

STIMULI TO THE REVISION PROCESS

Stimuli articles do not necessarily reflect the policies
of the USPC or the USP Council of Experts

USP's Nomenclature Initiatives

Angela G. Long, M.S.; Andrzej Wilk, Ph.D.; Matthew Van Hook, J.D.; Shawn C. Becker, M.S.,
RN

ABSTRACT The purpose of this *Stimuli* article is to update *USP–NF* users about recent USP nomenclature initiatives. These initiatives include: (a) a revision of general information chapter *Nomenclature* 〈 1121 〉; (b) recommendations from the Monograph Naming Advisory Group on the implementation, education, and communication of the *USP Monograph Naming Policy for Salt Drug Substances in Drug Products and Compounded Preparations*, which becomes official May 1, 2013; (c) a new Nomenclature Guideline that will provide additional information about how the USP Nomenclature, Safety and Labeling Expert Committee¹ names drug products; and (d) a new “Compendial Nomenclature” area of the USP website that provides the naming decisions of the Nomenclature, Safety, and Labeling Expert Committee in a timely manner.

Background

In the interest of achieving a uniform and consistent process for the naming of compendial articles (drug substances and drug products, for small molecule drugs, biologics, excipients, and dietary supplements), the Nomenclature, Safety, and Labeling Expert Committee applies standard naming approaches to articles appearing in the *USP–NF* for consistency in establishing titles of drug product monographs. These general naming approaches are outlined in general information chapter *Nomenclature* 〈 1121 〉.

In the United States under the Federal Food, Drug, and Cosmetic Act (FDCA), the name given a drug (nomenclature) plays a critical role. Both the *United States Pharmacopeia (USP)* and the *National Formulary (NF)* are recognized as official compendia. A drug (which includes both FDCA and Public Health Service Act biologics) with a name recognized in *USP–NF* must comply with compendial identity standards or be deemed adulterated, misbranded, or both. In addition, such drugs also must comply with compendial standards for strength, quality, and purity, unless labeled to show all respects in which the drug differs. See FDCA 501(b) and 502(e)(3)(b), and the Food and Drug Administration (FDA) regulations at 21 CFR 299.5. The FDCA requires all legally marketed drugs to have an “established name” (which is a nonproprietary name, other than the applicable systematic chemical name), which is almost always tied to the drug name recognized in *USP–NF*. USP plays an

important role, with FDA, in creating such names/nomenclature, which play a central role not only for enforceable compendial requirements, but also in FDA regulations. Note that oversight of proprietary or “brand” drug names remains the responsibility of FDA, working with applicants in the course of reviewing and approving new drug applications (NDAs), abbreviated new drug applications (ANDAs), and biologics license applications (BLAs). FDCA 502(e)(3) specifies how “established names” for drugs are created. FDA may establish such names by regulation under FDCA 508, but rarely does so. Instead, in the absence of a name specifically designated in a 508 rulemaking, the law recognizes the official title of a drug in *USP–NF* (and that is so even if USP does not designate a established name until after FDA has approved a drug or biologic, which might necessitate a change in the product's interim established name). As detailed in FDA regulations, the naming of an article in a USP compendium is the primary pathway for deriving official nonproprietary names. In particular, FDA regulations recognize the process by which USP develops established names for drug substances, which is normally through the work of the U.S. Adopted Names (USAN) Council, which in addition to USP includes the American Medical Association and American Pharmaceutical Association, with close cooperation by FDA (see 21 CFR 299.4(c), (d), and (e)). Accordingly, the regulated community “may rely on as the established name for any drug the current compendial name or the USAN adopted name listed in *USAN and the USP Dictionary of Drug Names*”² [21 CFR 299.4(e)].

While USP has had a role in monograph naming since its inception in 1820, a USP nomenclature committee was formed in 1986¹ to create appropriate established names for dosage forms and combination drug products, and to develop naming policies. The Expert Committee coordinates its work with the USAN Council, and it establishes a *Pronunciation Guide*, which also is utilized by USAN.

Changes to Nomenclature < 1121 >

The proposed changes to *Nomenclature < 1121 >*, also included in this issue of *Pharmacopeial Forum (PF)* 38(1), include, first and foremost, a proposal to move the general information chapter to a general test chapter below <1000>. The new number for the chapter is <8>. This reflects the mandatory nature of the chapter due to USP's legal authority in creating established names (see above). Main changes in the chapter include:

- An updated description of USP's role in law with amended references
- A revised *Monograph Naming Policy for Salt Drug Substances in Drug Products and Compounded Preparations* to clarify the definition of the active moiety. This definition applies to non-covalent chemical entities such as salts, complexes, and clathrates, but excludes covalently bound esters.
- General rules applied in the naming of drug products with clear definitions such as:
 - Rules for omitting route of administration in the name

- Rules for naming and labeling injections, where specific route (e.g., intravenous, intramuscular) is placed in the labeling rather than in the title
- Term “for” which is included in names to indicate that the product is a solid drug substance that must be dissolved or suspended in a suitable liquid to obtain a final dosage form
- Provision that creams, ointments, lotions, and pastes are applied topically, unless otherwise indicated in the name
- Clarification of rules for products administered vaginally (inserts) and rectally (suppositories)
- A system as a preparation of drug(s) in a carrier device that is applied topically or inserted into a body cavity, from which drugs are released gradually over an extended period of time, after which the carrier device is removed
- Definitions applied for concentrates
- A preparation
- “General Nomenclature Forms” that outline the general approaches the Nomenclature, Safety, and Labeling Expert Committee uses to establish monograph titles. This section lists examples of existing monograph titles or approved drug product names that illustrate the rules applied in creating these names. It should be noted that *USP–NF* has numerous examples of the nomenclature established before the expert committee was formed, and in some cases even before FDA established its processes for drug approvals. Details pertaining to some of these non-preferred terms are beyond the scope of the chapter, but are included in the Nomenclature Guidelines document that will be posted on the USP website.
- The delayed implementation schedule for changes of the official monograph titles has been removed from this chapter and will be included in the *General Notices*.

Nomenclature ⟨ 1121 ⟩ is consistent with the definitions in general information chapter *Pharmaceutical Dosage Forms* ⟨ 1151 ⟩. The general convention used in the naming of drug products is

[DRUG] [ROUTE OF ADMINISTRATION] [DOSAGE FORM]

There are exceptions based on historical naming conventions. For example, drug dosage form for an Injection is the physical form of the product in the container, usually a solution or a suspension. However, all injectable products are named as Injections with further specific rules that the route of administration “by injection” is further detailed by providing the injection site/tissue/organ in the labeling rather than in the name.

Implementation, Education, and Communication of the Monograph Naming Policy

The Monograph Naming Advisory Group (Advisory Group) was formed to engage representatives from FDA, healthcare practitioners, compounding organizations, and pharmaceutical manufacturers to assist USP in implementing the *Monograph Naming Policy for Salt Drug Substances in Drug Products and Compounded Preparations* (Monograph Naming Policy or policy). The focus of the Advisory Group's work is to determine the elements of the implementation of the policy, including communication and training to be addressed to ensure a thorough understanding of the Monograph Naming Policy, which becomes official May 1, 2013.

For many years, USP's Nomenclature Expert Committees followed the USP "Salt Nomenclature Policy" in establishing monograph titles for drug products. This policy directed that the specific salt form be included in the product title only if the strength of the article is expressed in terms of the salt and that the product name and strength should match. Although this approach led to inconsistency in naming, USP recommended, as early as 1978, that both the name (title) and the dose be expressed in terms of the active moiety. In 2007, on the basis of stakeholder and FDA input, USP revisited the Salt Nomenclature Policy. As a result, the Nomenclature Expert Committee strengthened its preference of the use of active moiety to express the strength of the product and changed the name of the policy to the *Monograph Naming Policy for Salt Drug Substances in Drug Products and Compounded Preparations*. The Expert Committee also decided to include the policy in *USP-NF* and to broaden understanding of the policy among all parties who may be affected by it, including the target audience. As with all proposed revisions to *USP-NF*, USP solicited comments on the revisions to *USP-NF* through the *PF* process.

The Nomenclature Expert Committee adopted the final policy in November 2007, which was then published in *USP-NF* in *USP 31-NF 26*, with a delayed official date of May 1, 2013. The policy also is posted on the USP website. This new policy has a delayed official date in order to allow USP time to inform stakeholders of the policy and provide manufacturers time to bring their products into conformance with the new policy. This policy is intended to promote consistent dosage form names beginning in 2013. Currently the policy is being applied in a go-forward manner. In the application of the policy, the Expert Committee can apply it retroactively and grant exceptions.

The Advisory Group focused on the implementation, education, and communications about the policy. The implementation and exceptions to the policy are posted in the Compendial Nomenclature section of the USP website. Education and communication efforts will be ongoing through May 2013, when the policy becomes official.

Nomenclature Guideline

The purpose of the Nomenclature Guideline is to provide supplemental information to the general approaches outlined in *Nomenclature* *USP-NF*. The Guideline will be posted on the

USP website. After general information about USP's drug naming activities, the Guideline provides an alphabetical listing of the types of drugs by type of dosage form. A general description of the dosage form is provided (which is derived from general information chapter *Pharmaceutical Dosage Forms* (1151)) followed by examples of drug names for the particular type of dosage form. The Guideline is first organized by chemical drugs, then biologics, then dietary supplements, and then excipients.

The document is designed for ease in revising and amending based on the comments received through USP's public comment process. The guideline will also provide a venue for presenting new and emerging nomenclature for dosage forms, products, formulations, and administration routes. Progress in development of "designer" excipients where properties are determined by degree of modification (including polymerization or degradation), additions, etc. will also be addressed in collaboration with the USP Excipient Expert Committee.

In the field of dietary supplements, USP has an important role in establishing nomenclature as a compromise of scientific definitions and names already widely used in the consumer market, including multi-national influences. Overlap of nomenclature between dietary supplements and prescription drugs, especially in modified-release dosage forms, will also be addressed.

It is anticipated that the Guideline will be posted in the Compendial Nomenclature section of the USP website in early 2012, shortly after the publication of this issue of *PF*.

Compendial Nomenclature Section of the USP Website

This new section of the USP website is to provide *USP-NF* users notice of naming decisions by the Nomenclature, Safety, and Labeling Expert Committee. Each month, the previous month's naming decisions will be posted so that users may see the naming decisions in a timely manner. The Nomenclature Guideline also will be posted in this location, as well as implementation information for the Monograph Naming Policy for Salt Drug Substances in Drug Products and Compounded Preparations.

CONCLUSION

USP's role in nomenclature is an important one, as outlined above. USP hopes that the broadening of information about these activities will help users better understand them and have access to information that has not been previously available.

REFERENCES

1. FDCA 501(b) and 502(e)(3)(b).
2. 21 CFR 299.5.
3. 21 CFR 299.4(c), (d), and (e).

4. USP. *USP Dictionary of USAN and International Drug Names*. 47th ed. Rockville, MD: USP; 2011:3.
5. 21 CFR 299.4(e).
6. USP. *Monograph Naming Policy for Salt Drug Substances in Drug Products and Compounded Preparations*. Available at: www.usp.org. Accessed 15 August 2010.
7. Bhattacharyya L, Cecil T, Dabbah R, et al. The value of USP public standards for therapeutic products. *Pharm Res*. 2004;21(10):1725–1731.

¹ The name of the Expert Committee has been changed over the years. Previous names have included Nomenclature Expert Committee and Nomenclature and Labeling Expert Committee. It is presently the Nomenclature, Safety, and Labeling Expert Committee. Members of the 2010–2015 Nomenclature, Safety, and Labeling Expert Committee can be found on USP's website.

² The dictionary is published under the title “*USP Dictionary of USAN and International Drug Names*”, and includes names approved outside the United States.