Strengthening Your Compendial Strategy

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U.S. Pharmacopeia

Quality and Regulatory Predictability: Shaping USP Standards

December 11, 2025

The views and opinions presented here represent those of the speaker and should not be considered to represent advice or guidance on behalf of the U.S. Food and Drug Administration.

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Overview

- Role of USP standards: Regulatory framework and patient health
- Why USP needs direct engagement with industry – the challenge
- When and how to engage with USP to shape public standards
- Why engage early with USP

Creating robust public standards to meet the needs of regulators, industry, patients

What is USP?

U.S. Pharmacopeia (USP) is a private, non-profit scientific organization responsible for developing quality standards for 200+ years.

USP standards in U.S. Federal law

Recognized under Federal Food, Drug, and Cosmetic Act of 1938 (FDCA), which sets the foundation for modern-day food and drug regulation

Naming & Identity

Drug deemed *misbranded* unless its label bears the established USP name

FDCA 502(e)

Strength, Purity & Quality

Drug deemed *adulterated* if strength or quality or purity falls below USP standards

FDCA 501(b)

Packaging & Labeling

Drug deemed *misbranded* unless it is packaged and labeled as prescribed by USP

FDCA 502(g)

USP standards address urgent public health risks

DEG/EG

- Added test for DEG/EG in ID section of at-risk drug components

Heparin

- Developed methods and RS to assist detection of over-sulfated chondroitin sulfate adulteration in Heparin products

Alcohol

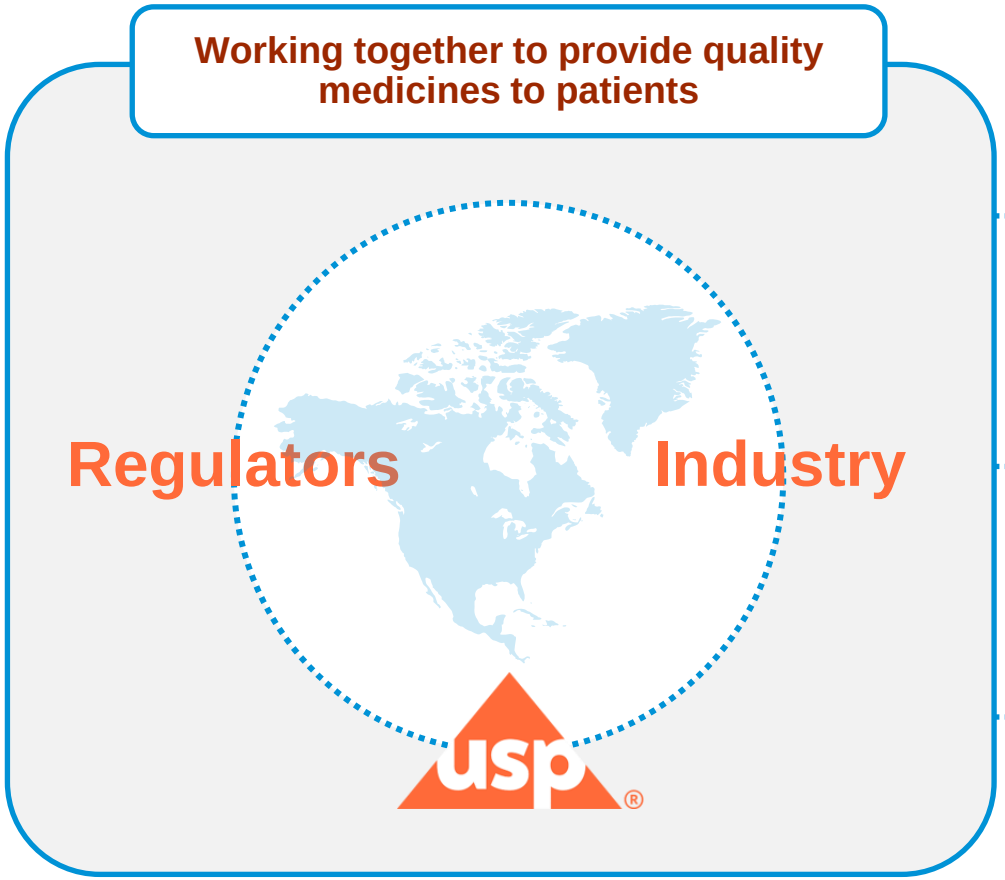
- Inclusion of a test for Methanol in the ID section of Alcohol and related monographs to address critical contamination in hand sanitizers and other products

Dextromethorphan

- Addition of chromatographic procedure in the ID section and RS to detect Levomethorphan in products containing Dextromethorphan

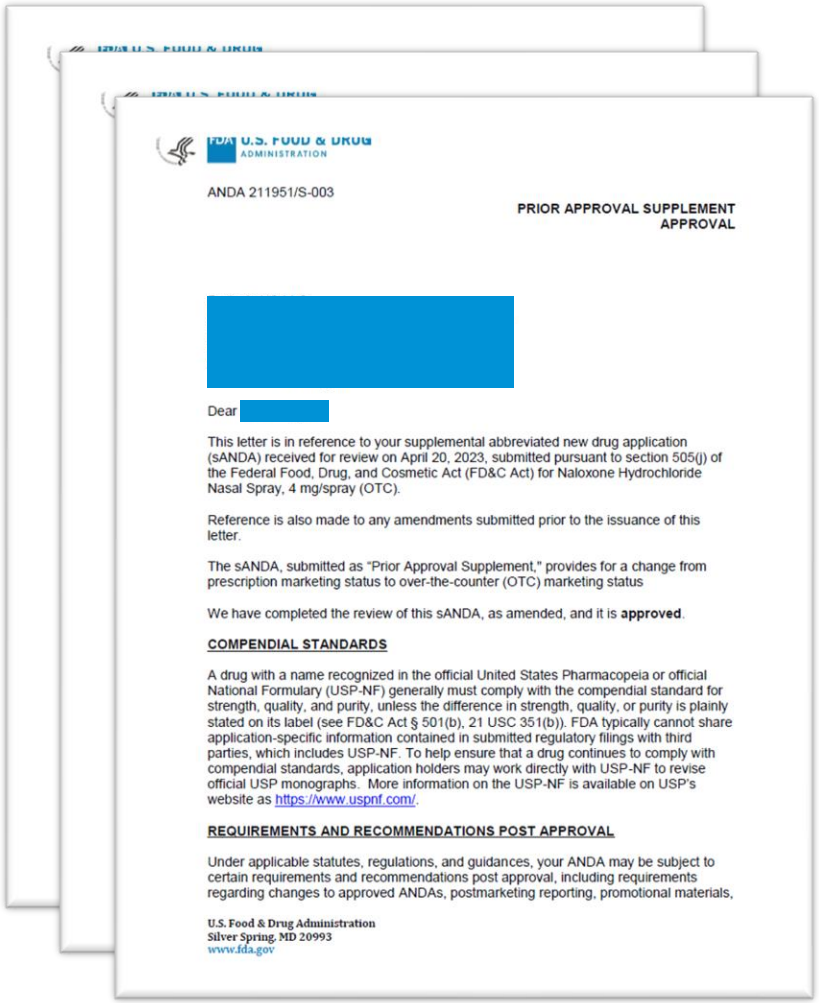
Quality and the supply chain

Quality issues in medicines can disrupt the supply chain, negatively impact patient access and threaten people's health.



- Demonstrate your company's dedication to quality and help protect patients.
- Help set the standard for manufacturing quality medicines and support patient access to needed therapies.
- Improve regulatory predictability by helping USP define critical quality attributes for medicines based on your approved product.

Information-sharing challenge



U.S. FOOD & DRUG ADMINISTRATION

ANDA 211951/S-003

PRIOR APPROVAL SUPPLEMENT
APPROVAL

[redacted]

Dear [redacted]

This letter is in reference to your supplemental abbreviated new drug application (sANDA) received for review on April 20, 2023, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Naloxone Hydrochloride Nasal Spray, 4 mg/spray (OTC).

Reference is also made to any amendments submitted prior to the issuance of this letter.

The sANDA, submitted as "Prior Approval Supplement," provides for a change from prescription marketing status to over-the-counter (OTC) marketing status

We have completed the review of this sANDA, as amended, and it is **approved**.

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standard for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website as https://www.uspnf.com/.

REQUIREMENTS AND RECOMMENDATIONS POST APPROVAL

Under applicable statutes, regulations, and guidances, your ANDA may be subject to certain requirements and recommendations post approval, including requirements regarding changes to approved ANDAs, postmarketing reporting, promotional materials,

U.S. Food & Drug Administration
Silver Spring, MD 20993
www.fda.gov

COMPENDIAL STANDARDS

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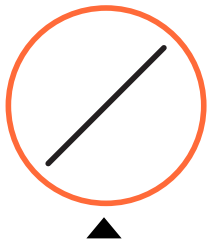
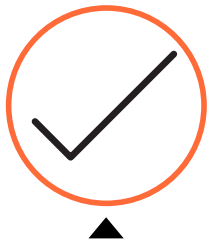
Sharing information with USP …



Myths

- Risks intellectual property and aids competitors
- Is too resource intensive
- Is unnecessary
- USP can't develop or revise a monograph **without my involvement**

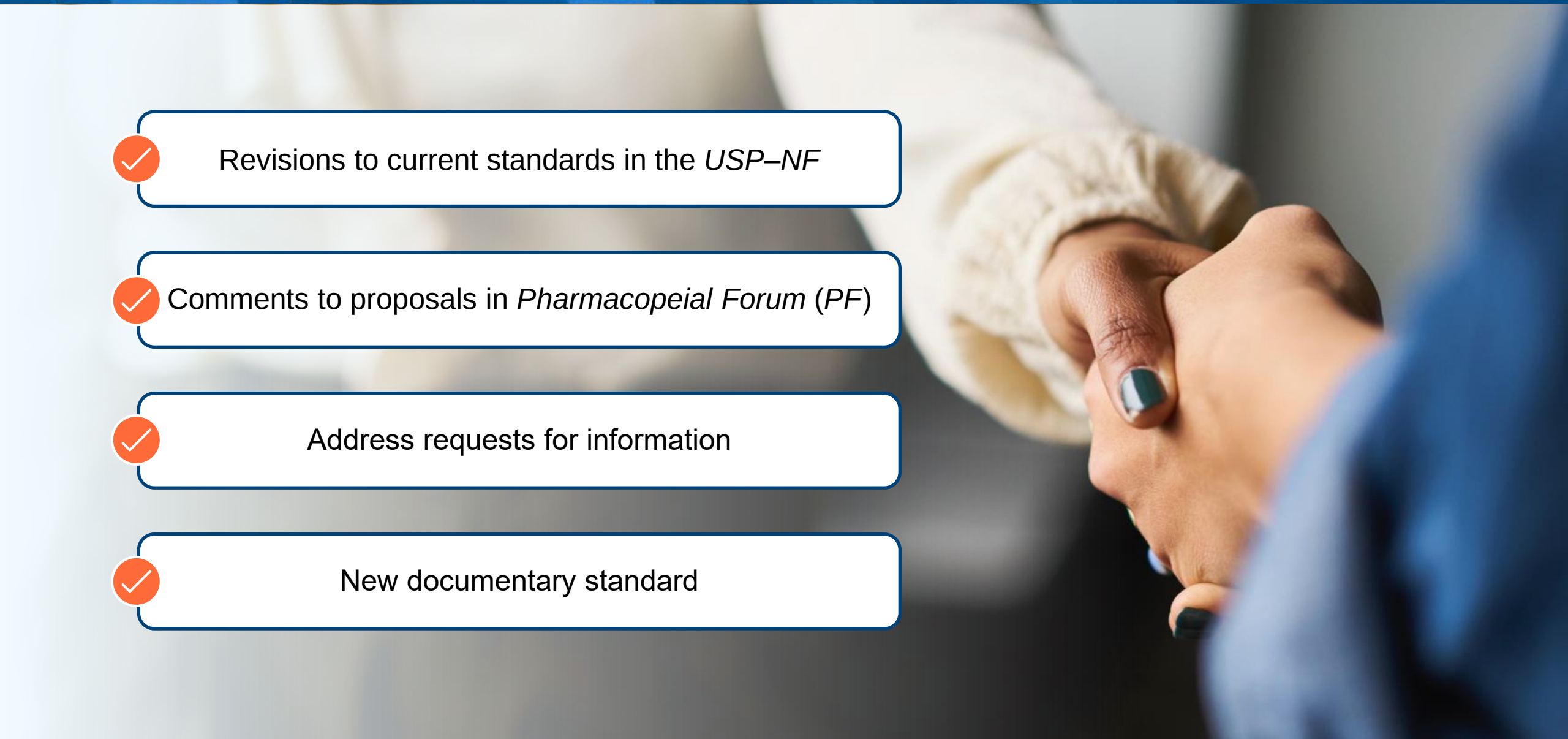
vs



Facts

- Helps ensure other products meet the same quality standards
- Reduces risk of non-compliance
- USP is an official compendium enforceable by FDA
- **Any FDA approved stakeholder** can engage USP to develop or revise monographs

Opportunities to engage

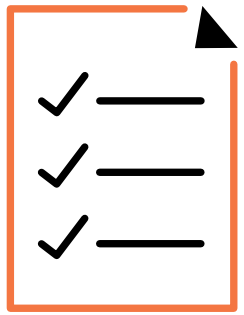


- Revisions to current standards in the *USP–NF*
- Comments to proposals in *Pharmacopeial Forum* (*PF*)
- Address requests for information
- New documentary standard

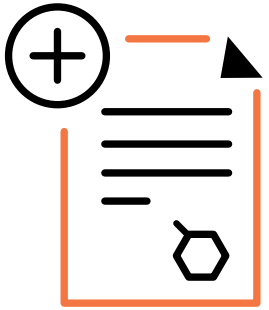
Ongoing monograph revision challenges

To ensure the quality of medicines, we are committed to the ongoing refinement of public standards… but we still face challenges

Partner resources/priority challenges



Information sharing



Monograph submissions

Monograph refinement: Ongoing revisions

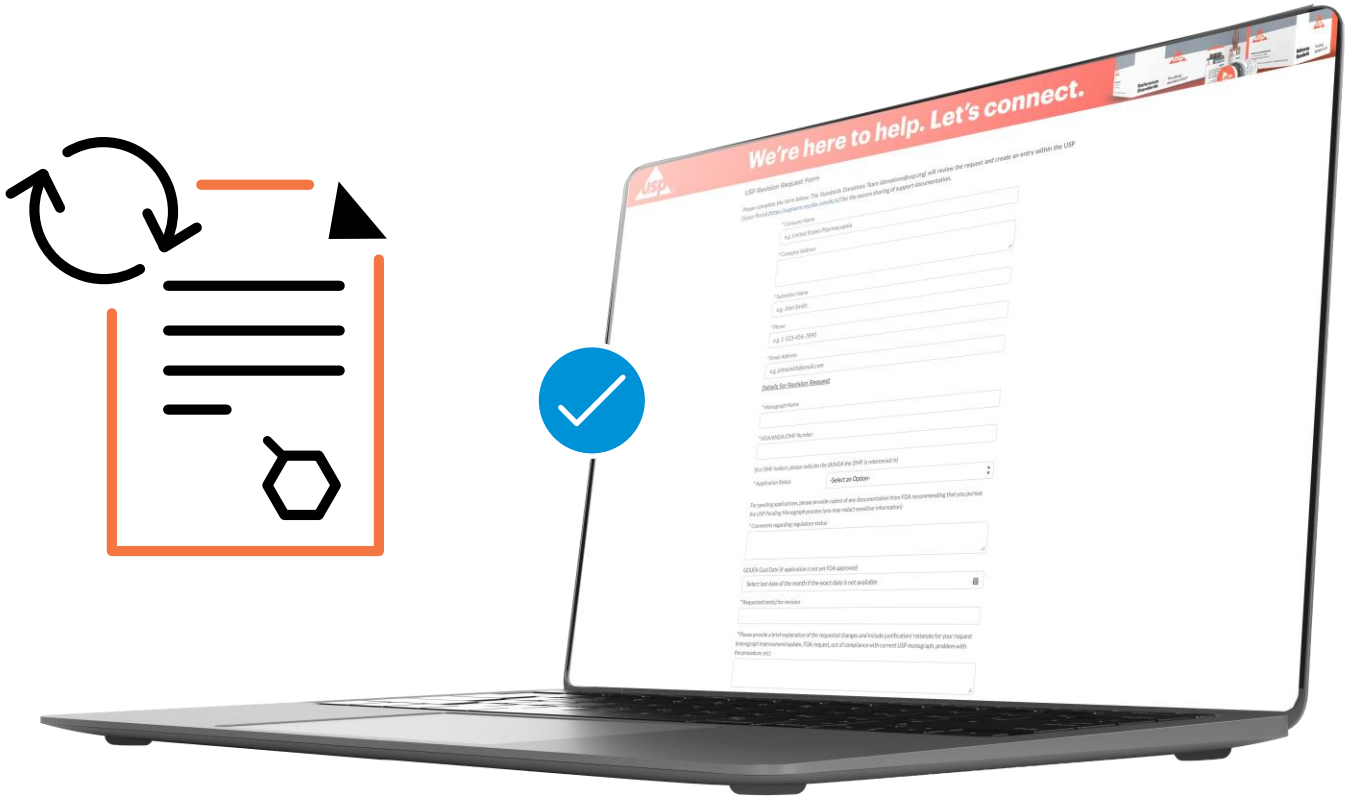
Targeted revisions to update, improve *USP–NF* standards

- Add or update ID
- Add organic impurities
- Replace animal testing where possible
- Replace outdated equipment
- Eliminate hazardous procedures and materials
- Add stability indicating procedures where appropriate
- Provide alternative procedures
- Align with ICH and regulatory expectations

Efforts to improve older standards and help ensure they are consistent with modern quality control practices and regulatory needs

Submitting a Revision Request

Easily submit Revision Requests online



uspharm.my.site.com/WebForm/s/webform?formName=RevisionRequest

Pending Monograph Program (PMP)

- Aligns updates to monographs with FDA approval of application under review
- Sponsors can initiate monograph revision for applications under review by FDA
- Primarily to revise existing monographs
- FDA may reference PMP in CR and/or Acknowledgement Letters

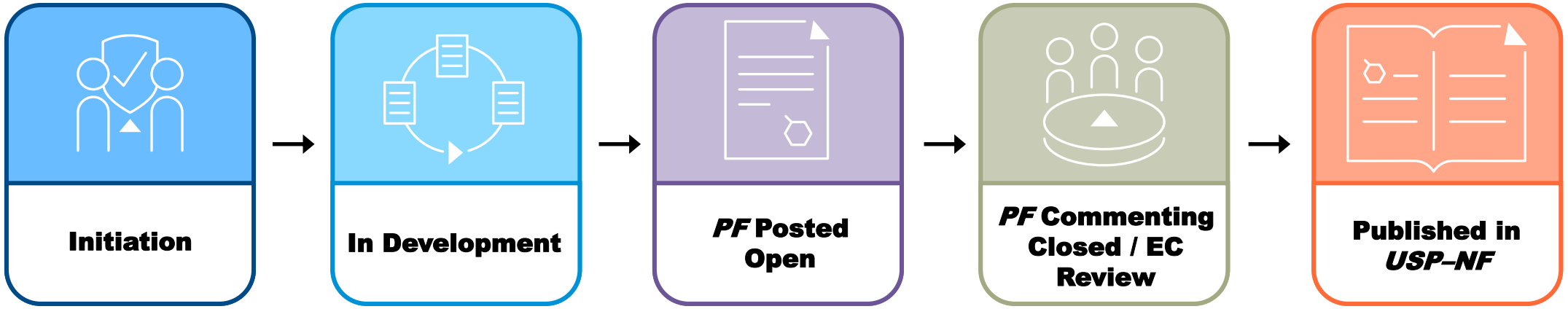
Additional information

– https://www.uspnf.com/pending-monographs

Submit request

– pendingrevisions@usp.org

USP monograph development stages



In development

USP activity

- Reviews submission package, begins drafting monograph, identifies needed reference materials and initiates procurement
- Engages with FDA on draft content proposal via Government Liaisons serving on Expert Committees

Where industry can engage

- USP may reach out to other known application holders associated with article
- View monographs that are in development before going to *PF*
- Other application holders can contact USP to discuss supporting monograph development

Proposed in *PF* for comment

USP activity

- Waiting and processing incoming comments on *PF* proposals

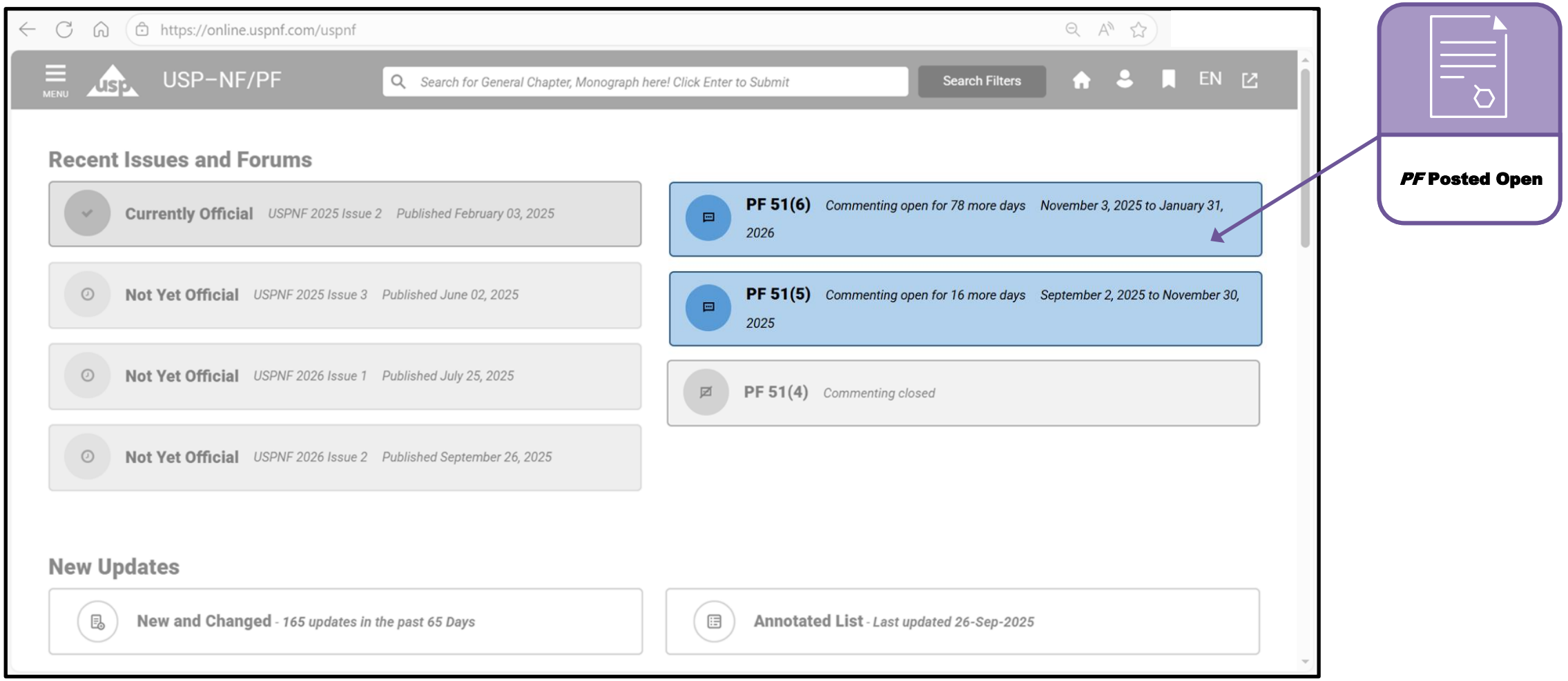
FDA

- Reviews draft monograph based, in part, on known approved applicants; provides necessary formal comments
- May also consider other applications under review when drafting comments

Where industry can engage

- Evaluating and commenting to USP on the proposal
- Submitting comments via *PF* during 90-day comment period

USP–NF / PF online



Expert Committee review

USP activity

- EC considers comments received from all stakeholders, including FDA
- USP publishes Notices (General Announcement – Call for Data) to specifically request information related to comments received from FDA

Where industry can engage

- View and respond to specific data request in timely manner
- Respond to USP's direct communication

Industry response to FDA comments

USP activity

- Posted on *USP–NF* website
- Additional outreach from USP to known approved application holders
- Responses accepted through email (pfcomments@usp.org or donations@usp.org)
- If unresponsive, the EC can decide to move the proposal forward

Example

Call for Data: Buprenorphine Injection (REF: 05-25-013-Z)

USP published a revision proposal for **Buprenorphine Injection** in Pharmacopeial Forum (PF), Vol. 51, No. 2., which introduced a new monograph for this drug product.

USP is interested in working with FDA approved applicants in order to help address the following comments provided by FDA:

- In the **IMPURITIES** section, we note that the acceptance criteria for "Buprenorphine 2,2'-dimer", and "Total degradation products" are different from what has been approved by the agency. We recommend revising the acceptance criteria to be consistent with what has been approved by the agency. We recommend that USP should contact the FDA approved applicants to obtain this information.

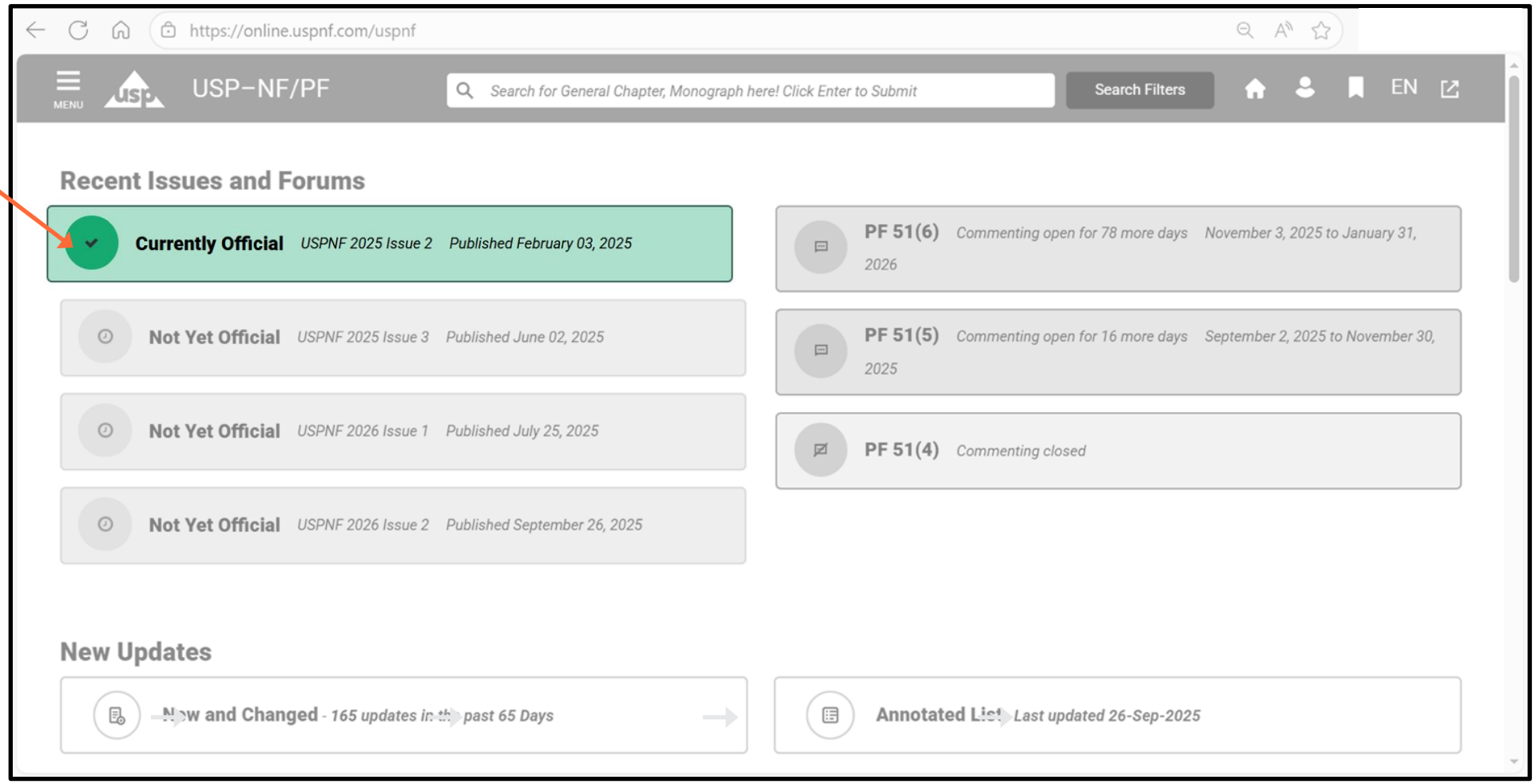
Publication in *USP–NF*

online.uspnf.com/uspnf

- Six-month minimum given for implementation
- Implementation timeline based on comments received from stakeholders
- Compliance issues discovered later can be addressed through future revision request

USP–NF / PF online.

Published in *USP–NF*

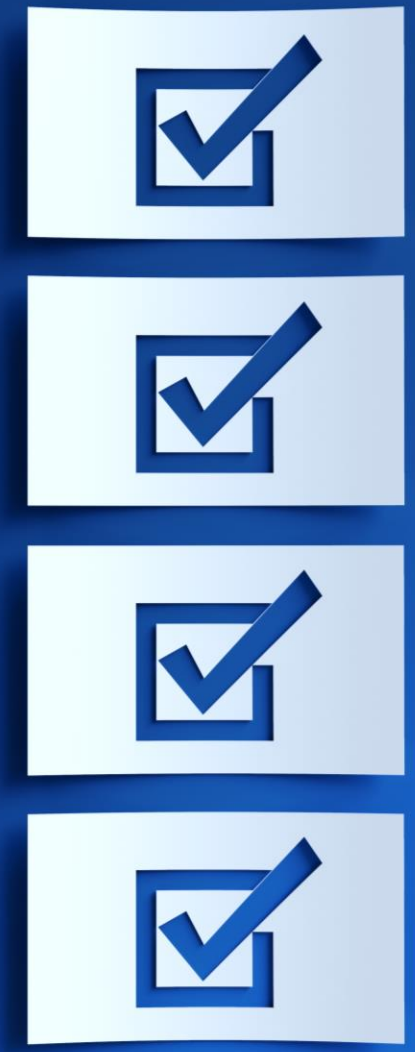


Addressing post-publication issues

- USP reaches out to known approved application holders
- USP proposes standards in *PF* to avoid any compliance issues
- Revision requests for accelerated revisions to address compliance issues are confirmed with FDA by USP before being accepted

Failure to participate in standards-setting processes could result in:

- Approved product may no longer comply with *USP–NF* / Federal law
- A request for revision to address any compliance issues will be required
- Compliance gap of unpredictable length



Initiation of monograph development

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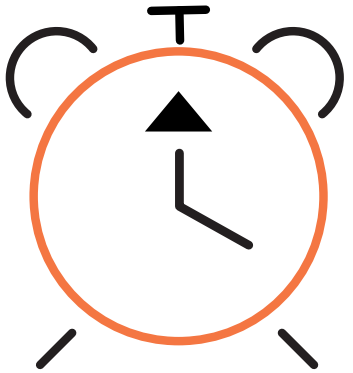
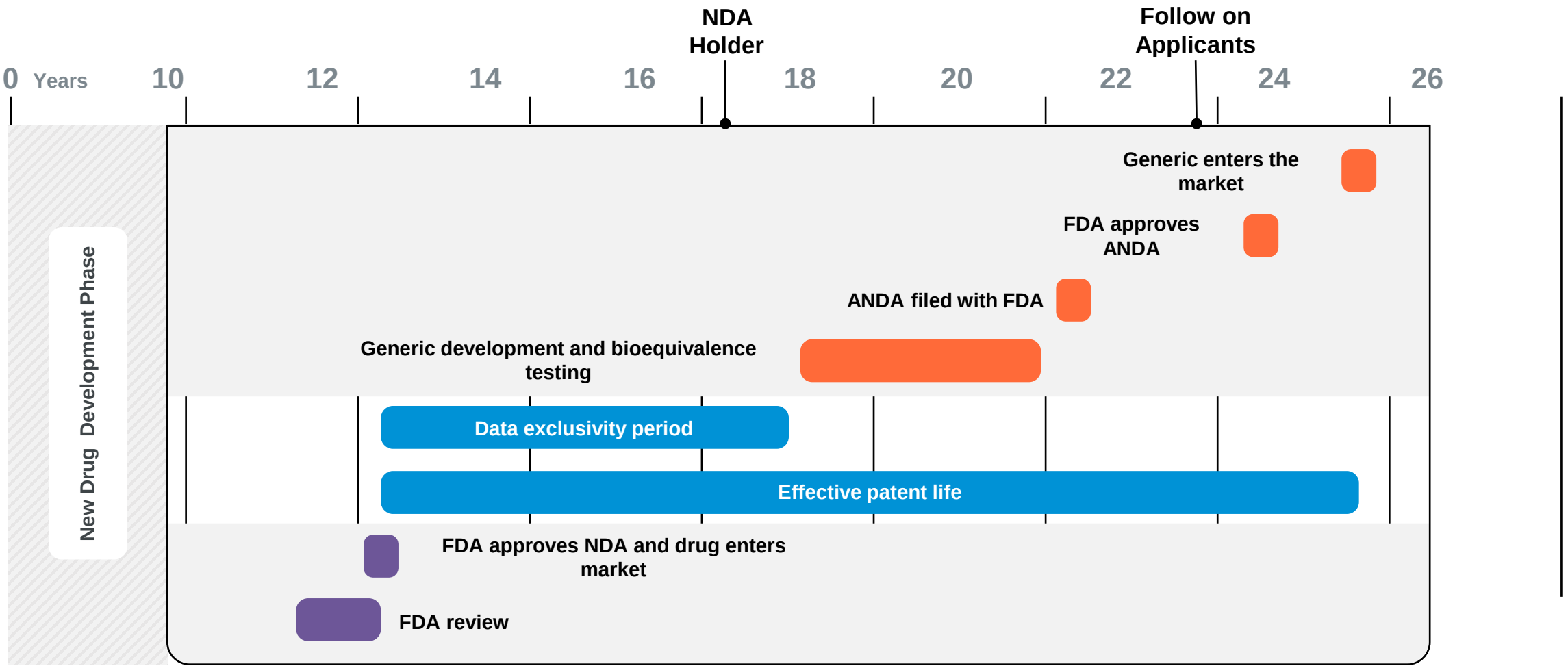
Initiation: Seeking submissions

Optimal timings

- Five years post-product launch when new chemical entity (NCE) exclusivities have generally expired OR five years before Generic Entry, depending on Drug Substance Patents (NDA)
- When analytical methods and processes have been optimized and approved by FDA (All)
- Upon receipt of Technical Review and Letter of Authorization linked to ANDA on file (DMF Holders)
- Revision requests submitted prior to approval via Pending Monograph Process

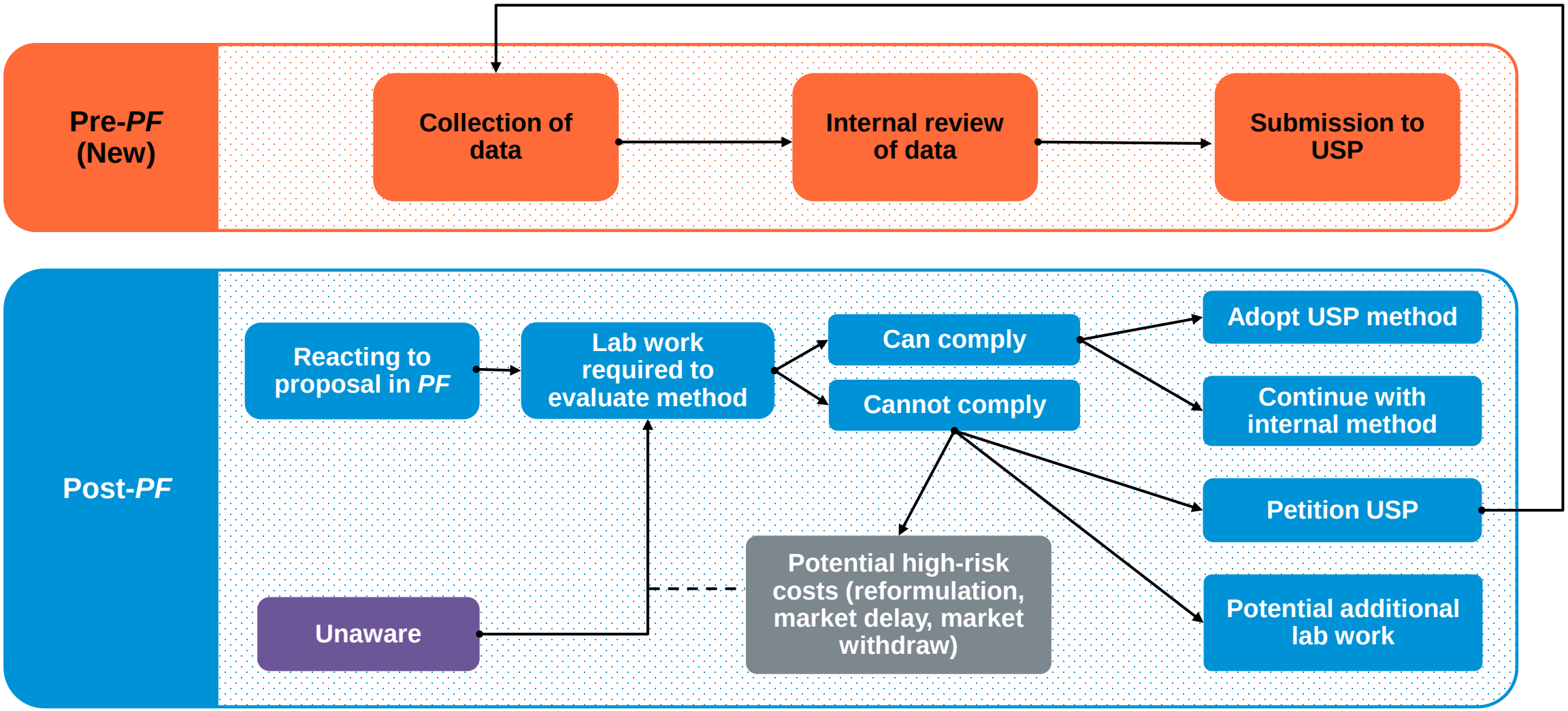


Regulatory lifecycle approach for monograph development



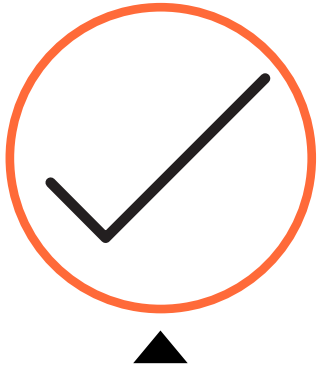
Submission timing changes depending on exclusivities, DS patents, PIV challenges

Submission pre- vs. post-*PF*



Key requested information

The requested information is typically listed in the 3.2.S. for drug substances and 3.2.P. for drug products in the FDA approved application (eCTD).



- US regulatory status
- Monograph content
  - Methods, shelf-life, acceptance criteria based on approved application
- Chemical/impurity information
- Validation data
- Stability data
- Certificates of Analysis
- Packaging/storage/labeling information
- Willingness to donate bulk reference material

Your data is protected by USP's Commitment to Confidentiality

Find more at USP.org

Seeking Submissions

Emerging Standards*

In Development

PF Posted Open for Comment

PF Commenting Closed / EC Review

Published USP-NF

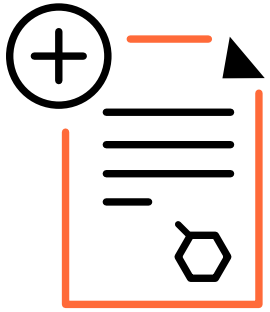
RS & Material Releases

usp.org/get-involved/usp-donations-program

Don't know where to get started? Contact donations@usp.org

Key takeaways

There are multiple opportunities to engage with USP



Sharing information with USP creates a robust public standard for all manufacturers

Sharing information early in your regulatory lifecycle avoids future compliance issues, increasing regulatory predictability

Regardless of the manufacturer, all patients have the right to quality medicines. When you donate to USP, your legacy of quality lives on.

Stay connected

donations@usp.org

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