



PENDING MONOGRAPHS GUIDELINE

Version 2.7, Effective November 1, 2011

1. BACKGROUND

The United States Pharmacopeial Convention (USP) Pending Monographs approach enables Web-based publication of monographs for articles (e.g., drug substances, excipients, and dosage forms) based on information in FDA applications and filings. The purpose of Pending Monographs is to have an official *USP* or *NF* monograph ready as soon as possible after FDA grants final product approval. The Pending Monographs approach enables monograph development to begin before FDA's approval process is complete, resulting in an official *USP* or *NF* monograph more rapidly than would be possible if monograph development started only after final FDA approval. Pending Monographs are considered authorized rather than official text because they are approved by the USP Council of Experts but are not part of an official compendium of the U.S. (*USP* or *NF*). A company is not permitted to label their article as "USP", "NF" or "USP-NF" on the basis of adherence to a Draft or Authorized Pending Monograph. Use of the "USP", "NF" or "USP-NF" labeling is permitted only in reference to official *USP-NF* monographs.

2. REQUIREMENTS

Monographs developed according to the Pending Monographs Guideline must meet the following criteria:

- Requests for Revision (see link at 3.1 below) will be accepted only from sponsors:
 - Who have filed or intend to file with FDA an Abbreviated New Drug Application (ANDA) or Abbreviated New Animal Drug Application (ANADA) within six months; or
 - Who have filed or intend to file with FDA a Biosimilar or Interchangeable Biologics License Application (a Public Health Service Act 351(k) BLA) within six months; or
 - Who have submitted a Drug Master File (DMF) for an article to FDA; or
 - Whose substance is or will be the subject of a Time and Extent Application or citizen petition to amend an FDA OTC drug monograph.
- A sponsor's intent to file an ANDA or ANADA or 351(k) BLA within six months must be established through documentation satisfactory to USP. Documentation of a DMF can be confirmed by providing a copy of the DMF filing letter.

- Unless USP determines otherwise, if the proposed monograph includes the use of a new USP Reference Standard then USP will not publish the proposed monograph on its Web site until it has received the necessary reference material bulk candidate(s).
- If the sponsor wants to maintain confidentiality, the submission should include a request that some part(s) or the entire proposed Request for Revision be viewed only by USP and FDA for a specified time before Web publication in draft for public comment.
- If the sponsor has filed or intends to file an ANDA or ANADA or 351(k) BLA, it must agree to inform USP promptly of any changes or additions that should be made to a pending monograph as a result of the regulatory review and approval process (including, but not limited to, providing USP with the dissolution test included in the approved product specifications). This will ensure consistency between the Pending Monograph and the private specification approved by FDA.
- The sponsor of the Request for Revision should follow the General Information for All Submissions and the appropriate Submission Guideline for the article (e.g., small molecules, biologics/biotechnology substance or product) and should label the Request "Pending Monographs." The timing of the Request for Revision should be consistent with USP's timeline for working with potential generic applicants as outlined in the General Information for All Submissions.

3. PROCESS

1. The Request for Revision will be reviewed in accordance with USP's usual process.
2. If USP decides to proceed with the revision and has received the bulk candidate(s) for needed reference material(s), then the Draft Pending Monograph will be developed and published on the USP Web site for a 90-day comment period. Any USP Reference Standard developed in support of a Pending Monograph may be available for sale at any time before or after website publication of the Draft or Authorized Pending Monograph.
3. Following the 90-day comment period, the USP Council of Experts will consider public comments as part of the balloting process and the USP Nomenclature Expert Committee will approve the title (if not approved previously). If approved by the relevant Expert Committee(s), the draft version becomes an Authorized Pending Monograph and it will be published on USP's Web site. To the extent applicable, an Authorized Pending Monograph will be subject to the assumptions, definitions and default conditions contained in the General Notices and Requirements section of the *USP-NF*. If not approved as an Authorized Pending Monograph, then USP staff will work with the relevant Expert Committee(s) and the sponsor to determine the most appropriate next step(s).
4. The Authorized Pending Monograph remains on the USP Web site until FDA approval of the sponsor's application or an application incorporating the DMF has been granted. When FDA approves such drug product application, the corresponding Authorized Pending Monograph for the drug product, drug substance and/or excipient will be eligible to become an official *USP* or *NF* monograph. Unless otherwise determined by USP, any associated official USP

Reference Standard must be available before the monograph can become official.

5. If approved by the relevant Expert Committees of the USP Council of Experts, the Authorized Pending Monograph will advance to official status in the *USP-NF* via a Revision Bulletin posted on USP's Web site. The monograph will be official and legally enforceable as a *USP* or *NF* monograph as of the date specified in the Revision Bulletin, which generally will be six months after the posting of the Revision Bulletin. If the Authorized Pending Monograph is not approved for official adoption, then USP staff will work with the relevant Expert Committee(s) and the sponsor to determine the most appropriate next step(s).
6. If there is an existing official *USP* or *NF* monograph, then information from the Authorized Pending Monograph will be merged with the existing monograph, as appropriate, to create a monograph that reflects all FDA-approved articles (see the Guideline for Submitting Requests for Revision to *USP-NF*). This revision to the existing monograph will advance to official status in the *USP-NF* via a Revision Bulletin and will be official immediately upon posting consistent with USP's Guideline on Use of Accelerated Processes for Revisions to the *USP-NF*.

If FDA approval is received prior to the end of the 90-day comment period, then upon expiration of the comment period the Draft Pending Monograph will be eligible to advance directly to official status in the *USP-NF* through the processes described in Paragraphs 6 and 7 above, without the need to be approved first as an Authorized Pending Monograph. Similarly, if FDA approval is received after the end of the comment period but prior to balloting as an Authorized Pending Monograph, the Draft Pending Monograph may be advanced directly to official status in the *USP-NF* without approval as an Authorized Pending Monograph.

Sometimes ANDA and ANADA and 351(k) BLA applicants are required to make changes to methods, acceptance criteria, or other portions of their submission during the regulatory review process. As stated above, the Pending Monograph Guideline requires sponsors to notify USP about such changes so that USP can make appropriate changes to the Pending Monograph posted on USP's Web site. If changes are made during the 90-day comment period, USP may extend the comment period to allow additional time for comments. If changes are made to an Authorized Pending Monograph, USP will republish the Pending Monograph as a draft on USP's Web site for a 90-day notice and comment period. If a sponsor withdraws its application from FDA, USP will remove the Draft or Authorized Pending Monograph from the USP Web site

4. REVISION HISTORY

Version 2.7 Effective November 1, 2011

Section: Process

Change: Clarified that if there is an existing official *USP* or *NF* monograph, and the Authorized Pending Monograph is merged into the existing monograph to accommodate the Pending Monograph donor, the Revision Bulletin revising the existing monograph will become official immediately. This is consistent with USP's Guideline on Use of Accelerated Processes for Revisions to the *USP-NF*, which allows an immediate official date where a monograph is revised via a Revision Bulletin to accommodate an article which otherwise would be out of compliance with the existing standards. Also clarified

that if FDA approval is received after the end of the 90-day comment period but before balloting as an Authorized Pending Monograph, the Draft Pending Monograph will be eligible to advance directly to official status.

Version 2.6 Effective August 1, 2010

Section: Requirements

Changes:

- Specified that Requests for Revision will also be accepted from sponsors of Public Health Service Act 351(k) BLAs, reflecting enactment of healthcare reform legislation which includes establishment of a new approval pathway for biosimilar and interchangeable biologics (Public Law 111-148, signed by President Obama March 23, 2010).
- Clarified that the timing of the Request for Revision should be consistent with USP's timeline for working with potential generic applicants.

Section: Process

Change: Added a reference to 351(k) BLAs among those applicants who may be required by FDA to make changes to their submissions during the regulatory review process.

Version 2.5 Effective May 1, 2010

Section: Background

Change: Clarified that excipients are eligible for the Pending Monographs approach and can ultimately result in an official *NF* monograph.

Change: Specified that use of the "USP", "NF" or "USP-NF" labeling is permitted only in reference to official *USP-NF* monographs.

Section: Process, Paragraphs 6, 7 and 8

Change: Clarified that excipients are eligible for the Pending Monograph approach and can ultimately result in an official *NF* monograph.

Version 2.4 Effective October 1, 2009

Section: Process, Paragraph 8

Change: Specified that the default official date for the *USP* monograph will be six months after the Revision Bulletin posting.

Version 2.3 Effective July 1, 2009

Section: Requirements

Change: Added the reference to the General Information to All Submissions document and removed the reference to the USP Guideline for Submitting Requests for Revision to the USP-NF.

Section: Process, Paragraph 2

Change: Clarified that USP Reference Materials associated with a Pending Monograph may be released any time before or after the monograph has been published either in Pending or Authorized status.

Section: Process, Paragraph 3

Change: Clarified that a Draft Pending Monograph may move directly to official status without advancing to an Authorized Pending Monograph if FDA approval is obtained during the comment period.

Sections: Process, Paragraphs 5 and 7

Changes: Clarified that in the event that the proposed monograph is not approved for advancement from Draft to Authorized or from Authorized to Official status, USP staff will work with the relevant Expert Committee(s) and the sponsor to determine the most appropriate next step(s).

Version 2.2 Effective March 1, 2009

Sections: All

Changes: Minor clarifications to the document were made throughout. There were no substantive changes to content.

Version 2.1 Effective May 14, 2008

Sections: All

Changes: The language of the document was simplified to make it easier to understand. There were no substantive changes to content. Frequently Asked Questions were moved to a separate document.

Version 2.0 Effective April 1, 2008

Sections: All

Change: The Guideline was reformatted to a new style

Section: "Why is the Guideline being modified?"

Changes: The approach and Guideline were modified in the following ways:

- Clarification of what constitutes "intent to file" with the FDA;
- A requirement that the Sponsor promptly inform USP of any changes to methods or specifications resulting from the regulatory review and approval process, to ensure consistency between the monograph and the private specification approved by FDA;
- Utilization of USP's Revision Bulletin process to move a Pending Standards monograph to official status upon product approval, to allow such monographs to become official more quickly than under the proposed Interim Revision Announcement process formerly utilized; and

- A requirement that the bulk material necessary to develop any accompanying USP Reference Standard be received by USP prior to posting a proposed Pending Monograph on the Web site, to help ensure that such USP Reference Standard will be available at the time the product is approved and the monograph becomes official.

Version 1.1 Effective June 14, 2007

Section: Requirements

Change: Added a requirement for review and approval of the title by the USP Nomenclature Expert Committee.

Version 1.0 Effective February 23, 2007

Initial Guideline was posted.