Closing out GDUFA II-Summary of DMF Performance

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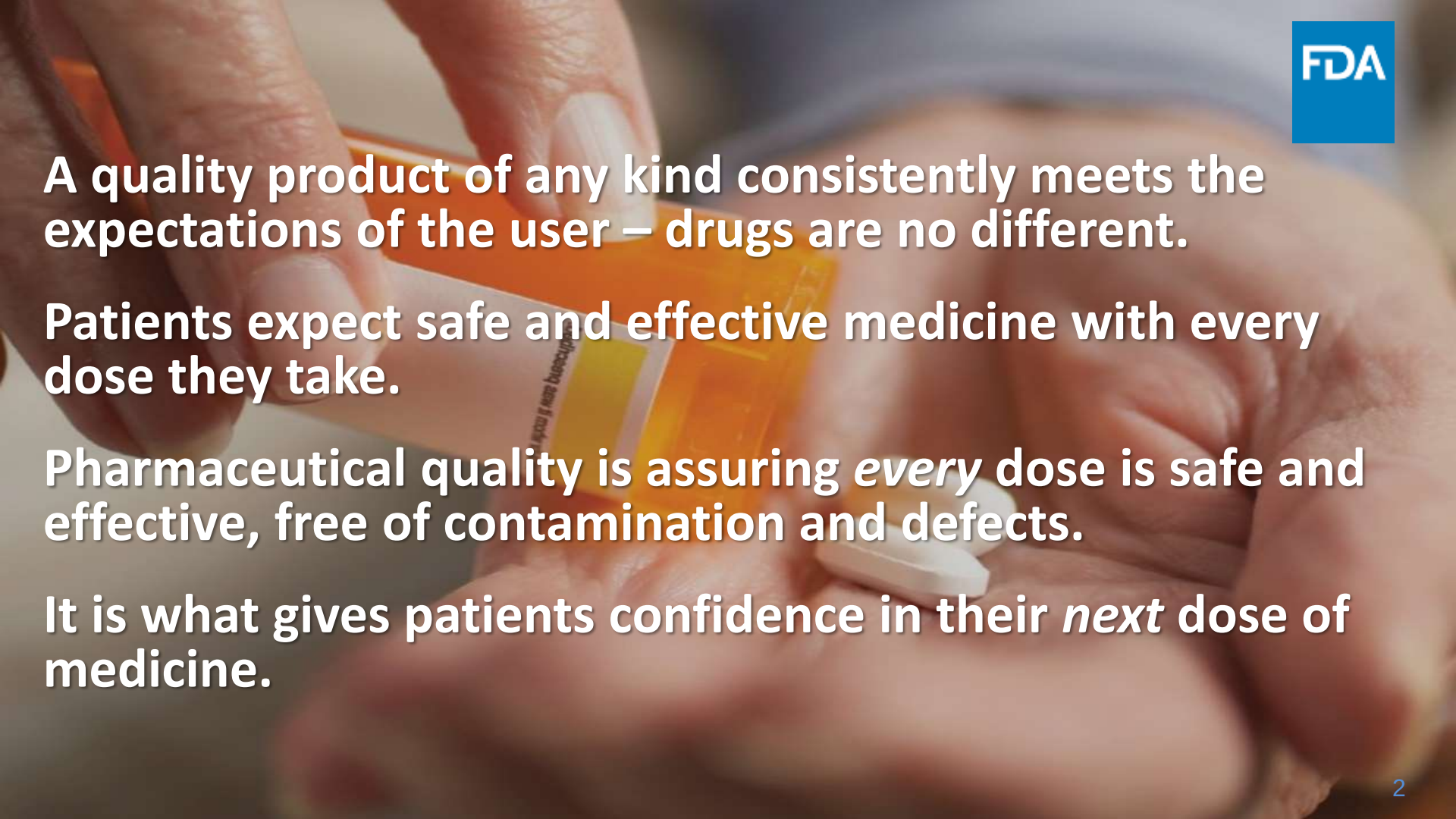
SBIA DMF Workshop: GDUFA III Enhancements and Structured Data Submissions– November 30, 2022



A quality product of any kind consistently meets the expectations of the user – drugs are no different.

Patients expect safe and effective medicine with every dose they take.

Pharmaceutical quality is assuring *every* dose is safe and effective, free of contamination and defects.

It is what gives patients confidence in their *next* dose of medicine.

Objectives

- **GDUFA I & II Accomplishments**
  - Completeness Assessment (CA)
  - First Adequate Letter (FA)
  - No Further Comments Letter (NFC)
  - Teleconference (T-Con)
- **Opportunities into GDUFA III**
  - Navigating the Unsolicited Amend arena
  - Secure email and its benefits
- **Resource Links**

Completeness Assessment (CA)

for GDUFA I & II

Historical CA Data

GDUFA I

	FY 13	FY 14	FY 15	FY 16	FY 17
Total #of DMFs Completed	1780	802	714	531	458
Total Full CAs	938	550	546	449	388
R01 with status “Complete”	219	241	246	242	257
%R01 Complete	23.3	43.8	45.0	53.9	66.2

GDUFA II

	FY 18	FY 19	FY 20	FY 21	FY 22
Total #of DMFs Completed	384	454	303	412	397
Total Full CAs	326	397	244	354	360
R01 with status “Complete”	164	172	126	225	247
%R01 Complete	50.3	43.3	51.6	63.6	68.6

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GDUFA II Data for Subsequent Cycle

	FY18	FY19	FY20	FY21	FY22
Total Full CAs	326	397	244	354	360
R01 with status "Complete"	164	172	126	225	247
R02 with status "Complete"	150	207	103	169	134
%R01 +R02 with status "Complete"	96.3	95.5	93.9	95.6	96.0

- The average first cycle completes are around 56%.
- Over 95% are found complete after two cycles.

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Completeness Assessment (CA)

GDUFA II Performance

- Complete the initial completeness assessment review for 90 percent of Type II API DMFs within 60 days of the later of the date of DMF submission or DMF fee payment.

	FY 18	FY 19	FY 20	FY21	FY22
DMF Submissions	384	454	303	412	397
Met Goal	364	422	300	404	391
Metric	94.8%	93.0%	99.0%	98.1%	98.5%

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Key Highlights

First Adequate Ltr (FA)

&

No Further Comments Ltr (NFC)

GDUFA II Performance

- **DMF First Adequate Letters**: Once a DMF has undergone a full scientific review and has no open issues related to the review of the referencing ANDA, FDA will issue a First Adequate Letter.
- **No Further Comments Letters**: Once a DMF has undergone a complete review and the ANDA referencing the DMF has been approved or tentatively approved, FDA will issue a no further comment letter.

	FY 18	FY 19	FY 20	FY21	FY22	Total
First Adequate Letter	189	198	213	254	318	1172
No Further Comments Letter	974	800	1336	703	748	4561

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Key Highlights

Teleconference (T-Con)

GDUFA II T-con Performance

Fiscal Year	FY17	FY18	FY19	FY20	FY21	FY22
Total number of meetings requested	20	12	6	3	4	8
Total number of meetings Granted	18	11	6	3	0	3
Median response time (in days) to grant meeting or grant with written response	14	28	21	10	n/a	22

Email Exchange (EE)

GDUFA II Email Exchange (EE) Performance

Fiscal Year	FY18	FY19	FY20	FY21	FY22
Total Initial EE completed	60	65	80	66	46
Median days to response-Initial EE	12	16	9	13	11
Total Follow-up EE completed	10	2	16	5	8
Median days to response-Follow-up EE	10	12	8	11	16

Unsolicited Amendments Issues & Tips

DMF Unsolicited Amendment Issues

- Poorly timed unsolicited amendments continue to adversely impact application timelines.
- Can result in goal date extensions or unnecessary CR letters to the DMF and applicant.
- Most unsolicited amendments do not need to be submitted at the time they are received.
- Communication between the applicant and DMF holder regarding the DMF submission and application timelines is the best solution

Tips to avoid Unsolicited Amendment Issues

- DMF holders and applicants should share the following information in a timely way:
  - Plans to submit changes to the DMF
  - Key expected action dates and priorities for the referencing application(s)
  - Know the current status of your DMF – FA letters, NFC letters, real time updates from DMFOGD@FDA.HHS.GOV
  - FDA can share DMF status information with authorized parties to the DMF

Tips to avoid Unsolicited Amendment Issues

- If it is not clear whether an unsolicited DMF submission will impact an application timeline do the following:
  - Reach out to your customers to get information on application timelines
  - Reach out to DMFOGD so we can provide helpful guidance on submission timing

- Understand the consequences of a poorly timed DMF amendment to your customer's ANDA
  - Goal date extension (extended from the date the DMF amendment is received)
  - Length of extension determined by nature of the amendment (major or minor)
  - Potential loss of an exclusivity (forfeiture date)
  - Withdrawal of a DMF amendment will not restore an already extended goal date

Benefits of secure email link with the FDA

Secure Email Address

- DMF holders and agents can greatly facilitate communication by having a secure email address.
- Secure email allows FDA to provide DMF communications electronically.
- Contact SecureEmail@fda.hhs.gov for information on how to become a secure email partner with the FDA.

The Change Over

From GDUFA II to GDUFA III

What is same

&

What is new

GIII: What is the same

- Completeness Assessment (CA)
- No Further Comments letter (NFC)
- First Adequate letter (FA)
- Email Exchange (EE)
- Teleconference (T-con): Largely the same with one minor timeline change.

GDUFA III: What is new

DMF Assessment Program Enhancements

DMF review prior to ANDA submission:

The DMF holder would provide a "request for review" 6 months prior to the original ANDA's planned submission date for applications that meet one of the following criteria: All patents and exclusivities will expire within 12 months of the planned submission date, no more than 3 approved ANDAs, drug shortage, public health emergency, or sole source product. The "request for review" process is available to newly submitted DMFs, and previously unreviewed DMFs that will be referenced in an original ANDA to be submitted in 6 months. A DMF holder can also submit a "request for review" for a PAS to add a new API source, provided the product is related to drug shortage or public health emergency.

Assessment of DMF solicited off-cycle amendments:

1. FDA will assess solicited DMF amendments related to original ANDAs and PASs upon receipt even if the original ANDA or PAS in which the DMF is referenced is not currently under assessment.
2. Such assessments will be conducted based on the assessment status of the DMF and other disciplines in the related ANDAs, with priority being given to those amendments related to ANDAs for which acceptability of the DMF assessment may result in an approval.

Link to GDUFA III Commitment letter: https://www.fda.gov/media/153631/download

Resources

- GDUFA III Commitment Letter: https://www.fda.gov/media/153631/download
- Review of Drug Master Files in Advance of Certain ANDA Submissions Under GDUFA, Guidance for Industry, Draft Guidance: https://www.fda.gov/media/162019/download
- GDUFA II Drug Master Files (DMFs): https://www.fda.gov/drugs/forms-submission-requirements/gdufa-ii-drug-master-files-dmfs
- GDUFA III Drug Master File (DMF) Review Enhancements: https://www.fda.gov/industry/generic-drug-user-fee-amendments/gdufa-iii-drug-master-file-dmf-review-enhancements


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