

USP Excipients Stakeholder Forum
Wednesday, November 13, 2019

Pending Monographs for Excipients

Amber Day
Program Manager, Standards Operations



Agenda

Topics of Discussion

- ▶ What is the PMP?
- ▶ Submission Requirements
- ▶ Types of Pending Monographs
- ▶ Resources
- ▶ Examples of FDA Letters



What is the Pending Monograph Process?



- ▶ The traditional USP revision process addresses products that are already approved
- ▶ The Pending Monograph Process (PMP) is used to revise existing, or create new, USP-NF monographs to accommodate products under review by FDA
- ▶ Provides an efficient mechanism for industry, FDA, and USP alignment in the drug approval and monograph development processes
- ▶ Program was designed in close collaboration between USP and FDA, and based on feedback from industry
- ▶ Minimizes delays in updating USP monograph
- ▶ USP communicates with FDA monthly to share information on pending applications in progress

Application Requirements



- ▶ Sponsor must have submitted application with FDA, examples
 - ANDA
 - BLA
 - ANADA
 - Other application types on case-by-case basis (505b2 NDAs)
- ▶ Sponsor must agree to provide necessary reference materials
- ▶ Sponsor must provide USP with information on changes to their FDA application
- ▶ USP will share sponsor name and title of monograph being revised with FDA



Additional Submission Information

USP will also request the following information to facilitate processing of the request



- ▶ Supporting data and information
 - See [Guideline for Submitting Requests for Revision to the USP–NF](#)
- ▶ Copies of correspondence from FDA recommending use of pending process
 - Recommendation from FDA not necessary prior to submitting pending request for revision
 - Sponsors should contact USP as soon as possible
- ▶ Information on estimated application approval and/or review date



Types of Pending Monographs



There are 3 application types

1. New Pending Monograph
2. Pending Revision--Comment Required
3. Pending Revision—No Comment Required ★



New Pending Monographs (NPM)



Features

- ▶ Published in PF
 - In-Process Revisions
- ▶ Includes note that they are “contingent on FDA approval of product meeting specifications”
- ▶ Associated RS developed using sponsor provided material
 - RS maybe available in USP Store before monograph is official
- ▶ Will be included on deferrals list until associated FDA application is approved
 - Must be republished in PF after 2 years



Pending Revision -- Comment Required (CR)

Features

- ▶ Used for any revision requests that may impact other manufacturers
- ▶ Published in PF
 - In-Process Revisions
- ▶ FDA may cite PMP in Acknowledgement, Information, or Complete Response letter
- ▶ Posted as Notice of Intent to Revise
- ▶ Becomes official via Revision Bulletin



Pending Revision -- No Comment Required (NCR)

Features

- ▶ For compliance-related revisions
- ▶ Requested revisions must not impact other manufacturers
- ▶ **Not** published for public comment in PF
- ▶ FDA may cite PMP in Acknowledgement, Information, or Complete Response letter
- ▶ Posted as Notice of Intent to Revise
- ▶ Becomes official via Revision Bulletin

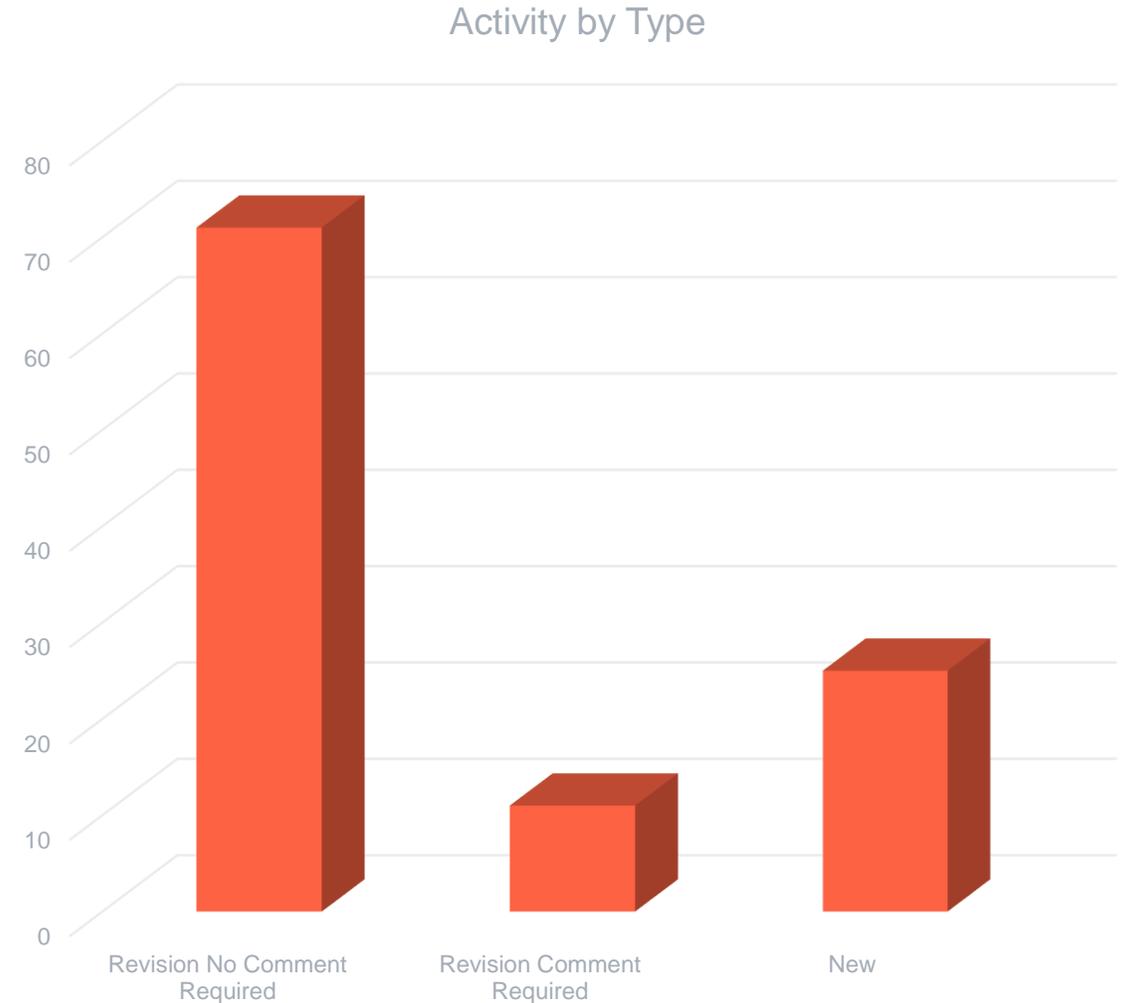


Pending Revisions -- No Comment Required

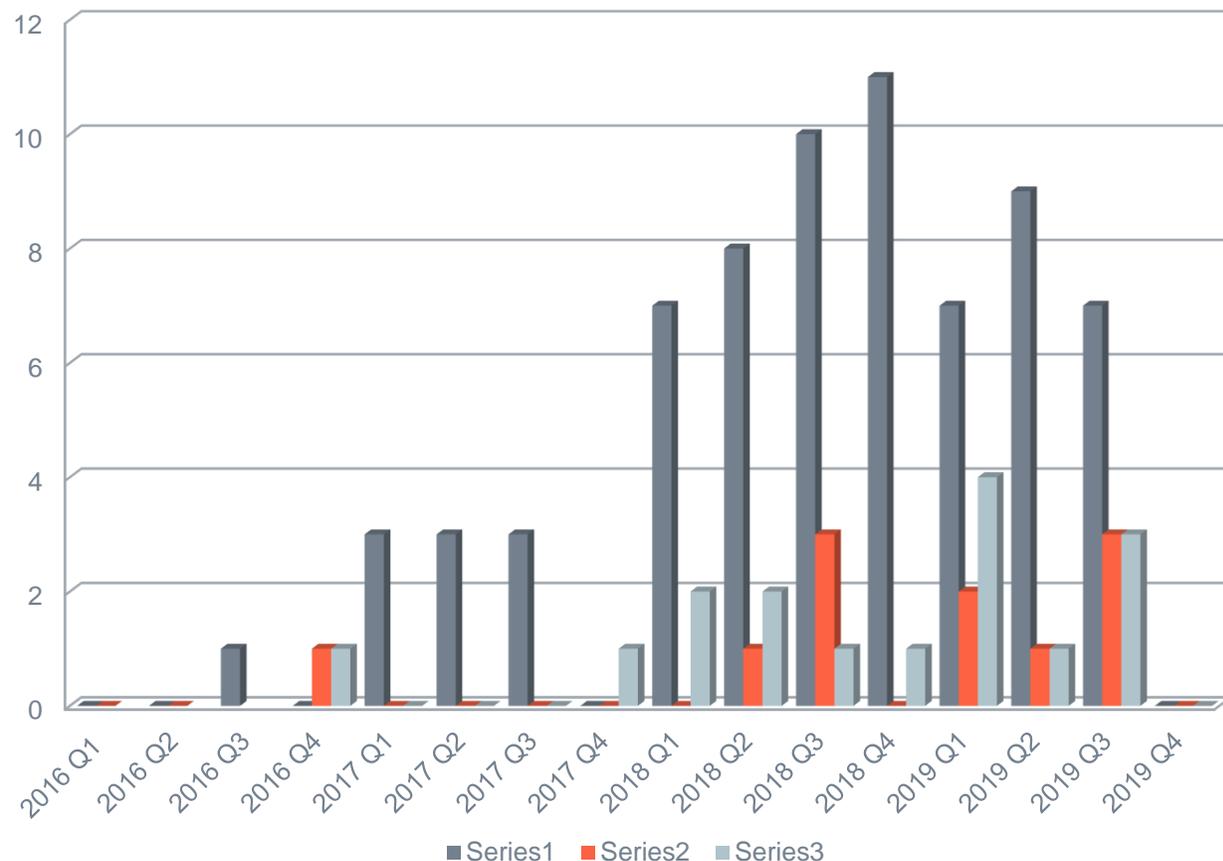


Additional Information

- ▶ No Comment Required Revisions are the most frequently used pending vehicle
- ▶ Frequently used to add dissolution test or widen acceptance criteria
 - Have been used for more novel revisions
- ▶ USP's goal is to notify FDA of the NITR posting date:
 - By the mid-point in the ANDA application process
 - Or 4-5 months prior to the GDUFA date
 - Sponsor should contact USP ASAP to facilitate this, due to short time frame



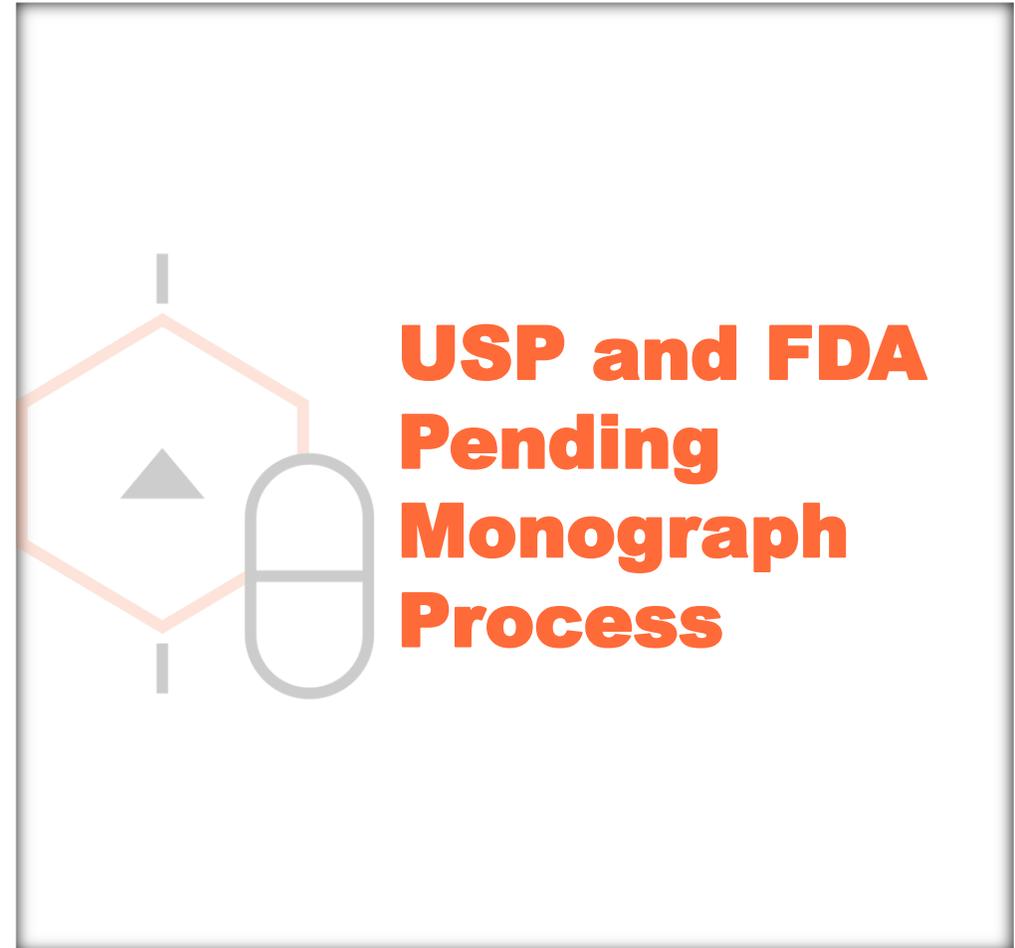
PMP Revisions Activity



Notes

- ▶ First PMP NCR Revision become official in Fall 2017
- ▶ FDA began citing PMP in letters to applicants in late 2017
- ▶ Expect pending NCR to be utilized more frequently than accelerated revision process
- ▶ In 2019 began using PMP to prepare updates to USP for tentatively approved items

- ▶ Process documented in [Pending Monograph Guideline](#)
- ▶ [FDA Draft Guidance](#) published on July 2019
- ▶ [Guideline for Submitting Requests for Revision to the USP–NF](#)



Letter Samples





FDA Acknowledgement Letter

A drug with a name recognized in the USP National Formulary (USP–NF) generally must comply with applicable compendial standards or the drug will be deemed adulterated, misbranded, or both. (See section 501(b) and 502(e)(3)(b) and (g) of the Federal Food, Drug, and Cosmetic Act (FD&C Act); also 21 CFR 299.5(a) and (b)). Such drugs must also comply with compendial standards for strength, quality, and purity, unless labeled to show all respects in which the drug differs or they will be deemed adulterated. (See section 501(b) of the FD&C Act and 21 CFR 299.5(c)). If the proposed specifications for your product do not conform with an applicable official USP monograph, you are advised to contact USP upon receipt of this Acknowledgement Letter to initiate a monograph revision through the USP Pending Monograph Process (PMP). Please note that initiation of the PMP does not mean that the proposed specifications will necessarily be approved by FDA; revisions to the USP monograph will be contingent upon FDA approval of the proposed specifications in this application.

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

- ▶ Note: PMP will be referenced in all ANDA applications, regardless if it is needed or not. Applicant should review USP monograph to determine if revision to monograph is needed

▶ Example of Reference to PMP in Information Request

2. We acknowledge that the recommended dissolution acceptance criteria for your product, [REDACTED] [REDACTED] differ from the USP. Please initiate a revision to an official monograph for [REDACTED] [REDACTED] [REDACTED] to the USP under the USP Pending Monograph Process. Until your product is in alignment with the dissolution specifications (method and acceptance criteria) in the USP monograph, include the following statement in the description section on Labeling: *FDA approved dissolution specifications differ from the USP dissolution specifications.*

Send your submission through the Electronic Submission Gateway

<http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/default.htm>.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission:

▶ Example of Reference to PMP in Complete Response Letter

FDA Comment:

“Please note that a drug with a name recognized in the USP National Formulary (USP–NF) generally must comply with applicable compendial standards or the drug will be deemed adulterated, misbranded, or both. (See section 501(b) and 502(e)(3)(b) and (g) of the Federal Food, Drug, and Cosmetic Act (FD&C Act); also 21 CFR 299.5(a) and (b)). Such drugs must also comply with compendial standards for strength, quality, and purity, unless labelled to show all respects in which the drug differs or they will be deemed adulterated. (See section 501(b) of the FD&C Act and 21 CFR 299.5(c)). Because the proposed specifications for your product do not conform to the USP monograph for [REDACTED] with regard to the specified impurity [REDACTED] acceptance criterion, you are advised to contact USP upon receipt of this communication to initiate a monograph revision through the USP Pending Monograph Process (PMP). Please note that initiation of the PMP does not mean that the proposed specifications will necessarily be approved by FDA; revisions to the USP monograph will be contingent upon FDA approval of the proposed specifications in this application.”

Stay Connected

301-816-8501 | pendingrevisions@usp.org



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Thank You



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