
POLICY AND PROCEDURES

OFFICE OF GENERIC DRUGS

Prioritization of the Review of Original ANDAs, Amendments, and Supplements

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PURPOSE

This MAPP describes how the review of original abbreviated new drug applications (ANDAs), ANDA amendments, and ANDA supplements will be prioritized within the Office of Generic Drugs (OGD) and the Office of Pharmaceutical Quality (OPQ).¹ This MAPP is a revision of MAPP 5240.3 Rev. 4 *Prioritization of the Review of Original ANDAs, Amendments, and Supplements* (November 9, 2017).

BACKGROUND

On October 18, 2006, OGD issued MAPP 5240.3 *Review Order of Original ANDAs, Amendments, and Supplements*. That MAPP set forth certain modifications to OGD’s earlier “first-in, first-reviewed” approach to the review of ANDAs, amendments, and supplements. The Food and Drug Administration (FDA) has continued to revise that MAPP to reflect approaches to the review of ANDAs, amendments, and supplements designed to prioritize submissions that would have a meaningful impact on generic drug access. These approaches stem from a variety of legislative and regulatory initiatives including the Food and Drug

¹ Certain original ANDAs may qualify for an 8-month goal date under section 505(j)(11) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(11)) if a pre-submission of facility information is made in accordance with that provision. This MAPP does not describe the pre-submission of facility information or procedures for determining qualification for the 8-month review period, but does include among its prioritization factors the factors reflected in section 505(j)(11)(A)(i) and (ii).

Administration Safety and Innovation Act (FDASIA),² the FDA Reauthorization Act of 2017 (FDARA),³ and the Commissioner’s Drug Competition Action Plan.

This MAPP establishes public health priorities (or “prioritization factors”) that may qualify an original ANDA, amendment, or supplement for a priority review.

POLICY

Prioritization of the review of submissions to OGD will be carried out as described in the paragraphs below.

1. If an *original* ANDA or amendment to an original ANDA meets one of the prioritization factors in this MAPP, the submission will be eligible for a “priority review.” A priority review will be granted to an ANDA *supplement* or amendment to an ANDA supplement if the supplement submission relates to a drug shortage or public health emergency, is subject to a statutory mandate or other legal requirement, or FDA determines that a delay in making the change described in the supplement would impose an extraordinary hardship on the applicant.⁴
2. FDA will only evaluate whether a priority review may be granted if (1) there is an explicit request from the applicant at the time of submission⁵ that includes the prioritization factor or factors under which the applicant believes the submission qualifies for priority review; or (2) in the absence of an explicit request from the applicant, FDA determines that the submission relates to a drug shortage or public health emergency, or that the submission meets the requirements of section 505(j)(11)(A) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

FDA will only consider a request for priority review when (1) the cover letter to the submission clearly states “Priority Review Requested” and references the ANDA number; (2) the basis for the request is consistent with this MAPP; (3) the applicant clearly and briefly states the basis for the request, including the prioritization factor(s); and (4) the applicant includes sufficient supporting documentation for the request.

² Public Law 112-144. FDASIA includes the Generic Drug User Fee Amendments of 2012 (GDUFA I) and, by reference, the Generic Drug User Fee Act Program Performance Goals and Procedures (GDUFA I Commitment Letter).

³ Public Law 115-201. FDARA includes the Generic Drug User Fee Amendments Act of 2017 (GDUFA II) and, by reference, the GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022 (GDUFA II Commitment Letter).

⁴ In accordance with 21 CFR 314.97, 21 CFR 314.70(b)(4) applies to ANDAs.

⁵ FDA evaluates each submission for prioritization at the time of submission, and applicants must request priority review for each submission.

3. Submissions that are eligible for a priority review may receive either a shorter goal date or an expedited review, as defined below in this MAPP. If FDA has received a submission and assigned the submission a goal date, FDA will not adjust the goal date for that submission even if FDA subsequently grants the submission priority review (e.g., if a submission newly qualifies for priority review at some point after its receipt under the *submissions related to drug shortages* prioritization factor described below).
4. Submissions that qualify for priority review under multiple factors in this MAPP do not receive an additional benefit relative to submissions that qualify under one factor.
5. If one drug product (e.g., one strength) under an original ANDA, amendment, or supplement submission qualifies for priority review under one or more of the prioritization factors in this MAPP, the entire submission will be eligible for priority review.
6. Submissions involving facilities that are subject to a recommendation of Official Action Indicated generally will not be considered for a priority review, except in certain cases in which it is determined that the submission must be prioritized to address a public health concern. These determinations will be made by the OGD Regulatory Project Manager (OGD RPM) and OGD management in consultation with other FDA personnel as necessary, including the OPQ Regulatory Business Process Manager (OPQ RBPM).

Prioritization Factors

- **Submissions for which there are not more than three approved drug products**

Submissions for drug products for which there are not more than three approved drug products listed in FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book")^{6,7} and for which there are no blocking patents or exclusivities listed for the reference listed drug (RLD).⁸ In other words, if there are fewer than four approved therapeutically equivalent drug products, including the RLD, listed in the Orange Book, and if there are no blocking patents or unexpired exclusivities for the RLD in the Orange Book, a submission can qualify under this factor.

⁶ The Orange Book is available at <https://www.accessdata.fda.gov/scripts/cder/ob/>.

⁷ "Approved drug products" include drug products listed in both the "Active Section" and the "Discontinued Section" of the Orange Book, unless the approval is voluntarily withdrawn under 21 CFR 314.150(c) pursuant to a published *Federal Register* notice. Generally, an approved product is added to the "Discontinued Section" when the applicant notifies FDA of the product's not-marketed status.

⁸ For purposes of this MAPP, a patent to which an applicant has solely submitted a statement under section 505(j)(2)(A)(viii) of the FD&C Act (21 U.S.C. 355(j)(2)(A)(viii)) will not be considered a blocking patent.

- **Applications containing a paragraph IV certification**

For applications containing a paragraph IV certification,⁹ FDA will prioritize submissions that will be ready for final approval at or before the goal date for that submission and that fit within one of the categories described in the sub-bullets below.¹⁰ To receive priority review, an applicant must clearly state in the cover letter to its submission that the submission is a request for final approval and provide adequate documentation to show that the application will be eligible for final approval at or before the goal date for that submission. In order for a priority review to be granted, litigation updates (e.g., notification of court actions or written consent to approval) must be appropriately documented and submitted to FDA in accordance with 21 CFR 314.107; if legal action was not filed by the patent owner(s), the New Drug Application (NDA) holder, or the exclusive patent licensee within 45 days of their receipt of the notice of the paragraph IV certification, the applicant should submit documentation after the 45-day period elapses stating that no legal action was taken by the patent owner(s), NDA holder, or exclusive patent licensee.¹¹ If an applicant fails to timely submit its documentation, FDA may not be able to grant priority review. FDA will prioritize submissions that will be ready for final approval at or before the goal date for that submission in the following circumstances:

- Submissions from applicants who satisfy the statutory definition of first applicant¹² at the time of submission. To qualify for prioritization, these applicants must summarize in the submission cover letter the basis for the priority review request and provide any required documentation to confirm the application will be ready for final approval at or before the goal date for that submission. FDA will prioritize submissions under this factor until the 180-day exclusivity period¹³ has expired, been extinguished, or been relinquished.
- Submissions from subsequent applicants who were blocked from final approval by 180-day exclusivity qualify for prioritization once the relevant 180-day exclusivity period has been triggered. FDA will prioritize submissions under this factor until the 180-day exclusivity period has expired.

⁹ See section 505(j)(2)(A)(vii)(IV) of the FD&C Act (21 U.S.C. 355(j)(2)(A)(vii)(IV)).

¹⁰ FDA will no longer automatically prioritize upon original submission all ANDAs that contain a paragraph IV certification, are submitted on the first day that any valid paragraph IV-containing application for the drug in question is submitted, and are received as substantially complete (i.e., submissions that have “first filer” status). Rather, FDA will prioritize such ANDA submissions if they meet the criteria described under this factor.

¹¹ See also the draft guidance for industry, *ANDA Submissions – Amendments and Requests for Final Approval to Tentatively Approved ANDAs* (January 2019). 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>.

¹² See section 505(j)(5)(B)(iv)(II)(bb) of the FD&C Act (21 U.S.C. 355(j)(5)(B)(iv)(II)(bb)).

¹³ See section 505(j)(5)(B)(iv) of the FD&C Act (21 U.S.C. 355(j)(5)(B)(iv)).

- Other submissions containing a paragraph IV certification that do not otherwise qualify for prioritization under either of the two sub-bullets above, if there are fewer than four approved therapeutically equivalent drug products, including the RLD, listed in the Orange Book at the time the submission is received by FDA. This includes submissions containing a paragraph IV certification for drug products for which FDA has determined that 180-day exclusivity has been extinguished and this has been documented on FDA's Paragraph IV Certifications List (<https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/patent-certifications-and-suitability-petitions>).

- **Submissions for which final approval is dependent on the expiration of a patent or NDA exclusivity**

Submissions for noncomplex products that are dependent on the expiration of a patent (i.e., the submission contains a paragraph III certification) or NDA exclusivity period for final approval where the original ANDA submission is submitted between 24 and 36 months prior to the expiration of the last applicable patent or exclusivity period. For complex products,¹⁴ submissions that are dependent on the expiration of a patent or NDA exclusivity period where the original ANDA submission is submitted between 36 and 48 months prior to the expiration of the last applicable patent or exclusivity period. FDA will prioritize submissions under this factor if there are fewer than four approved therapeutically equivalent drug products, including the RLD, listed in the Orange Book.

- **Submissions related to drug shortages**

Submissions that could help mitigate or resolve a drug shortage and prevent future shortages, including submissions related to products that are listed on FDA's Drug Shortage List at the time of the submission.

- **Submissions that are subject to special review programs such as the President's Emergency Plan for AIDS Relief (PEPFAR)**

This may include submissions for antiretroviral drug products that could help address the global HIV/AIDS epidemic. For an original submission to qualify for prioritization under this factor, the submission may not contain a paragraph IV certification.

¹⁴ "Complex products" generally include products with complex active ingredients, complex formulations, complex routes of delivery, or complex dosage forms. See the GFUDA II Commitment Letter.

- **Submissions related to public health emergencies**

Submissions that either could help address a public health emergency declared by the Secretary of the U.S. Department of Health and Human Services under section 319 of the Public Health Service Act (42 U.S.C. 247d), or anticipated under the same criteria as apply to such a declaration.

- **Submissions related to certain government purchasing programs**

Submissions related to certain government purchasing or procurement activities, including expiration-date extensions or packaging changes usually requested by the Government-Wide Quality Assurance Program.

- **Submissions subject to statutory mandates or other legal requirements**

Submissions that are subject to federal or state mandates or other legal or regulatory actions, as necessary to comply with those requirements.¹⁵

- **Supplements for which a priority review is requested under 21 CFR 314.70(b)(4)**

Under 21 CFR 314.70(b)(4), an applicant may ask FDA to grant a priority review to “a supplement for public health reasons or if a delay in making the change described in [the supplement] would impose an extraordinary hardship on the applicant.” For priority reviews, “extraordinary hardship on the applicant” will be interpreted to include the following:

- Catastrophic events such as explosion, fire, or storm damage to manufacturing facilities.
- Events that could not have been reasonably foreseen by the applicant and for which the applicant could not have planned. Examples include:
 - An abrupt discontinuation of the supply of an active ingredient, packaging material, or container closure system.

¹⁵ This category includes legally required changes in formulation or labeling. However, if the applicant submits a supplement under 21 CFR 314.70(b) for changes that require approval prior to the distribution of the product made with the changes and the supplement involves facilities that are subject to a recommendation of Official Action Indicated, the supplement will not be considered for a priority review.

- The relocation of a facility or a change in an existing facility because of a catastrophic event.¹⁶

- **Submissions for “sole source” drug products**

Submissions for drug products for which (1) there is only one approved drug product listed in the Prescription Drug Product List (i.e., the “Active Section”) of the Orange Book and that product is approved under an ANDA (i.e., the RLD is in the “Discontinued Section” and there is not more than one ANDA in the “Active Section”); (2) the approved ANDA for the drug product listed in the “Active Section” was not approved pursuant to a suitability petition under section 505(j)(2)(C) of the FD&C Act; (3) there are no blocking patents or exclusivities for the RLD; and (4) the submission does not qualify for prioritization under any other factor.

RESPONSIBILITIES

- OGD RPMs and OPQ RBPMs will have the overall responsibility for applying the prioritization policy outlined in this MAPP to the review of specific submissions within OGD and OPQ.
 - OGD RPMs will coordinate with OPQ RBPMs the prioritization of an original ANDA or supplement containing the quality review (chemistry, microbiology, etc.) to ensure consistent prioritizations across offices.
 - OGD RPMs will coordinate the prioritization of OGD reviews with the OGD disciplines.
 - OPQ RBPMs will coordinate the prioritization of OPQ reviews with the OPQ disciplines.
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PROCEDURES

- During a filing review of an original ANDA or new strength supplement, the OGD Division of Filing Review staff will identify submissions that request prioritization based on one of the criteria set forth in this MAPP and communicate that information to the relevant OGD staff, including the OGD RPM.

¹⁶ In the absence of a catastrophic event, the applicant should contact OGD early in the planning stage of a contemplated relocation or change.

- Submissions that request prioritization but do not go through a filing review within OGD will be assessed for prioritization purposes at the time they are submitted, by the OGD RPM, OGD labeling review project manager, or the OPQ RBPM. To ensure consistent prioritizations across offices, the OGD RPM, OGD labeling review project manager, and OPQ RBPM will communicate prioritization information to each other and to the relevant OGD and OPQ staff.
- OGD and OPQ staff may also identify submissions that appear to meet the criteria for prioritization for a drug shortage or public health emergency, or meet the requirements of section 505(j)(11)(A) of the FD&C Act and will communicate that information to the relevant OGD RPM and OPQ RBPM.
- Determinations about prioritizing a review will not be made until a submission is received for review as discussed in 21 CFR 314.101(b).
- OGD RPMs will coordinate with the Office of Generic Drug Policy, OGD review disciplines, and the OPQ RBPMs to ensure that submissions are prioritized according to this MAPP.

DEFINITIONS

Blocking Patent: any patent that an ANDA applicant is required to address with a paragraph III or paragraph IV patent certification.

Expedited Review: FDA will strive to act on an ANDA as soon as possible, including prior to the goal date if possible. An expedited review, though, does not result in a shorter goal date.

Priority Review: FDA will either (1) give a shorter goal date or (2) grant an expedited review.

Shorter Goal Date: In accordance with the GDUFA II Commitment Letter, FDA commits to one of the following (1) for original ANDAs, an 8-month goal date; (2) for major amendments, a 6- or 8-month goal date; or (3) for prior approval supplements, a 4- or 8-month goal date.

EFFECTIVE DATE

This MAPP becomes effective upon the date of publication and applies to all submissions, including those pending with FDA as of that date, unless otherwise noted.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
08/01/2014	1	Updated to describe how the review of ANDAs, ANDA amendments, and ANDA supplements will be prioritized for review within OGD and OPQ.
03/07/2016	2	Updated to include the prioritization of sole source drug products, reflect the reorganization of OPQ, and revise certain forfeiture time frames consistent with FDASIA.
06/27/2017	3	Updated to include (1) the prioritization of generic products for which there are fewer than three ANDAs approved for the RLD and (2) certain external references.
11/09/2017	4	Updated to revise responsibilities and procedures; modernize language; and add a new prioritization factor, prioritization policy, and definitions section.
1/30/2020	5	Updated to revise and clarify the policy section and revise prioritization factors.