

INTRODUCTION

This guideline is published pursuant to Section 9.04(a) of the Rules and Procedures of the 2005-2010 Council of Experts. It is intended to provide guidance to Sponsors submitting information to support a Request for Revision to the *United States Pharmacopeia* and *National Formulary (USP–NF)*. A Request for Revision may be for the creation of a new monograph or a revision to an existing official monograph. The purpose of this guideline is to promote optimal submissions by Sponsors and facilitate development and finalization of a Revision. Sponsors of Requests for Revision, whether for new monographs or revision of existing or proposed monographs, should understand that a Request for Revision will lead to a public standard that may incorporate comments from other parties and will ultimately be determined by the assigned USP Expert Committee. As a result, it may differ from the original Request for Revision and may no longer reflect the private standard of the submitting Sponsor.

Procedures for submitting Requests for Revision for a new USP-NF monograph

Where no USP–NF monograph exists for an article, a Sponsor may submit a Request for Revision on its own initiative or be requested to provide a Request for Revision by USP staff. In either case, the provision of information by a Sponsor is voluntary. When received, USP assigns the Request for Revision to a Scientific Liaison who will work with the Sponsor to ensure that the Request for Revision contains the appropriate information and background materials.

At times, issues of timing and intellectual property arise regarding a monograph. Under USP’s Intellectual Property Policy, available on USP’s website, USP respects intellectual property rights and adheres to all applicable laws regarding protection of intellectual property. A Sponsor may specifically request that certain portions of a Request for Revision be kept confidential. This request will be honored, and the designated confidential information will be exempt from disclosure under USP’s Document Disclosure Policy, also available on the USP website.

Availability of timely, high quality revisions to USP–NF requires the active participation of Sponsors and can be resource-intensive. To assist Sponsors, USP will: (1) send a Sponsor the draft monograph based on their Request for Revision prior to publication in the Pharmacopeial Forum; (2) where acceptable to the Expert Committee, invite a Sponsor to participate in the relevant Expert Committee’s deliberations on the Request for Revision; and (3) with Sponsor and Expert Committee approval, invite an FDA reviewer to attend Committee deliberations of the Request for Revision.

Under USP’s approach for developing standards for articles pending FDA approval (SAPFA), a new monograph may be developed and published on USP’s website even if the article has not yet received FDA approval, as long as the Sponsor is seeking such approval. More information on the SAPFA approach can be found in a separate Guideline available on USP’s website.

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Organization of this Guideline Following this Introduction is a Glossary section which provides definitions for terms commonly used in this Guideline. The remainder of the Guideline is divided into four chapters: (1) monographs for Small Molecule drug substances and products; (2) monographs for biologics/biotechnology drug substances and products; (3) monographs for excipients; (4) monographs for vaccines, and (5) monographs for blood, blood components and blood products. Additional sections may be added, as appropriate. Recommendations are duplicated in several of the chapters to allow manufacturers of specific articles (e.g., active ingredients, excipients) to access the recommendations in their entirety.

Procedures where a USP–NF monograph does exist or a proposal for a new monograph has appeared in PF A Sponsor may submit a Request for Revision to revise an official or proposed 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 USP General Chapters. The Request for Revision should include rationale, description of the proposed change, and supporting data, where needed. The rationale can be editorial, science-based, or economic-based. Because revisions to monographs in USP–NF can be resource intensive, Sponsors should request revisions to existing procedures only when the change represents a significant improvement. Description of the proposed change and data needed to support a change are described in specific sections of this guideline.

Flexible monograph approach At times, an ingredient and/or a drug product, including dietary supplement ingredients and products and biologicals and biotechnological ingredients and products, exhibit different attributes that have been determined by the FDA not to impact their safety and/or efficacy, i.e., their identity as official ingredients and products. Examples include different polymorphic forms, 1 impurities, hydrates, and dissolution cases. In these instances, USP will allow different tests, procedures, and/or acceptance criteria reflecting these different attributes within a single monograph, with suitable validation, under its flexible monograph approach.²

The flexible monograph approach may be used in conjunction with USP’s SAPFA approach, described above, to allow a proposed revision to a monograph incorporating the new tests, procedures or acceptance criteria to be published on USP’s website even if the Sponsor of the Request for Revision does not have FDA approval at the time but is seeking such approval. As noted above, the SAPFA approach is discussed in more detail in a separate Guideline available on the USP website.

¹ Crystalline forms have different arrangements and/or conformations of the molecules in the crystal lattice. Amorphous forms consist of disordered arrangements of molecules that do not possess a distinguishable crystal lattice. Solvates are crystal forms containing either stoichiometric or nonstoichiometric amounts of a solvent. If the incorporated solvent is water, the solvate is commonly known as a hydrate. For further information, see the FDA’s Guidance for Industry on ANDAs: Pharmaceutical Solid Polymorphism—Chemistry, Manufacturing, and Controls Information. Rockville, MD; 2004.

² For additional information on the adoption of the flexible monograph approach by USP’s Council of Experts Executive Committee, see Policies and Announcements. *Pharm Forum*. 2005;31(3):690–691.

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USP acknowledges that use of the flexible monograph approach will result in the inclusion of tests and procedures in a monograph that are not applicable to all manufacturers of that article. The General Notices of USP–NF currently state that an article must pass all tests to be compliant. USP is currently revising the General Notices to accommodate the flexible monograph approach. For example, the revised General Notices will include a statement to the effect that when an impurity test or procedure that is not applicable to all manufacturers of that article is included in a monograph, the test need not be performed if the supplier of the article has demonstrated that the given impurity is not formed by or utilized in the synthetic route used for the manufacture of that article. Similarly, the revised General Notices will state that when a test or procedure that relates to the physical character of an article (such as a particle size test or specific surface area test) is included in a monograph and is not applicable to a manufacturer of that article, the test need not be performed.

Sponsors of Requests for Revision are encouraged to utilize the flexible monograph approach where applicable, together with the SAPFA approach . For specific questions, please contact the appropriate USP Scientific Liaison.

Submissions USP requests that Sponsors provide a Request for Revision electronically, via e-mail or computer disc (CD), as well as a printed copy using either PDF or a Windows-based application. Because USP uses Microsoft Office products, submissions in these formats are preferred. Documents also may be submitted in HTML, SGML, or XML formats. Draft Requests for Revision should be complete and include all supporting information and software applications/versions used to prepare the Request for Revision.