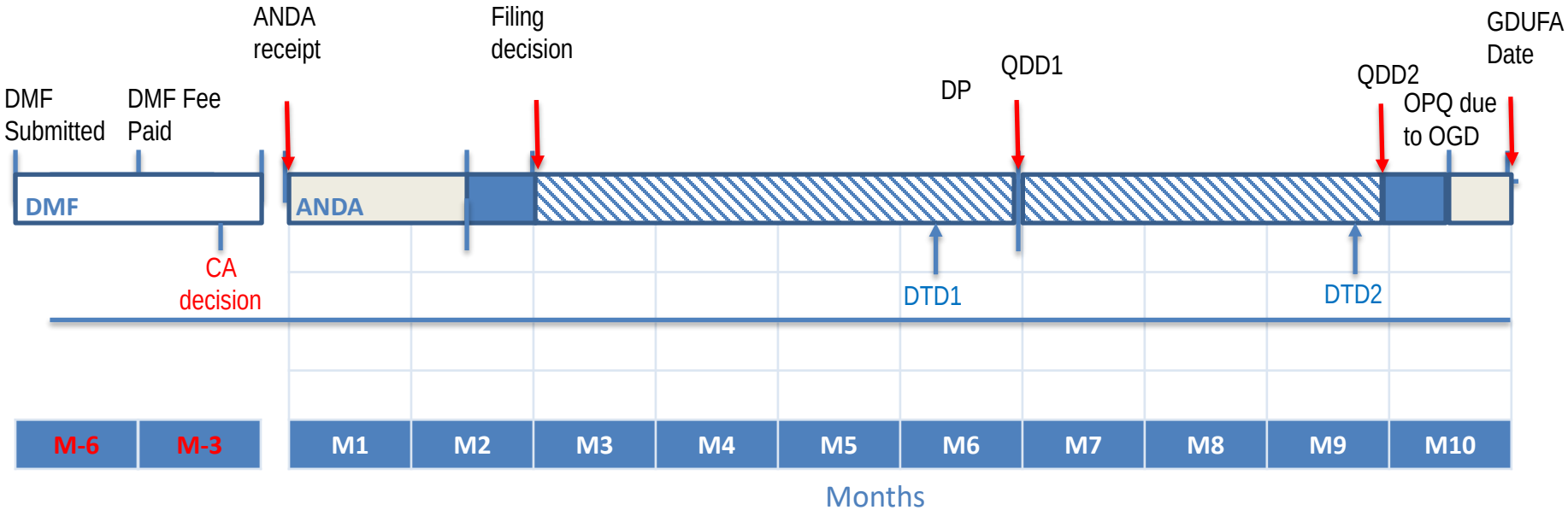
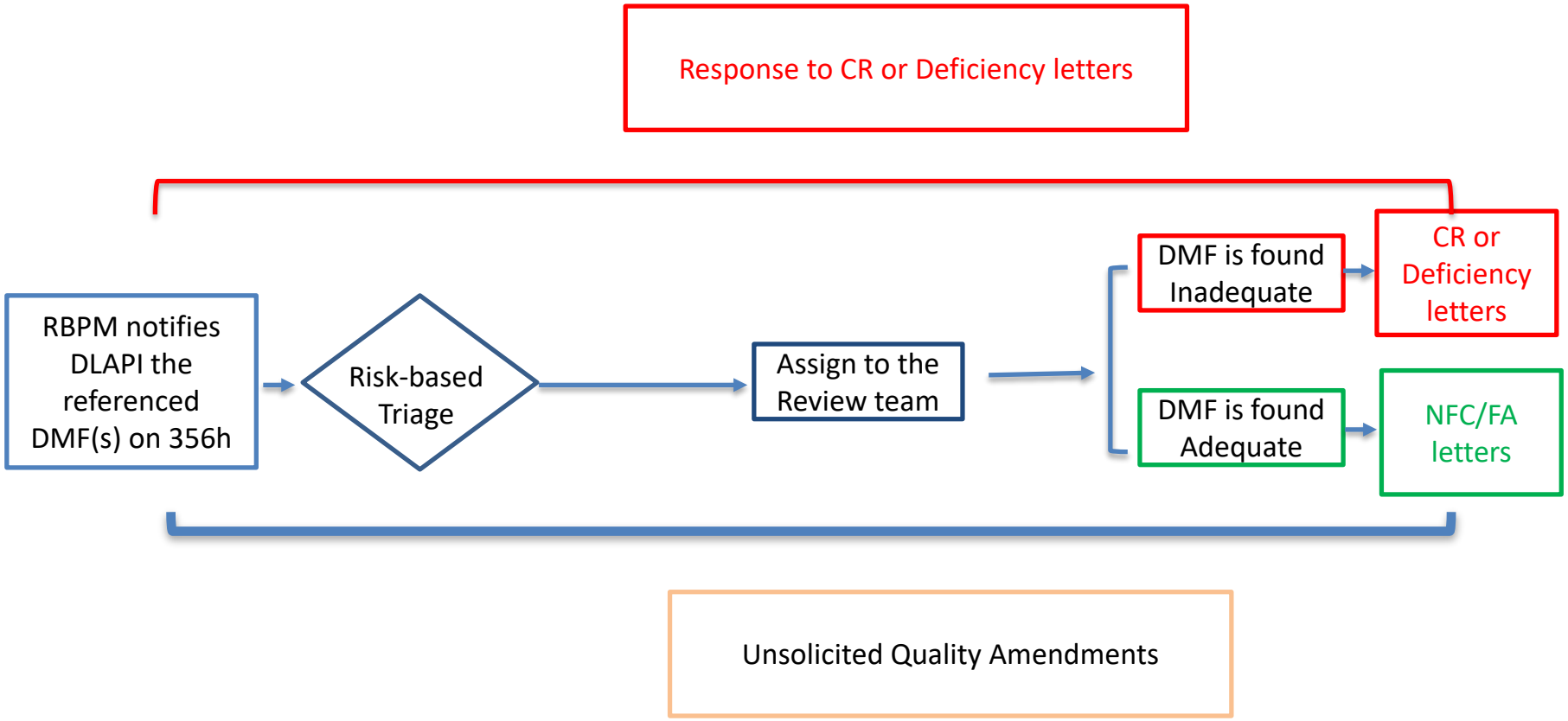
Road Map for the First cycle approval



Where is the DMF: With OGD With OPQ With OPQ/DMF under review

The life cycle of Type II DMF Assessment



Algorithm of Internal Due Dates for Type II DMF Assessments

To coordinate with other disciplines with the Agency, DLAPI developed the following internal dates. These internal due dates will allow the drug product reviewers to update their assessments based on the DMF assessment. It also gives RBPMs sufficient time to process the letters and to prepare FDA Actions.

Quality Due Date: QDD

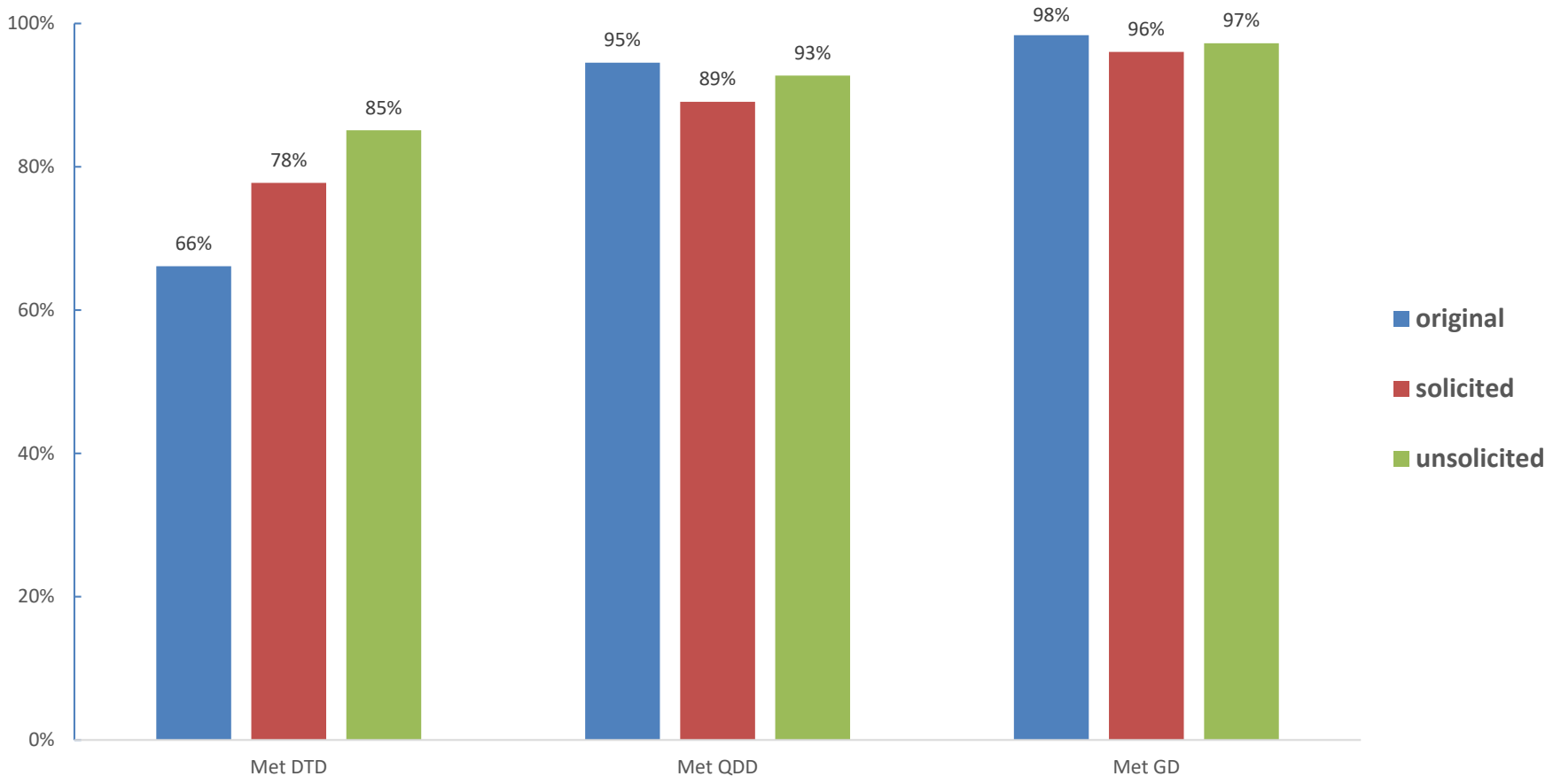
QDD1* =Receiving Date +180 days
QDD 2* =Receiving Date +270 days

DMF Target Date: DTD

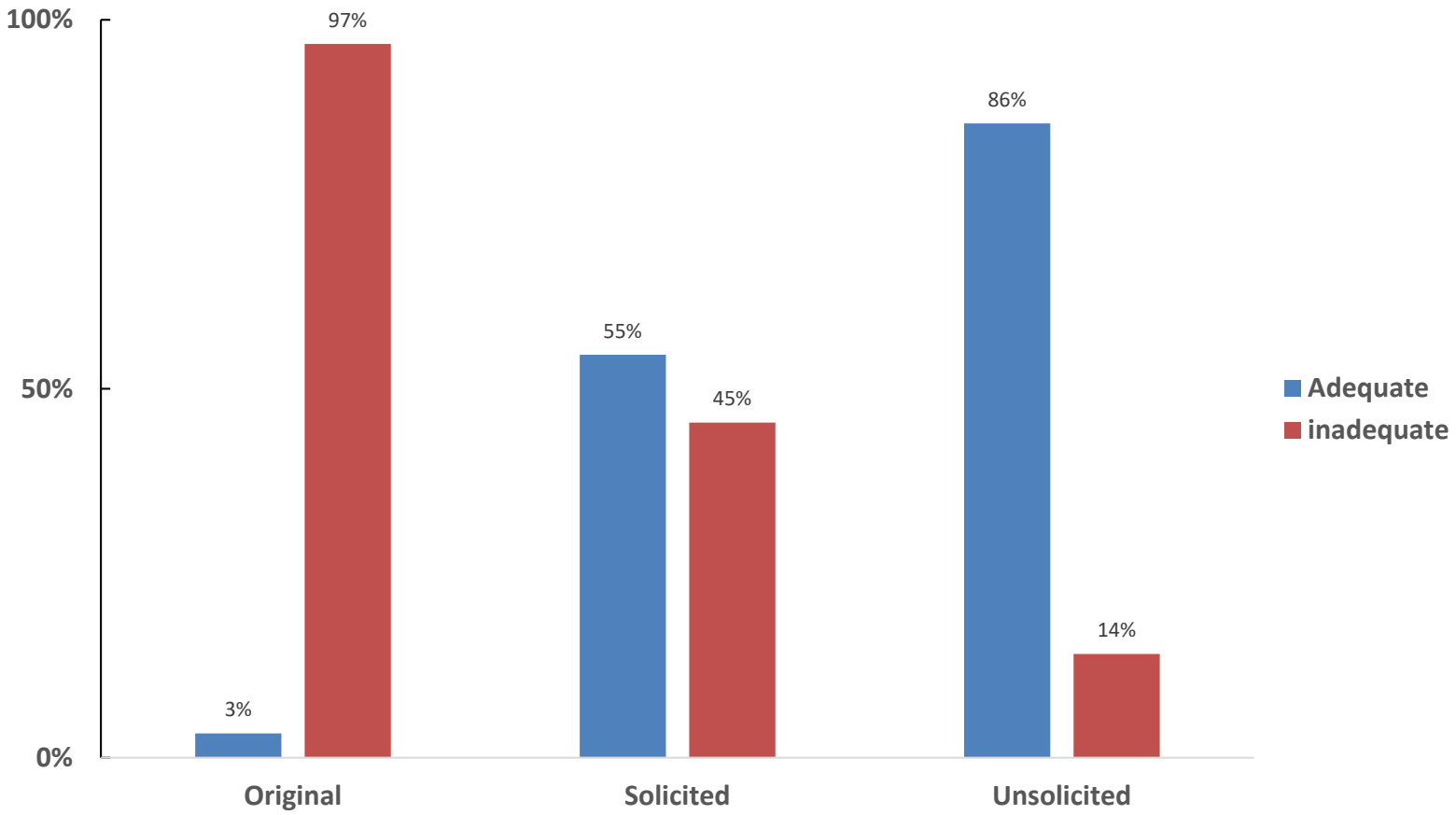
DTD1 =QDD1 -20 days
DTD2 =QDD2 -7 days

*Based on 10 months review window

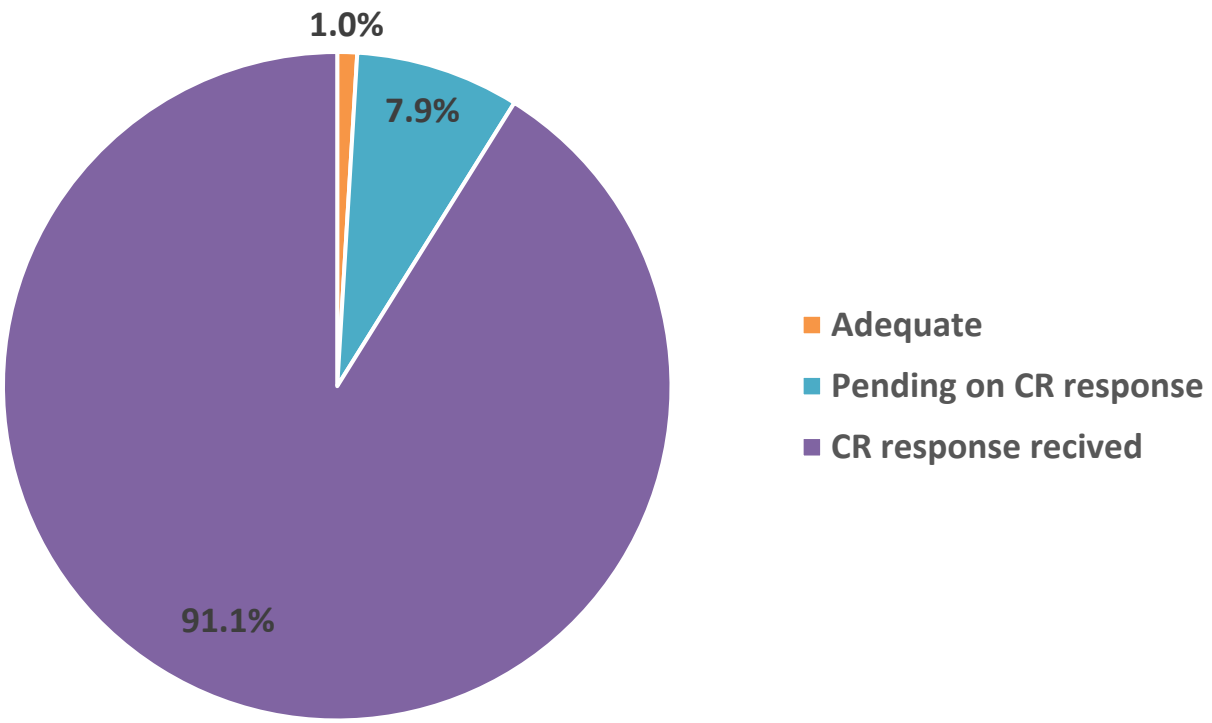
DMF Completion Rate by Type of DMF and by Internal Due Dates (FY 2019)



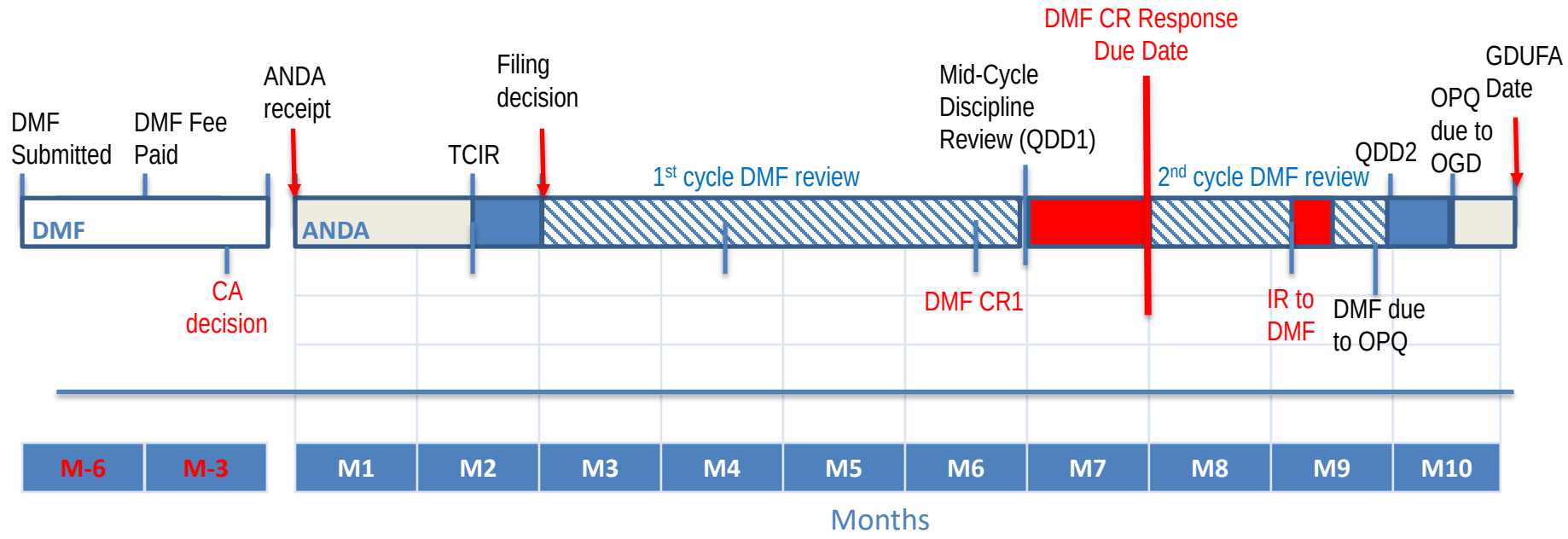
Adequacy Rate by DMF Submission Type (FY2019)



Outcomes of 1462 First Cycle Original DMFs (FY 2013-FY 2019)



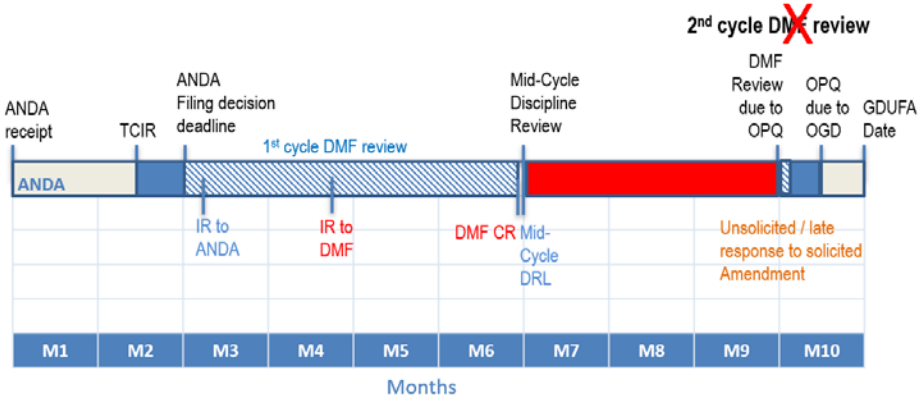
Proposed Strategy for the First Cycle Approval

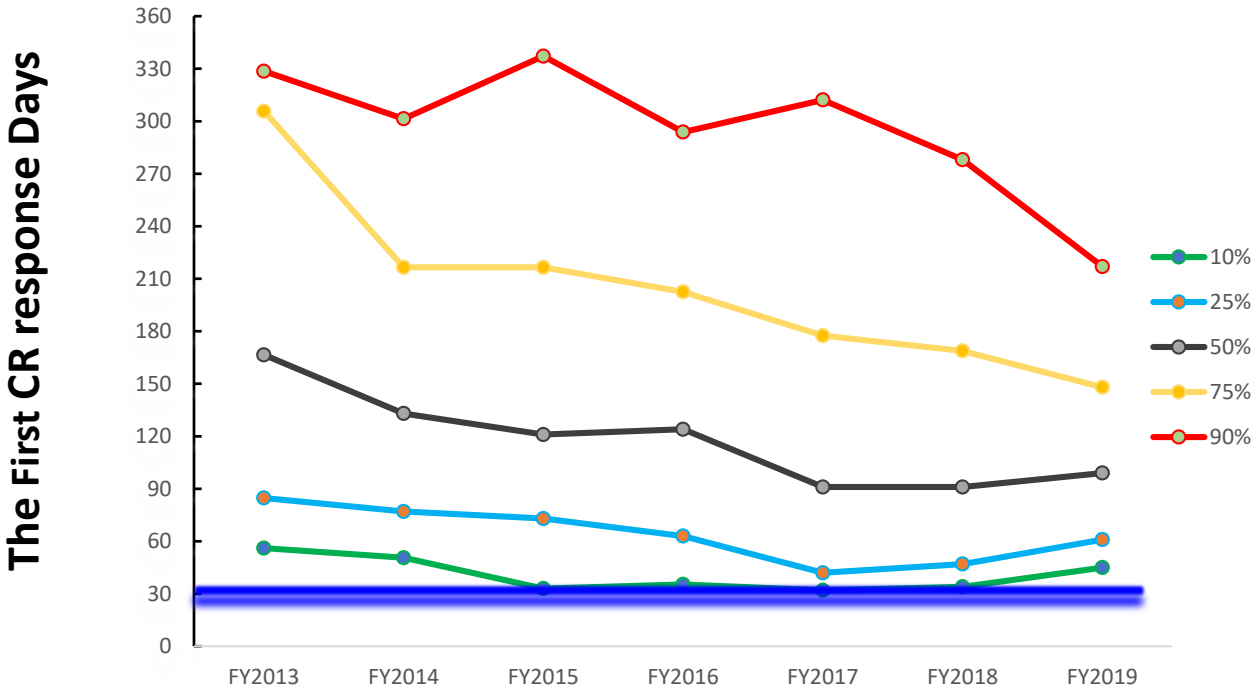


Outgoing communications: FDA to ANDA FDA to DMF holder

Where is the DMF: With OGD With OPQ With OPQ/DMF under review With DMF holder

Majority of the First CR Letter Response are longer than 90 Days





Information from Complete Response Letter

GDUFA DMF COMPLETE RESPONSE LETTER

Dear CONTACT:

This communication is in reference to your Type II Drug Master File (DMF) ###### for SUBJECT OF DMF, submitted pursuant to 21 CFR 314.420 of the Federal Food, Drug, and Cosmetic Act. This DMF was reviewed under the letter of authorization dated MONTH DAY, YEAR in support of NAME OF APPLICANT's abbreviated new drug application (ANDA). Also, this DMF was reviewed under the letter of authorization dated MONTH DAY, YEAR in support of NAME OF APPLICANT's ANDA OR supplemental new drug application (sNDA).

Reference is also made to your submission(s) dated MONTH DAY, YEAR.

IF THE REVIEW OF ANY AMENDMENT WAS DEFERRED TO THE NEXT REVIEW CYCLE, INCLUDE THE FOLLOWING SENTENCE:
We acknowledge receipt of your amendment dated MONTH DAY, YEAR which was not reviewed for this letter. You may incorporate applicable sections of the amendment by specific reference as part of your response to the deficiencies cited in this letter.

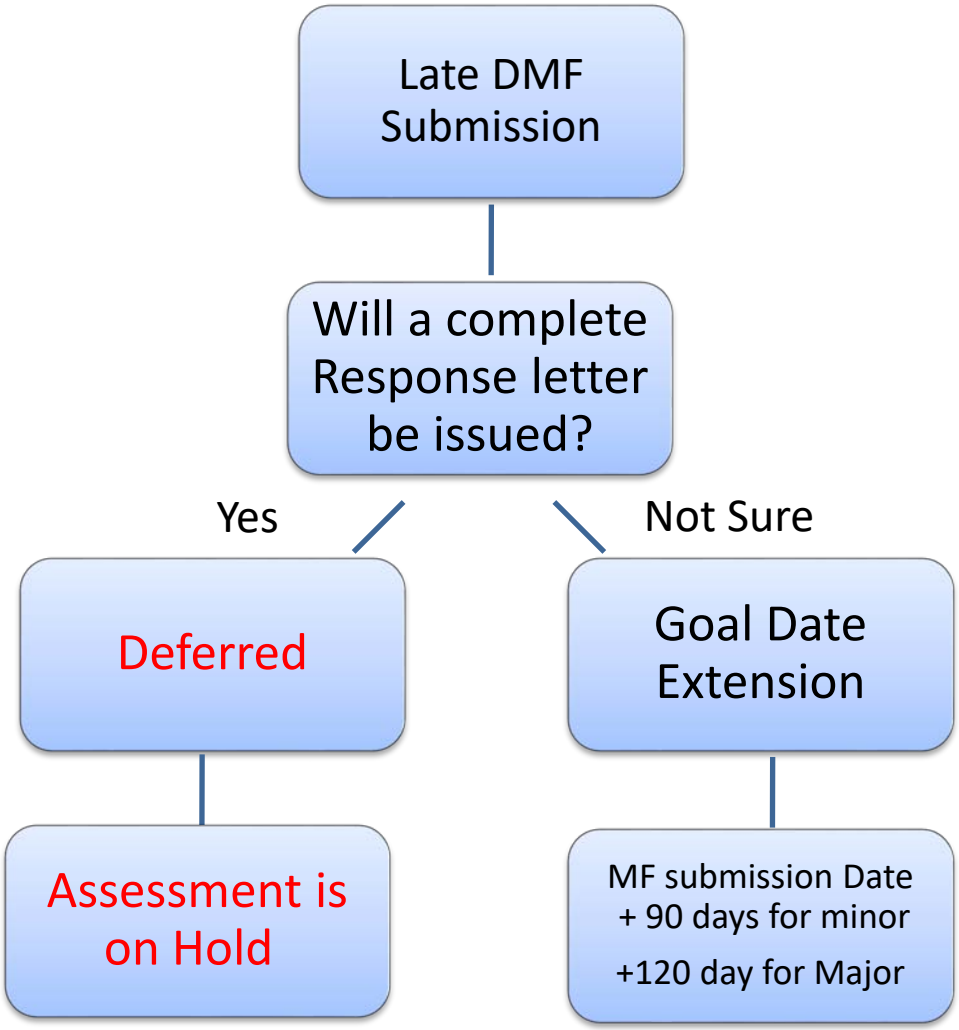
We have completed our review of this Type II DMF and have determined that it is not adequate in its present form. We have described our reasons for this conclusion below and, where possible, our recommendations to address these issues.

In order to keep the DMF review aligned with the referencing application(s), we recommend that you communicate with your customer(s) regarding the action timelines for their application(s) and coordinate your response accordingly. We recommend that your response to this letter be submitted no later than 90-days **[USE IF NO MAJOR DMF DEFICIENCIES] OR** no later than 120-days **[USE IF THERE IS ONE OR MORE MAJOR DMF DEFICIENCIES]** before any referencing ANDA's goal date(s). Please note that if your response contains either gratuitous information not requested by FDA or information that requires a more thorough review as determined by FDA, the existing review goals may be extended or a Complete Response letter may be issued for any referencing ANDA.

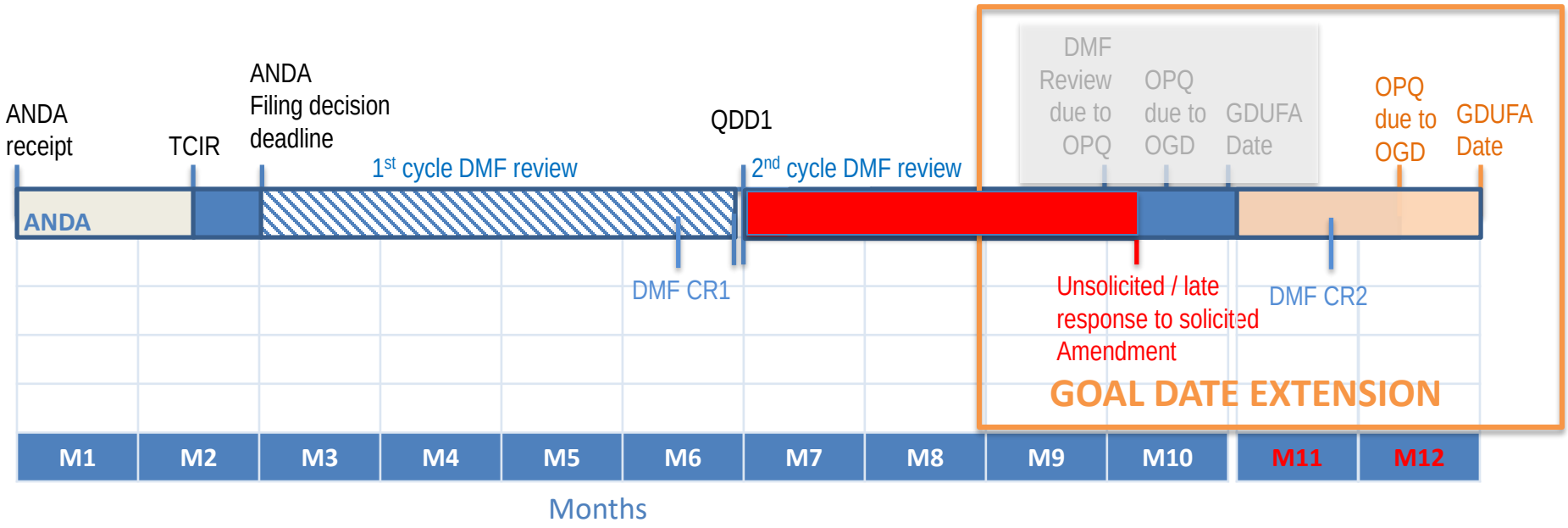
- **The First Page:**
- The status of DMF is not adequate yet
- The assessment was completed or was deferred
- The Applicant whose application is under reviewing

- **The Last Page:**
- CR response Date
  IQ minor=The earliest goal date-90 days
  IQ Major= The earliest goal date-120 days

Internal Process of Late Submissions



Late DMF Response/Amendment Results the Goal Date Extension



Outgoing communications: FDA to ANDA, FDA to DMF

Where is the DMF: With OGD | With OPQ | With OPQ/DMF under review | With DMF holder

Industry Actions

- On receipt of a complete response letter, DMF holder should follow the instructions in the letter and submit a CR response in a timely manner

- For DMF holders, before submitting an unsolicited DMF amendment, consider disclosing the submission date to your customers.

- For ANDA holders, consider informing the corresponding DMF holder regarding your pending goal date.

- Late submission may cause an extension of the goal date.

Conclusions

- In FY 2019 submission study, 3% of original DMF submissions, 55% solicited DMF submissions, and 86% unsolicited DMF submissions are found adequate. Over 96% of DMF assessments met the GDUFA goal dates.

- In the last six years, the Agency issued 1462 CR letters for original DMF submission. Less than 10% of DMF CR responses were submitted within 30 days. The average first CR response time is dropped from 190 days (FY 2013) to 114 days (FY 2019), decreasing about 40%.

Conclusions

- The average CR response time is over 90 days, and the CR responses are identified as the late submission.

- Late CR responses or unsolicited amendments don’t allow the second cycle DMF review, which decreases the first-cycle approval rate.

- Submit CR response promptly and communicate with Applicants effectively will allow the second cycle DMF review and improve the DMF adequacy rate.

Acknowledgement

- Olivia Oh
- Viktor Fedotov

Thank You!

- Send questions regarding this poster to: DMFWorkshop2021@fda.hhs.gov by 2/15/2021 for inclusion in the poster Q&A session on *March 3rd*
- A follow-up webinar for both posters/presentations is scheduled on April 9, 2021. Questions can be sent to the above email by 3/19/2021 for the webinar.
- Please refer to the following posters for cross-referenced materials: *Metrics on DMF Assessments – Productivity, Output, and Metrics*
- Please refer to the following presentations on March 3rd and 4th for additional information: *Effective Communication Strategies For Drug Master Files*