# 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 abbreviated new drug applications (ANDAs), ANDA amendments, and ANDA supplements will be prioritized for review within the Office of Generic Drugs (OGD) and the Office of Pharmaceutical Quality (OPQ).

This MAPP is a revision of MAPP 5240.3 Rev 2, *Review Order of Original ANDAs, Amendments, and Supplements* (March 11, 2016). This MAPP also supersedes MAPP 5240.1, *Requests for Expedited Review of Supplements to Approved ANDAs* (November 1, 1995). Information relevant to this MAPP is contained in the Draft Guidance for Industry, *ANDA Submissions: Amendments and Easily Correctable Deficiencies Pursuant to GDUFA* (July 11, 2014) and the Guidance for Industry entitled *ANDA Submissions: Prior Approval Supplements Pursuant to GDUFA* (October 17, 2016).

## 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 modifications described in the previous versions of this MAPP were driven by increases in the volume of ANDAs and related submissions to OGD, as well as an increase in the complexity of those submissions. In recent years, the volume and complexity of submissions have continued to increase, and OGD has continued to pursue a science/risk-based approach to the review of submissions. Consistent with the Agency's ongoing focus on product quality, the

quality review for generic submissions is now handled by OPQ. In light of these changes, the need has arisen for further modifications to OGD's prioritization of submissions within the review process.

The review of generic drug submissions is also subject to the Generic Drug User Fee Amendments of 2012 (GDUFA). Under GDUFA, the Agency agreed to review and act upon certain percentages of original ANDAs, amendments, and supplements within certain timeframes.

As part of its GDUFA implementation, the Agency has recently issued the Draft Guidance for Industry on *ANDA Submissions: Amendments and Easily Correctable Deficiencies Pursuant to GDUFA* (July 11, 2014). This guidance replaces the December 2001 Guidance for Industry entitled *Major, Minor and Telephone Amendments to Abbreviated New Drug Applications.* FDA has also issued the Guidance for Industry entitled *ANDA Submissions: Prior Approval Supplements Pursuant to GDUFA* (October 17, 2016).

## POLICY

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

- For purposes of this MAPP, "expedited review" means that a submission will receive heightened review priority as determined by the OGD Division of Project Management staff (including the Regulatory Project Manager (RPM)) and OGD management. Expedited review may be granted following a request from the applicant (including where expedited review is requested for a supplemental ANDA under 21 CFR 314.70(b)(4)), or at OGD's initiative. In either case, the granting of expedited review must be consistent with the criteria set forth in this MAPP.

- Inquiries about expedited review should be directed to the OGD RPM consistent with the procedures described in MAPP 5200.3 Rev. 1, Responding to Industry Inquiries with Respect to Abbreviated New Drug Applications in the Office of Generic Drugs.

- The prioritization criteria outlined below apply at all stages of review. Determinations about expedited review may be made at the time a submission is received or thereafter.

- Submissions involving facilities that are subject to a recommendation of Official Action Indicated (OAI) will not be considered for expedited review, except in certain cases where it is determined that the submission must be expedited to address a public health concern. These determinations will be made by the OGD Division of Project Management and OGD management in consultation with other Agency personnel as necessary.

- Submissions that do not receive expedited review will be reviewed in the order in which they are received, to the extent possible and unless otherwise determined by the Agency.

- All determinations regarding priority of submissions within the review process will be consistent with the Agency's GDUFA review metrics, the GDUFA Program Performance Goals and Procedures (the GDUFA Commitment Letter), and the Draft Guidance for Industry on *ANDA Submissions: Amendments and Easily Correctable Deficiencies Pursuant to GDUFA* (July 11, 2014).

- The review of grouped supplements will continue to be handled as described in MAPP 5015.6 Rev. 1, *Review of Grouped Product Quality Supplements* (April 19, 2016).

## Prioritization of Review

1. Submissions containing patent certifications pursuant to 21 CFR 314.94(a)(12)
    - Generic products for which there are fewer than three ANDAs approved for the reference listed drug (RLD) and for which there are no blocking patents or exclusivities on the RLD may receive expedited review. For purposes of this MAPP, a patent to which an applicant has solely submitted a statement under 21 USC 505(j)(2)(A)(viii) will not be considered a blocking patent.

    - Submissions that contain a Paragraph IV certification, but become eligible for approval during the review period as a result of no blocking patents or exclusivities (including 180-day exclusivity) and no applicable stays, may receive expedited review if no other generic version of the same reference listed drug (RLD) has yet been brought to market under an approved ANDA. The absence of any blocking patent, exclusivity period or stay must be appropriately documented in order for expedited review to be granted. In the case of 180-day exclusivity, "no exclusivity" means that the 180-day exclusivity has been relinquished, or has been waived, or that forfeiture of the exclusivity has been established.

    - Submissions that contain a Paragraph IV certification, that are submitted on the first day that any valid Paragraph IV application for the drug in question is submitted, and that are received as substantially complete (*i.e*. submissions that have "first filer" status) may receive expedited review. OGD and OPQ will seek to complete review of these submissions in a manner that would permit tentative or final approval within 30 months of filing (or 36, as specified by the Food and Drug Administration Safety and Innovation Act (FDASIA).

- Where a submission contains a Paragraph IV certification and has "first filer" status as described above, and also contains a Paragraph III certification, the "first filer" status will govern for purposes of granting expedited review.

- Where a submission's approval is dependent on the expiration of a patent (*i.e.* the submission contains a Paragraph III certification), or is dependent on the expiration of an exclusivity period, OGD and OPQ will seek to complete review of the submission in a manner that would permit approval prior to the last applicable patent expiration date or exclusivity date. However, with regard to ANDAs submitted on or after October 1, 2014:

    i. ANDAs submitted within one year of the last applicable patent expiration date or exclusivity date will not be considered for expedited review, and no assurances can be provided that review will be completed in a manner that would permit approval by the last applicable patent expiration date or exclusivity date. This provision may be subject to exception in certain cases where it is determined that the submission must be expedited to address a public health concern. These determinations will be made by the OGD Division of Project Management and OGD management in consultation with other Agency personnel as necessary.

    ii. ANDAs submitted more than 30 months in advance of the last applicable patent expiration date or exclusivity date will not be considered for expedited review.

2. 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 Current Drug Shortages Index at the time of the submission, may receive expedited review.

3. Submissions that are subject to special review programs such as the President's Emergency Plan for AIDS Relief

    - Submissions in this category may receive expedited review.

4. Submissions related to public health emergencies

    - Submissions that could help address a public health emergency declared by the Secretary of the Department of Health and Human Services, or anticipated under the same criteria as apply to such a declaration, may receive expedited review.

5. 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, may receive expedited review.

6. Submissions subject to statutory mandates or other legal requirements

    - Submissions that are subject to federal or state mandates or other legal or regulatory actions may receive expedited review as necessary to comply with those requirements. Note: This category includes legally required changes in formulation or labeling. However, supplements submitted following actions taken by FDA field staff against applicants who put changes into effect that are required to have approved supplements under 21 CFR 314.70(b) will not be considered for expedited review.)

7. Supplements for which expedited review is requested under 21 CFR 314.70(b)(4)

    - Under 21 CFR 314.70(b)(4), an applicant "may ask FDA to expedite its review of 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 purposes of expedited review, "extraordinary hardship on the applicant" will be interpreted to include the following:

        i. Catastrophic events such as explosion, fire, or storm damage to manufacturing facilities.

        ii. Events that could not have been reasonably foreseen by the applicant, and for which the applicant could not have planned. Examples include:

            1. Abrupt discontinuation of supply of an active ingredient, packaging material, or container closure system.

            2. Relocation of a facility or change in an existing facility because of a catastrophic event. (In the absence of a catastrophic event, the applicant should contact OGD early in the planning stage of a contemplated relocation or change.)

8. Submissions for "sole source" drug products

    - Submissions for drug products for which there is only one approved drug product listed in the Prescription Drug Product List (the "active section") of FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations*

(the "Orange Book") and for which there are no blocking patents or exclusivities may receive expedited review, except where the approved drug product was approved pursuant to a suitability petition under section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act.

## RESPONSIBILITIES

- OGD Division of Project Management staff, supervised by OGD management, will have overall responsibility for applying the prioritization policy outlined in this MAPP to the review of specific submissions within OGD and OPQ.

- OGD Division of Project Management staff and Regulatory Support staff, CDER Drug Shortages staff, and OPQ Regulatory Business Project Managers (OPQ RBPMs) will notify the OGD RPM of any submissions that appear to satisfy the criteria for prioritization set forth in this MAPP.

- The OGD Division of Project Management staff will coordinate prioritization of OGD reviews with the OGD disciplines.

- The OGD Division of Project Management staff will coordinate prioritization of the quality review (chemistry and microbiology) with the OPQ RBPMs.

## PROCEDURES

- During filing review within OGD, OGD Regulatory Support staff will identify submissions that appear to meet the criteria for prioritization set forth in this MAPP, and will communicate that information to the relevant OGD RPM.

- During filing review within OGD, the OGD Division of Project Management staff may also identify submissions that appear to meet the criteria for prioritization set forth in this MAPP, and will communicate that information to the relevant OGD RPM.

- Submissions that do not go through filing review within OGD will be assessed for prioritization purposes at the time they are submitted, either by the OGD Division of Project Management staff or the OPQ RBPMs. In the latter case, the OPQ RBPM will notify OGD Division of Project Management staff of prioritization status.

- Determinations about expedited review will not be made until a submission is received.

- After a submission is received, OGD Division of Project Management staff will coordinate with OGD review disciplines and the OPQ RBPMs to ensure that submissions are prioritized according to this MAPP.

- Where an applicant requests expedited review (including expedited review of a supplement under 21 CFR 314.70(b)(4)), OGD Division of Project Management staff will evaluate those requests. Any request for expedited review should be submitted to the relevant OGD RPM. Consideration for these requests will be given only when the submission and cover letter clearly state "Expedited Review Requested" and reference the ANDA number (where applicable); the basis for the request is consistent with this MAPP and is clearly and briefly stated by the applicant; and sufficient supporting documentation is included.

## EFFECTIVE DATE

This MAPP becomes effective upon the date of publication, and applies to all submissions, including those pending with the Agency 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 OPS/OPQ |
| 03/07/2016 | 2 | Updated to include prioritization of sole source drug products, reflect the reorganization of CDER's Office of Pharmaceutical Quality, and revise certain forfeiture timeframes consistent with the Food and Drug Administration Safety and Innovation Act of 2012. |
| 6/27/2017 | 3 | Updated to include prioritization of generic products for which there are fewer than three ANDAs approved for the reference listed drug (RLD) and update certain external references. |