

POLICY

OFFICE OF PHARMACEUTICAL QUALITY

Requests for Expedited Review of New Drug Application and Biologics License Application Prior Approval Supplements Submitted for Chemistry, Manufacturing, and Controls Changes

Table of Contents

PURPOSE.....1
POLICY1
RESPONSIBILITIES4
REFERENCES.....5
EFFECTIVE DATE.....5
CHANGE CONTROL TABLE.....5

PURPOSE

This MAPP outlines the policies of the Office of Pharmaceutical Quality (OPQ) for granting or denying a request to conduct an expedited review for new drug application (NDA) and biologics license application (BLA) prior approval supplements (PASs) that (1) involve chemistry, manufacturing, and controls (CMC) changes and (2) are managed by OPQ.¹ This MAPP specifies both the criteria that OPQ uses to make an expedited review designation and the roles and responsibilities of the OPQ quality assessment team members for making this designation.

POLICY

- In this MAPP, an *expedited review* means that OPQ will strive to assess and act on the PAS before the Prescription Drug User Fee Act (PDUFA) goal date associated with that PAS. It should be noted, however, that an expedited review designation for either an NDA PAS or a BLA PAS does not change the PDUFA goal dates associated with that PAS.
- If a public health need arises, OPQ may designate the PAS for expedited review with or without a request from an applicant. The scope of this MAPP includes

¹ Although OPQ also manages certain abbreviated new drug application (ANDA) supplements, these supplements should be prioritized according to MAPP 5240.3 Rev. 3 *Prioritization of the Review of Original ANDAs, Amendments, and Supplements*.

-
- both expedited review requests received internally and from an NDA or BLA applicant.
- OPQ will consider requests from an applicant for an expedited review of a PAS on a case-by-case basis. However, OPQ will only consider expedited review requests that clearly state the basis for the request.
 - OPQ may designate a PAS for expedited review at the time it receives the PAS or anytime thereafter. If the OPQ quality assessment team receives a request for expedited review after OPQ has received and initially processed the PAS, OPQ will consider the request and may expedite the review of that PAS, as appropriate.
 - If OPQ grants an expedited review for a PAS, that PAS's review completion date will depend on both the availability of OPQ's resources and the provisions of the PAS.
 - If OPQ determines that a multidisciplinary team should participate in the assessment of a PAS designated for expedited review, the OPQ Office of Program and Regulatory Operation's Regulatory Business Project Manager (OPQ RBPM) will notify all appropriate sub-office assessment divisions and inspection divisions of the need to expedite the PAS.
 - OPQ will not consider a request for an expedited review that involves a facility that is subject to a recommendation of Official Action Indicated, unless an expedited review will help address a public health concern. The OPQ RBPM and appropriate Branch Chief (BC) or Review Chief, in consultation with other personnel as necessary, will determine if FDA must expedite the review to address the public health concern.
 - OPQ will consider an expedited review request for a PAS that falls into one or more of the following categories:
 - *Drug shortages*: Submissions that could help mitigate or resolve a drug shortage or prevent future shortages, including requests related to products that are listed on FDA's "Current and Resolved Drug Shortages and Discontinuations Reported to FDA" index,² may receive expedited review.
 - *Special review programs*: Submissions that are subject to a special review program, such as the President's Emergency Plan for AIDS Relief, may receive expedited review.
 - *Public health emergencies*: Submissions that could help address a public

² This index is available at <https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>.

health emergency declared by the Secretary of the U.S. Department of Health and Human Services, or anticipated under the same criteria, may receive expedited review.

- *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.
- *Statutory mandates or other legal requirements:* Submissions that are subject to Federal or State mandates or other legal (e.g., regulatory) actions may receive expedited review as necessary to comply with those requirements. (Please note: This category also includes any legally required changes in formulation or labeling. However, PASs submitted under 21 CFR 314.70(b)(4) or 601.12(b)(4) in response to feedback from FDA about CMC changes that were not reported appropriately (e.g., certain CMC changes reported to an application as changes being effected supplement rather than a PAS) will not be considered for expedited review.
- *Extraordinary hardship on the applicant:* Under 21 CFR 314.70(b)(4) or 601.12(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 it would impose an extraordinary hardship on the applicant.” Submissions received from an applicant who has experienced one or more of the following extraordinary hardships may receive expedited review:
 - A catastrophic event that incapacitates the applicant’s ability to manufacture a drug product, such as an explosion, a fire, or storm damage to their manufacturing facilities.
 - Events that could not have been reasonably foreseen by the applicant and for which the applicant could not have planned, such as:
 - An abrupt discontinuation of the supply of an active ingredient, the packaging material, or the product’s container closure system. If an applicant experiences one or more of these discontinuations, the PAS should document the date the applicant received notice of the discontinuation.
 - The relocation of a facility or a change in an existing facility because of a recent catastrophic event.

RESPONSIBILITIES

- The OPQ Drug Shortage Coordinator will:
 - Act as OPQ's point of contact for all drug shortage or potential drug shortage situations related to products mentioned in NDA PASs and BLA PASs.
 - Coordinate with the appropriate Drug Shortage Staff on expedited review requests related to drug shortages.

- The OPQ RBPM will:
 - For expedited requests related to an extraordinary hardship designation, collaborate with the Office of New Drug Products (ONDP) BC or the Office of Biotechnology Products (OBP) Review Chief about whether the situation meets the criteria for an extraordinary hardship, thereby ensuring a consistent designation.
 - For all other expedited requests, notify the BC of the expedited review request and how the request was received (i.e., whether FDA raised the request internally or whether the applicant made the request either in the original PAS or in an amendment).
 - Update Panorama with the expedited review request decision to either grant or deny the request. If the expedited review request is granted, the OPQ RBPM will document, in Panorama, the reason for the grant. If the expedited request based on a hardship claim is denied, the OPQ RBPM will document the reason for that denial.
 - Notify the requestor of the decision (i.e., whether the expedited review request was granted or denied).
 - Notify the OPQ quality assessment team of the expedited review status.

- The ONDP BC or OBP Review Chief (or their designee) will:
 - For claims related to extraordinary hardship, work with the RBPM to determine whether the PAS should be expedited.
 - For all granted expedited requests, support the expedited review of the submission.

- The OPQ/ONDP/OBP Review Team will:
 - Expedite the assessment of the submission if the expedited review request is granted. If the expedited review request is denied, the assessment of the submission will follow OPQ’s established practices.

REFERENCES

- MAPP 5240.3 Rev. 3 *Prioritization of the Review of Original ANDAs, Amendments, and Supplements.*³

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revision(s)
6/11/99	Initial	N/A
5/21/18	1	(1) Reflects OPQ’s roles and responsibilities for reviewing expedited review requests for NDA and BLA PASs (2) Updates the policy for processing FDA expedited review requests for NDA and BLA PASs (3) Renders obsolete the “Expedited Review Request Documentation Form,” which was referenced in MAPP 5310.3 <i>Requests for Expedited Review of NDA Chemistry Supplements</i> and was used to document an expedited review decision (4) Addresses BLA PASs, which were not addressed in MAPP 5310.3 <i>Requests for Expedited Review of NDA Chemistry Supplements</i>

³ We update MAPPs periodically. To make sure you have the most recent version of a MAPP, check the Manual of Policies & Procedures (CDER) web page at <https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/ucm2007329.htm>.