Your Generics & Biosimilars Industry

The Generic Drug User Fee Amendments (GDUFA III)

Background:

Congress first enacted the Generic Drug User Fee Amendments (GDUFA) in 2012. GDUFA is based on an agreement negotiated by FDA and representatives of the generic drug industry to address the growing number of regulatory challenges and resource gaps that created delays in the review of generic drug applications.

GDUFA aims to put FDA's generic drug program on a firm financial footing by enabling FDA to assess user fees to fund critical and measurable enhancements to the performance of FDA's generic drugs program, bringing greater predictability and timeliness to the review of generic drug applications. As a direct outcome, the generic drugs program has increased patient access to safe, high-quality, and affordable generic medicines.

Today, ninety percent of the prescriptions filled in the United States were filled with generic medicines, accounting for $330 billion in saving just in 2020 alone.

The initial authorization and subsequent reauthorization(s) are provided below:

- Authorization of Generic Drug User Fee Amendments (GDUFA I) – FY2013 to FY2017
- Reauthorization of the Generic Drug User Fee Amendments (GDUFA II) – FY2018 to FY2022
- Reauthorization of the Generic Drug User Fee Amendments (GDUFA III) – FY2023 to FY2027 (pending)

The GDUFA III negotiated agreements will further strengthen and build upon the good work and lessoned learned from GDUFA I and GDUFA II. The quick glance below highlights the new enhancements agreed upon between industry and FDA. The GDUFA III Commitment Letter can be found here.

GDUFA III at a Glance:

Advancing Approvals:

- Imminent Action

    - FDA will continue assessment of an Abbreviated New Drug Application (ANDA) past the goal date if, in FDA's judgment, it may be possible to approve or tentatively approve an ANDA within 60 days after the goal date

- Extension of Goal Dates
    - FDA will use Information Request (IR) and Discipline Review Letter (DRL) to facilitate an approval or tentative approval (TA) action. GDUFA III defines IRs and DRLs as follows:
        - Information Request (IR) is a communication that is sent to an applicant during an assessment to request further information or clarification that is needed or would be helpful to allow complete of the discipline assessment.
        - Discipline Review Letter (DRL) is a letter used to convey preliminary thoughts on possible deficiencies found by a discipline assessor and/or assessment team for its portion of the pending application at the conclusion of the discipline assessment.
- Pre-submission Facility Correspondence (PFC)
    - Modification to the timeline for including analytical studies used to support an application.
- Classification of Majors
    - FDA will issue a Manual of Policies and Procedures (MAPP) on the process for Reclassification of Facility-Based Major Complete Response Letter (CRL) Amendments on or before June 30, 2024.
- Controlled Correspondence
    - Expanded the scope to include regulatory and/or scientific advice after issuance of a CRL or TA, or after ANDA approval.

Facility Inspections:

- Post-Warning Letter Meetings
    - ANDA applicants may request a meeting with FDA to seek the Agency's feedback on the applicant's plan to remediate facility deviations identified in a warning letter.
- Reinspection Metrics
    - FDA will reinspect a facility within the agreed upon timelines after a request for reinspection is submitted by the applicant.
- Reclassification of Major for Facility Only Action

- FDA will make a decision on a request for reclassification of a Facility-Based Major CRL Amendment within 30 days from the date of submission for priority amendment and within 60 days for standard amendments.

Drug Master File (DMF):

- Advance Submission of Certain Category of DMFs
  - A DMF holder may submit a request for assessment 6 months prior to the planned ANDA submission.
  - A DMF holder may submit a request for assessment 6 months prior to the planned submission date for a Post Approval Supplement (PAS) to add a new Active Pharmaceutical Ingredient (API) source.
- Off-Cycle Review of Solicited DMF Amendments
  - FDA will assess solicited DMF amendments related to original ANDAs and PASs upon receipt even if the original or PAS is not currently under assessment.
  - FDA will issue a MAPP on the prioritization of FDA assessment of solicited DMF amendments on or before June 30, 2024
- FDA will ensure the DMF assessment comments submitted to the DMF holder are issued at least in parallel with the issuance of review comments relating to the DMF for the ANDA.
- Unsolicited DMF Amendments
  - FDA will assist with coordination of an unsolicited amendment to avoid introducing delays to the ANDA's the DMF supports.
- API-Excipient Mixtures
  - FDA will issue guidance clarifying the regulatory status of an API-Excipient mixtures for GDUFA purposes.

Different Types of Meetings:

- Product Development Meetings:
  - Prospective applicants can request a pre-ANDA submission Product Development Meeting. The scope of the Product Development Meeting is to provide a forum for a scientific exchange on specific issues in which FDA will provide targeted advice regarding an ongoing ANDA development program.

- Depending on available resources, FDA may grant a prospective applicant a product development meeting concerning development issues other than those described in the prior sub-bullet.
- FDA will conduct Product Development Meetings in accordance with the agreed upon metrics.

- Pre-Submission Meetings:
  - Prospective applicants may request a Pre-Submission Meeting with the FDA. The scope of the Pre-Submission Meeting is to provide an applicant the opportunity to present unique or novel data or information that will be included in the ANDA submission.
  - FDA will grant a Pre-Submission Meeting if the applicant was granted a Product Development Meeting for the same complex generic product or FDA believes that the meeting would improve the assessment efficiency.
  - FDA will conduct Pre-Submission Meetings in accordance with the agreed upon metrics

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- Mid-Cycle Review Meetings and Enhanced Mid-Cycle Review Meetings:
  - ANDA applicants for a complex generic product who were granted a Product Development Meeting may within 7 days of receiving the last mid-cycle DRL submit a request for either a Mid-Cycle Review Meeting or an Enhanced Mid-Cycle Review Meeting.
    - Mid-Cycle Review Meetings:
      - The scope of the Mid-Cycle Review Meeting is for the applicant to ask for the rationale for any deficiency identified in the mid-cycle DRL(s), and /or to ask questions related to FDA's assessment of the data or information in the ANDA. No new data or information can be presented at this meeting.
      - FDA will hold the Mid-Cycle Review Meeting within 30 days after the date the applicant submits a meeting request.
    - Enhanced Mid-Cycle Review Meeting
      - The scope of the Enhanced Mid-Cycle Review Meeting is for the applicant to ask questions related to a proposed scientific path to address possible deficiencies identified in the mid-cycle DRL(s). The applicant may ask questions

about potential new data or information to address any possible deficiencies.

- FDA will discuss the data and information but will not provide substantive assessment of data or information provided by the applicant.
- FDA will hold the Enhanced Mid-Cycle Review Meeting within 90 days after issuance of the last mid-cycle DRL.
- FDA will extend the ANDA goal date by 60 days if an applicant requests this type of meeting. FDA will also extend the response due date for the relevant DRL(s) by recalculating the response dates to align with the meeting.

- Post-CRL Scientific Meetings:
  - ANDA applicants can request a Post-CRL Meeting for a complex generic product or for issues that in FDA's judgement would be best addressed with a Post-CRL Scientific Meeting and would not be adequately addressed through a Controlled Correspondence.
  - The scope of the Post-CRL Meeting is to provide an applicant scientific advice on possible approaches to address deficiencies identified in a CRL related to establishing equivalence, such as new equivalence study needed to address the design deficiency in the CRL, a new approach that is different from that submitted in the ANDA, a new comparative use human factor study, or a new approach to demonstrating sameness of a complex active ingredient.
  - ANDA applicants are eligible for a Post-CRL Scientific Meeting even if they have not had a Product Development Meeting.
  - FDA will hold the Post-CRL Scientific Meeting within 90 days after the date the meeting is granted. FDA will grant or deny the meeting request with 14 days after receipt of the meeting request.

Product Specific Guidance (PSG)

- FDA will continue to issue PSG identifying the methodology for generating evidence needed to support ANDA approval.
- FDA will continue to develop and issue standard and complex PSGs as follows:

    - For all complex products approved in new drug applications (NDAs) on or after October 1, 2022, a PSG will be issued for 50% of such NDA products within 2 years after the date of approval and for 75% of such NDA products within 3 years after the date of approval.
    - FDA will continue to develop PSGs for complex products approved prior to October 1, 2022, for which no PSG has been published.
    - For all non-complex products approved in NDAs on or after October 1, 2022, that contain a new chemical entity, a PSG will be issued within 2 years after the date of approval for 90% of such products.
- FDA will seek public input on prioritization of PSGs annually during the public meeting on research prioritization.
- FDA will make available on its website information on how the Agency prioritizes the development of PSG's,
- Industry may identify PSGs that FDA should prioritize via the Controlled Correspondence pathway.
- ANDA applicants or a prospective applicant may request a PSG teleconference to obtain Agency feedback on the potential impact of a new or revised PSG on its development program. The scope of the meeting is to provide a forum in which industry can discuss the scientific rationale for an approach other than the approach recommended in the PSG to ensure the proposed approach complies with the relevant statutes and regulations.
- FDA will hold a 60 minute PSG teleconference within 30 days after the receipt of the meeting request. If further feedback is needed after the teleconference, the applicant may utilize the Controlled Correspondence pathway or request an additional meeting.

Suitability Petition Metrics:

- FDA will enhance the review and response times for suitability petitions.
- FDA will conduct a completeness assessment within 21 days after receipt of the original petition or the receipt of the IR response.
- FDA will prioritize the review of suitability petitions according to the agreed upon criteria and metrics.

Guidance and MAPPs:

- FDA will draft or modify relevant MAPPs to reflect the commitments and goals in the GDUFA III Commitment Letter, including, but not limited to directing project

managers, assessors, and other assessment program staff to actively work towards an action for ANDA's with missed or extended goal dates and revise MAPP 5200.12 Communicating ANDA Review Status Updates with Industry to include communications related to imminent action on or before April 30, 2023.

- FDA will issue a Federal Register Notice on or before April 30, 2023, to solicit public comment on the content of Appendix A in the guidance for Industry titled ANDA Submissions – Amendments to ANDA under GDUFA (July 2018). FDA will use evaluations and or training to assure consistency in ANDA amendment classification.
- FDA will issue a MAPP on the process for Reclassification of Facility-Based Major CRL Amendments on or before June 30, 2024.
- FDA will issue a MAPP on the prioritization of FDA assessment of solicited DMF amendments on or before June 30, 2024.
- FDA will issue guidance clarifying the regulatory status of API-excipient mixtures for GDUFA purposes.

Sustainability of GDUFA Program Resources:

- Resource Capacity Planning
    - FDA will continue activities to mature the Agency's resource capacity planning function, including utilization of modernized time reporting to support the implementation of the Capacity Planning Adjustment (CPA).
    - FDA will publish an implementation plan by the end of second quarter of FY 2023 that will describe how resource capacity planning and time reporting will continue to be utilized during GDUFA III.
    - FDA will provide annual updates and document in the annual GDUFA Financial Report how the CPA fee revenues are being utilized.
    - FDA and industry agreed upon caps for the CPA to mitigate creating entry barriers.
    - By the end of FY 2025, an independent contractor will complete and publish an evaluation of the resource capacity planning capability.

Improving the Hiring of Review Staff:

- FDA will hire 128 staff in FY 2023 of GDUFA III to ensure the negotiated commitments are attained.