



USP Guideline for Submitting Requests for Revision to *USP–NF* General Information for All Submissions

A. INTRODUCTION AND PURPOSE

This document, together with the accompanying Submission Guidelines for various types of compendial articles, are intended to provide guidance on how to submit information to support creation of a new monograph or a revision to a proposed or existing official monograph in the *United States Pharmacopeia* and *National Formulary (USP–NF)*. All such requests will be handled in accordance with Section 7.04 and other provisions of the [2015-2020 Rules and Procedures of the Council of Experts](#) (CoE Rules), which govern all aspects of USP's standards-setting processes. The purpose of this document and the Submission Guidelines is to promote optimal submissions from sponsors to facilitate development and finalization of a public standard in accordance with the processes outlined in the CoE Rules.

B. SCOPE OF *USP–NF*; ADMISSION POLICY

USP's policy is to include in *USP–NF* standards for all articles that are legally marketed in the U.S, including biologics, which are considered a subset of drugs by FDA and USP. This scope effectively encompasses any drugs considered legally marketed by the FDA, such as pursuant to an NDA, ANDA, BLA, NADA, ANADA, or provisions related to compounding or the OTC monograph system, as well as tissue-based products marketed under 21 CFR Part 1271 or cleared under the 510(k) device pathway. It is also USP's policy that each such article (drug product or drug substance, whether prescription, over-the-counter, or compounded; or excipient; or dietary supplement) should have a *USP–NF* monograph that includes USP Reference Standards (RS) approved as being suitable for use as a comparison standard in such monograph tests or assays.

Information to support new and revised compendial standards is often submitted by manufacturers whose articles are already FDA-approved or otherwise legally marketed (e.g. FDA OTC monograph system, tissues and tissue-based products). To further compendial modernization and optimize the role of compendial standards, USP in certain cases also works with manufacturers whose articles are undergoing clearance through the FDA review and approval process or otherwise. This is discussed further in the section below on "Articles Undergoing FDA Review & Approval."

USP recognizes that some manufacturers may not wish to sponsor a standard until an article approaches multi-source status. Although there may be circumstances meriting the development of a standard by USP without a sole-source sponsor, it is USP's policy to first seek to work exclusively with an FDA-approved manufacturer (typically the relevant patent holder) until approximately five years prior to potential generic entry. If at that time the manufacturer remains unwilling or unable to provide the necessary information or material, USP may work



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with another manufacturer willing to sponsor a submission or begin development internally. This time frame is intended to give due regard to applicable intellectual property/patent considerations,¹ while advancing the public policy goal of ensuring that a public monograph and any component RS are available when FDA reviews and approves any follow-on or multi-source versions.

C. CONFIDENTIALITY, DOCUMENT DISCLOSURE AND INTELLECTUAL PROPERTY POLICIES

USP has established policies and rules that provide the highest safeguards to confidential information submitted by sponsors during the course of the revision process. USP's confidentiality policies and the CoE Rules require both USP expert volunteers and staff involved in USP's standards-setting process to maintain the confidentiality of information submitted to USP by a third party. Below is a brief summary and link that provides additional information on each of the specific policies, provisions of the CoE Rules, and procedures concerning confidentiality.

USP Code of Ethics Confidentiality Policy

The [USP Code of Ethics](#) applies to USP employees, expert volunteers and representatives. The Confidentiality Policy in the USP Code of Ethics obligates everyone at USP to protect confidential information and proprietary information, whether generated by USP or by third parties, unless disclosure is authorized or legally mandated. All information about USP and our compendial activities is considered confidential unless it is made publicly available by USP or it is known to be publicly available outside of USP.

Confidential information consists of information that is not available to or intended for the public to view and can fall within, but is not limited to, the following categories:

- financial, scientific or medical information; customer information;
- supply and service information; marketing information;

¹ In many cases, sole-source manufacturers who prefer not to collaborate with USP in the initial years following FDA approval cite intellectual property/patent aspects as key considerations in deciding when to begin to collaborate actively with USP in development of a standard. As a general rule, in seeking to work as proactively as possible with such manufacturers, although non-patent exclusivity may also be considered, USP's standard-development time frame focuses on drug substance (active ingredient) patents listed in the FDA Orange Book, <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>. In cases of multiple drug substance patent listings, USP will generally focus on the patent with the later expiration date. Where sources are available to identify an earlier expiring drug substance or other patent as likely being key to the entry of generic or other follow-on versions, USP may use such earlier date.



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- correspondence between and among USP staff and members of its Board of Trustees, Council of Experts, and Expert Committees;
- personnel or consultant files;
- trade secrets; and,
- confidential information relating to manufacturing processes and other information which USP or a third party may deem confidential.

USP's confidentiality policy does not apply when a third party's information is required to be disclosed by law, regulation, rule, act or order of any governmental authority or agency, such as identifying country of origin on USP reference materials.

USP CoE Rules and Confidentiality

The [CoE Rules](#) reinforce the obligation of USP expert volunteers to maintain confidentiality during their standards-setting activities. Under Rule 2.06, CoE and EC members must maintain the confidentiality of all information they receive during the standards-setting process and are prohibited from disclosing any information for any purpose unless the information is already publicly available. **In cases of doubt as to the confidentiality of information, the information in question must be treated as confidential unless otherwise shown.** Under Rule 6.02, government liaisons to such Expert Committees and Expert Panels also have access to such information and are permitted to use it only for USP standards-setting purposes. USP expert volunteers and government liaisons sign a confidentiality agreement with USP reflecting these obligations.

USP Document Disclosure Policy

Under USP's Document Disclosure Policy, which is a part of the [Code of Ethics](#), USP provides disclosure of information and records regarding USP standards-setting activities to third parties upon request consistent with:

- The rights of individuals to privacy
- USP's need to protect the confidentiality of trade secrets and other proprietary commercial or financial information
- USP's need to promote frank internal deliberations and to pursue standards-setting activities without disruption



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USP will not disclose any document containing trade secrets or confidential commercial secrets, “if such documents have been specifically designated as such when submitted to USP”² Accordingly, sponsors should indicate in their Request for Revision whether any of the submitted documents or other information should be treated as confidential. Any submitted documents not clearly marked confidential will be subject to disclosure under the Document Disclosure Policy. As a general policy, USP undertakes to keep sponsor names confidential when providing documents under the Document Disclosure Policy, but USP reserves the right to disclose the identity of a sponsor at its discretion if circumstances warrant.

Intellectual Property

At times, issues of intellectual property arise regarding a monograph. Under USP’s Intellectual Property Policy, which is part of the Code of Ethics, USP respects intellectual property rights and uses its best efforts to adhere to all applicable laws regarding protection of intellectual property. USP is not, however, responsible for the protection or enforcement of intellectual property rights in the U.S. and elsewhere, and because USP’s standards are intended to be public standards available for the use and benefit of all parties, USP requests that sponsors disclose in their Requests for Revision whether any portion of the methods or procedures submitted is subject to patent or other sponsor-held intellectual property rights. In cases where patented methods, procedures or materials required for compendial tests and assays (such as RS or photomicrographs) are proposed, USP may seek assistance from the sponsor in obtaining clearance or license for use by any persons seeking to use or apply a USP public standard incorporating such method, procedure or material, and may consider other approaches including the solicitation of other Requests for Revision that use alternative methods or procedures. USP reserves the right to indicate in a resulting monograph or general chapter whether methods or procedures are subject to such intellectual property rights.

D. SUBMISSION PROCEDURES AND DEVELOPMENT PROCESS

Organization of the Submission Guidelines

There is a Submission Guideline for each class of compendial articles, as follows:

- Chemical Medicines
- Excipients

² However, the policy does allow documents submitted to USP by a third party containing trade secrets or confidential commercial secrets that ordinarily would be contained in a New Drug Application or Supplement thereto to be disclosed to the U.S. Food and Drug Administration upon its request in its review of any revision or proposed revision of the United States Pharmacopeia, National Formulary, or other USP compendium.



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- Biologics
- Non-Botanical Dietary Supplements
- Botanical Dietary Supplements

Procedures for Submitting Requests for Revision for a New *USP–NF* Monograph

Where no *USP–NF* monograph exists for an article, anyone may submit a Request for Revision or be asked to provide a Request for Revision by USP staff. When received, a USP staffer will work with the sponsor in accordance with the relevant Submission Guideline to ensure that the Request for Revision contains the appropriate information and background materials.

Procedures for Submitting Requests for Revision Relating to an Existing or Previously Proposed *USP–NF* Monograph

Interested parties may submit a Request for Revision to revise an official or previously proposed (in development) *USP–NF* monograph. Revisions may be directed at an entire monograph or specific monograph tests, procedures, and/or acceptance criteria. USP also welcomes revisions directed to changes in general chapters and the [General Notices and Requirements](#). The Request for Revision should be submitted as provided in the relevant Submission Guideline and include the rationale, description of the proposed change, and supporting data, where needed. Because revisions to monographs can be resource intensive, priority will be given to those revisions most likely to advance public health in terms of the timeliness, accuracy and utility of USP's public quality standards.

Accelerated Revisions

Certain situations may require that a Request for Revision be completed and become official more quickly than through USP's standard revision process. In such cases, the Request for Revision may be processed using one of USP's accelerated revision processes, in accordance with the USP [Guideline on the Use of Accelerated Processes for Revisions](#) to the *USP–NF* available on the USP Website.

Articles Undergoing FDA Review & Approval

USP will work with sponsors to develop monographs or monograph revisions for articles awaiting approval by FDA under USP's [Pending Monograph Guideline](#). These proposals will be published in the [Pharmacopeial Forum](#) (*PF*) for notice and comment where required in accordance with USP's typical Request for Revision processes. Following publication in *PF*, these proposals remain in an unofficial status until FDA approval of the market application held



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by the sponsor. For manufacturers with applications pending at FDA that either are or should be subject to an existing USP monograph, this ensures that FDA approval is not unnecessarily delayed or complicated because the article does not conform to the compendial monograph. For manufacturers with applications pending at FDA where no existing USP monograph exists, this allows a new monograph to become official as soon as possible following approval of the article.

The Request for Revision should be submitted in accordance with the relevant Submission Guideline and will be reviewed in accordance with USP's usual processes. If USP decides to proceed with the revision, then the proposal will be developed, balloted and published as provided in the Pending Monograph Guideline.

Relation of Standards to FDA-Approved Specifications

Although sponsors are understood to be voluntarily proposing the specifications and other aspects of what are essentially private standards, USP's mission is to establish public standards that help assure the identity and quality of medicines across manufacturers. Consistent with and in furtherance of this mission, USP is committed to doing all it reasonably can to assure that *USP–NF* standards and related methods are developed through an objective, independent, science-based process, and that the resulting official compendial standards not have the effect of favoring any manufacturer over others or putting any FDA-approved product out of compliance. Accordingly, in submitting a Request for Revision consistent with the Submission Guidelines, sponsors warrant and certify that the proposed test, methods and specifications are consistent with, and no more stringent than, those contained in sponsor applications or supplements submitted to and approved by FDA. Any proposed specifications that are more stringent than those approved by FDA in an initial application or prior supplement must be clearly identified and appropriately explained in the information provided to USP. In addition, if any specifications submitted by the sponsor deviate from ICH limits, Sponsor shall provide the justification for such deviation. If the deviation is not based on safety or other public health concerns, USP reserves the right to revert to ICH limits. In all cases, Sponsors should understand that the final official standard may differ from that originally submitted, because the Expert Committees are responsible for determining and approving content of *USP–NF*.

Reference Materials

When submitting a Request for Revision, a sponsor is asked to provide all appropriate information and background materials, including suitable bulk reference materials, in accordance with the requirements set forth in USP's [Guideline for Donors of USP Reference Standard Candidate Materials](#). If a sponsor is unwilling to provide such reference materials or



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for any reason such reference materials prove inadequate for compendial use, USP may source such materials elsewhere or develop appropriate reference materials in its own laboratories, and use any such materials and resulting RS as a component in USP monographs and as a part of USP's public compendial standards. Also note that USP RS are not reserved for use with any particular USP compendium or standard. Once a USP Expert Committee deems a particular USP RS suitable for use with a USP compendial standard, it becomes a component of any monograph in which it is called out (*see General Notices, §5.80, re USP–NF*). It is USP policy that any reference materials likely to be required for use with a *USP* or *NF* standard (approved by an Expert Committee as suitable for use as comparison standards in *USP* or *NF* tests and assays) either accompany a sponsor's submission, or be part of an overall monograph development commitment.