Facility Readiness: Goal Date Decisions Under GDUFA

Guidance for Industry

DRAFT GUIDANCE

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

October 2022
Generic Drugs

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance provides information to applicants on how FDA intends to assign a goal date based on a facility's readiness for inspection as certified on Form FDA 356h[2,3] submitted as part of an original abbreviated new drug application (ANDA)[4] under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)). This guidance explains how FDA incorporates a program enhancement agreed upon by the Agency and industry as part of the negotiations relating to reauthorization of the Generic Drug User Fee Amendments (GDUFA), as described in "GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2023-2027" (GDUFA III commitment letter).[5]

Under the commitment letter related to the GDUFA authorization for fiscal years 2018 through 2022 (under the Generic Drug User Fee Amendments of 2017),[6] a goal date was assigned without regard to facility readiness. In the GDUFA III commitment letter, FDA agreed to incorporate facility readiness into goal date assignment, such that FDA generally assigns a 15-month goal date and defers substantive assessment if a facility is not ready for an inspection at the time of application submission.[7,8] FDA may not be able to complete substantive assessment of an application unless all facilities are ready for inspection. Therefore, this change

[1] This guidance has been prepared by the Office of Pharmaceutical Quality (OPQ) and the Office of Generic Drugs (OGD) in the Center for Drug Evaluation and Research at the Food and Drug Administration.
[2] Form FDA 356h, titled *Application to Market a New or Abbreviated New Drug or Biologic for Human Use*, is available at https://www.fda.gov/media/72649/download.
[3] Form FDA 356h fulfills the 21 CFR 314.94(a)(1) application form requirement.
[4] For the purposes of this guidance, the term *original ANDA* refers exclusively to the application assessed during the first review cycle, including an application resubmitted after a refuse-to-receive action.
[5] The GDUFA III commitment letter is available at https://www.fda.gov/media/153631/download.
[6] Title III of the FDA Reauthorization Act of 2017, Public Law 115-52.
[7] See section I.A.3. of the GDUFA III commitment letter.
[8] OPQ and OGD generally use the terms *assessment* and *review* interchangeably. In this guidance, assessment means the process of both evaluating and analyzing submitted data and information to determine whether the application meets the requirements for approval and documenting that determination.

helps FDA to focus resources on substantially complete[9] applications that contain facilities ready for inspection.

This guidance does not apply to:

- Facilities involved in bioequivalence and clinical studies used to support an application
- Amendments submitted after a complete response or tentative approval letter
- Supplements or amendments to a supplement

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

The Generic Drug User Fee Amendments of 2012 (GDUFA I)[10] amended the FD&C Act to authorize FDA to assess and collect user fees to provide FDA with resources[11] to help ensure patients have access to quality, affordable, safe, and effective generic drugs. GDUFA fee resources bring greater predictability and timeliness to the review of generic drug applications. GDUFA has been reauthorized every 5 years to continue FDA's ability to assess and collect GDUFA fees, and this user fee program has been reauthorized two times since GDUFA I, most recently in the Generic Drug User Fee Amendments of 2022.[12] As described in the GDUFA III commitment letter applicable to this latest reauthorization, FDA has agreed to performance goals and program enhancements regarding aspects of the generic drug assessment program that build on previous authorizations of GDUFA. New enhancements to the program are designed to maximize the efficiency and utility of each assessment cycle, with the intent of reducing the number of assessment cycles for ANDAs and facilitating timely access to generic medicines for American patients.

[9] An application's substantial completeness is evaluated consistent with 21 CFR 314.101; information on FDA's policies and procedures for conducting a filing review to determine if an ANDA is substantially complete is available in the Manual of Policies and Procedures (MAPP) 5200.14 *Filing Review of Abbreviated New Drug Applications* (available at https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-manual-policies-procedures-mapp).

[10] Title III of the Food and Drug Administration Safety and Innovation Act, Public Law 112-144.

[11] User fees are available for obligation in accordance with appropriations acts.

[12] Enacted as Title III of Division F (the FDA User Fee Reauthorization Act of 2022) of the Continuing Appropriations and Ukraine Supplemental Appropriations Act, 2023.

A number of GDUFA III commitments are intended to reduce first assessment cycle facility-related delays that could delay application approval. The commitment outlined in this guidance sets the goal date to 15 months for an original ANDA containing a certification that a facility on Form FDA 356h is not ready for inspection. An applicant can amend its original ANDA to reset the 15-month goal date to a standard or priority assessment goal, as applicable,[13] once all facilities become ready for inspection. However, the commitment letter also explains that for an application that continues to include a facility not ready for inspection 30 days before the 15-month goal date expiration, FDA will reset the goal date for an additional 15 months (i.e., 30 months from the date of original ANDA submission). FDA agreed to assess and act on 90 percent of such ANDAs within 30 months of the date of the original submission as applicable.[14] Through the implementation of this commitment, FDA and industry aim to incentivize the submission of applications that include facilities ready for inspection to facilitate their timely assessment.

III. FACILITY READINESS: ASSESSMENT AND REPORTING

Under the GDUFA III commitment letter, FDA uses a facility's readiness for inspection designation in the Establishment Information section of Form FDA 356h to assign an application's goal date. Applicants should examine the accuracy of the facility information they submit on Form FDA 356h.

A. Applicant Assessment of Facility Readiness

Applicants should assess whether each facility is ready for inspection before checking the appropriate box on Form FDA 356h. FDA considers a facility that is ready for inspection to be one that complies with current good manufacturing practice (CGMP) requirements[15] and meets the following criteria related to the application product:

- Facility operations, methods, and product formulation are the same as those described in the application

[13] FDA considers an ANDA to be a priority ANDA if it meets the criteria listed in either section 505(j)(11) of the FD&C Act (which governs for ANDAs subject to that provision) or MAPP 5240.3 Rev. 5 *Prioritization of the Review of Original ANDAs, Amendments, and Supplements*. Section 505(j)(11)(D) of the FD&C Act reaffirms FDA's authority to "prioritiz[e] the review of other applications as [FDA] determines appropriate."

[14] GDUFA III commitment letter, section I.A.3.b., page 5

[15] For the purposes of this guidance, CGMP refers to the requirements in section 501(a)(2)(B) of the FD&C Act and 21 CFR parts 4, 210, and 211, as applicable.

- Data at the facility are complete and accurate, and are consistent with data in the application[16]

- The facility is ready for commercial manufacturing[17]

To assess these criteria during an inspection, FDA uses Compliance Program (CP) 7346.832 *Preapproval Inspections*.[18] Applicants may also find the considerations in CP 7346.832 (Part III, section 1, NDA/ANDA Inspectional/Audit Coverage, Objectives, and Techniques) useful when assessing facility readiness.[19] FDA provides additional facility readiness recommendations in the guidance for industry *Good ANDA Submission Practices* (January 2022), section V.D., Facilities.

FDA has experienced cases where facilities were not aware they were listed on Form FDA 356h.[20] This often results in a greater likelihood that a facility will be unprepared for an inspection. FDA recommends that applicants notify each facility that the facility is listed on the applicant's Form FDA 356h and inform the facility whether the applicant has checked the "yes" or "no" box in the Establishment Information Field 28 of Form FDA 356h to identify the inspection readiness of each manufacturing or testing facility listed.

When signing Form FDA 356h, an applicant certifies that the information in the application is complete and accurate. Inaccurate representation of facility readiness may cause a delay in or refusal to approve an application.[21]

B. Reporting Facility Readiness on Form FDA 356h

Form FDA 356h should be used to convey application-related facility information for manufacturing, packaging, and control sites for drug substance and drug product facilities.[22] Applicants should check the "yes" or "no" box in the "Is the site ready for inspection?" section of Field 28 (Establishment Information) on Form FDA 356h to identify the inspection readiness for each manufacturing or testing facility listed, including any reference to a manufacturing or testing facility associated with a drug master file.

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[16] See the guidance for industry *Data Integrity and Compliance With Drug CGMP; Questions and Answers* (December 2018). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[17] FDA considers *ready for commercial manufacturing* to mean that the establishment has a quality system that is designed to achieve sufficient control over the facility and commercial manufacturing operations for the product, among other elements further described in FDA Compliance Program 7346.832 *Preapproval Inspections*.

[18] Drug Compliance Programs are available at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/drug-compliance-programs.

[19] FDA considers it a best practice for all manufacturing facilities listed in an application to be ready for inspection at the time of submission. These considerations are useful when assessing facility readiness for a preapproval inspection.

[20] If a facility identified in an ANDA believes it was included in error and seeks to be removed from that ANDA, the facility should work with the ANDA applicant to be removed from the application.

[21] See section 505(j)(4)(A) and (K) of the FD&C Act; 21 CFR 314.127.

[22] For more information regarding which facilities should be listed on Form FDA 356h, see the guidance for industry *Identification of Manufacturing Establishments in Applications Submitted to CBER and CDER, Questions and Answers* (October 2019).

The "Is the site ready for inspection" section of Field 28 also includes an "N/A" box, but this box should not be checked for original ANDA submissions. Applicants should check the "N/A" box when they withdraw a facility from the application. FDA will not consider an applicant's estimated date of readiness (noted in Field 28) when assigning a goal date.

If the boxes in Field 28 are blank or incorrectly marked "N/A," both of which prevent a determination of facility readiness, FDA will seek clarification by issuing the applicant an information request (IR) letter. FDA will assign the application a 15-month goal date by default if the applicant does not respond within the time frame prescribed in the IR letter.[23]

IV. GOAL DATE ASSIGNMENT

When an original ANDA is submitted with a completed Form FDA 356h, FDA reviews the submission for facility readiness information, receives the application if substantially complete,[24] assigns the appropriate goal date,[25] and issues an acknowledgement letter.[26]

To implement the GDUFA III commitment,[27] FDA modified its procedures to incorporate facility readiness in goal date assignment. In cases when one or more facilities are not ready for inspection, FDA generally assigns a 15-month goal date and defers substantive assessment of the original ANDA and any unsolicited amendments until receipt of an amendment with an updated Form FDA 356h stating all facilities are ready for inspection.

Upon receipt of an amendment with Form FDA 356h certifying that all facilities are ready for inspection, FDA will reassign the appropriate standard or priority goal date (as applicable) calculated from the amendment receipt date. To facilitate goal date reassignment, FDA

[23] The GDUFA III commitment letter provides for FDA to communicate minor technical deficiencies (e.g., document legibility) and deficiencies potentially resolved with information in the ANDA at original submission within 10 days of original ANDA submission. If the applicant resolves those deficiencies within 10 days of such communication from FDA, those deficiencies will not be a basis for a refuse-to-receive decision under the terms of the commitment letter. See GDUFA III commitment letter, section II.A.2., at page 12 (https://www.fda.gov/media/153631/download).

[24] See 21 CFR 314.101(b)(2). See also the guidance for industry *Providing Regulatory Submissions in Electronic Format — Receipt Dates* (February 2014). These submissions are deemed to be submitted to FDA on the day when transmission to the Electronic Submissions Gateway (ESG) is completed, except when the submission arrives on a weekend, Federal holiday, or a day when the FDA office that will assess the submission is otherwise not open for business. In that case, the submission is deemed to be submitted on the next day when that office is open for business. Additional information concerning the FDA ESG is available at https://www.fda.gov/industry/electronic-submissions-gateway.

[25] GDUFA III commitment letter, section I.A.

[26] See 21 CFR 314.101(b)(2). FDA sends an ANDA acknowledgement letter when it has determined that the ANDA can be received for assessment.

[27] GDUFA III commitment letter, section I.A.3., page 5.

recommends the applicant state in the cover letter "**Facility Ready For Inspection**" along with the ANDA number.[28,29]

If the applicant does not submit an amendment with Form FDA 356h certifying all facilities are ready for inspection by 30 days before the goal date, FDA resets the goal date for an additional 15 months (i.e., 30 months from the date of original ANDA submission) and commences substantive assessment. FDA agreed to assess and act on 90 percent of such ANDAs within 30 months of the date of the original submission as applicable.[30]

[28] See the guidance for industry *ANDA Submissions — Amendments to Abbreviated New Drug Applications Under GDUFA* (July 2018) for additional recommendations on information to be included on the first page of the submission. See also the draft guidance for industry *Cover Letter Attachments for Controlled Correspondences and ANDA Submissions* (December 2021) (when final, this guidance will represent the FDA's current thinking on this topic).

[29] The application goal date is reset based on the calendar day after FDA receives the amendment certifying that all facilities are ready for inspection.

[30] GDUFA III commitment letter, section I.A.3.b., page 5.