

Role and Applicability of USP General Chapters Related to Compounding and Safe Handling of Hazardous Drugs

Summary

In December 2019, USP's standards on compounding and the safe handling of hazardous drugs will become official standards in the *United States Pharmacopeia–National Formulary (USP–NF)*. USP's compounding standards, provided in *USP–NF* General Chapters <795> *Pharmaceutical Compounding—Nonsterile Preparations* and <797> *Pharmaceutical Compounding—Sterile Preparations*, are required for medicines that are compounded in non-sterile and sterile environments. The standard on the safe handling of hazardous drugs, General Chapter <800> *Hazardous Drugs—Handling in Healthcare Settings*, is cross-referenced in <795> and <797> and therefore is only required in the context of compounding of hazardous drugs. The states have oversight over and regulate the practice of pharmacy, including pharmacy compounding. The U.S. Food and Drug Administration (FDA) cooperates with state authorities to address pharmacy activities that may violate the Federal Food, Drug, and Cosmetic Act (FD&C Act).

While the standard articulated in <800> is only required in the context of compounding, it is a science-based standard that can be utilized in healthcare settings beyond compounding at the discretion of regulatory authorities and other oversight organizations with jurisdiction over these settings. Accordingly, state agencies (e.g., State Boards of Pharmacy), other regulators (e.g., Occupational Safety and Health Administration), and oversight organizations (e.g., The Joint Commission) may make their own determinations regarding the applicability and enforceability of <800> for entities within their jurisdiction.

U.S. Law and Recognition of USP Standards in Compounding

The Food and Drug Administration Modernization Act (FDAMA), enacted in 1997, recognized the practice of compounding. FDAMA amended the FD&C Act to include section 503A on pharmacy compounding. Section 503A stipulates, among other things, that a drug product is exempt from certain provisions of the FD&C Act if it is compounded using bulk drug substances and ingredients that comply with the standards of an applicable *USP–NF* monograph, if a monograph exists, as well as the USP chapter on pharmacy compounding.

In 2013, section 503A was amended by the Drug Quality and Security Act (DQSA) to remove provisions that had been held unconstitutional by the U.S. Supreme Court in 2002. It clarified FDA's authority over drug compounding and reaffirmed USP's role under section 503A of the FD&C Act. Following enactment of the DQSA, FDA provided clarification of its views on the application of USP standards to pharmacy compounding and specifically referenced USP General Chapters <795> and <797> in the [*Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act Guidance*](#). In addition to the requirements in section 503A, many states have specifically incorporated references to USP general chapters.

USP General Chapters and Compounding Standards

USP's public standards for compounding include general chapters, compounded preparation monographs, and monographs for bulk drug substances and other ingredients.¹ In 1998, after decades of developing compounded preparation monographs, USP published in the *USP–NF* its first general chapter on compounding, *Pharmacy Compounding Practices*. As a result of FDAMA, USP in 2000

¹ For additional information on USP's standards for compounding go to:
<https://www.usp.org/sites/default/files/usp/document/about/usp-quality-standards-for-compounding.pdf>.

revised General Chapter <1161>, renumbering it to <795>.² In 2004, after several reports of adverse events that led to patient harm and death, USP published <797>, a new general chapter.³ This chapter was developed based on existing standards and guidelines at the time.⁴ Revisions to these chapters were published for public comment in March 2018 and July 2018, and the newly revised chapters were published in June 2019.

USP Standards for the Handling and Compounding of Hazardous Drugs

Both current versions of <795> and <797> contain standards for compounding hazardous drugs. Based on public health need and potential exposure of approximately 8 million U.S. healthcare workers to hazardous drugs each year,⁵⁶ the Expert Committee determined that it was important to expand this information. As a result, the Committee began developing a general chapter specific to hazardous drugs. Chapter <800>, first published for public comment in 2014, was created by incorporating the principles of hazardous drug compounding established in <795> and <797>. The chapter was also built upon guidance documents published by the National Institute for Occupational Safety and Health (NIOSH), the American Society of Health-System Pharmacists (ASHP), and the Oncology Nursing Society (ONS). Chapter <800> describes the practice and quality standards for handling hazardous drugs in healthcare settings and helps promote patient and worker safety as well as environmental protection.

Alignment of USP General Chapters and Applicability of General Chapter <800>

All three chapters, namely <795>, <797>, and <800>, are intended to become official on December 1, 2019, to ensure alignment. Chapters <795> and <797> cross-reference chapter <800>; therefore, for hazardous drugs, compounding activities that were subject to the requirements of <795> and <797> are now required to comply with the compounding standards in <800>. For other activities not in the scope of <795> and <797>, the standards in <800> are not required under the *USP–NF*. Nonetheless, the standards in <800> are broadly relevant to hazardous drug handling activities across all facility types. Therefore, USP supports adoption of the standards provided in <800> across other healthcare settings as deemed appropriate by government agencies and oversight organizations with jurisdiction over these settings.

Additional Resources

For additional information on how General Chapter <800> applies and its compendial status, see:

- [Compendial Applicability Video](#)
- [<800> FAQs](#) (FAQ #8 and #9)
- [FAQs on Identifying Official Text](#) (FAQ #8)

² Chapter <795> was subsequently revised several times, with the last revision published on June 1, 2019.

³ In 1990, FDA issued an Alert Letter to practitioners warning them of “the seriousness of ... undertaking the batch production of drug products intended to be sterile.” The letter was issued as a result of two outbreak events: 24 patients (4 of whom died) were infected from contaminated cardioplegic solution compounded in Lincoln, NE, and two patients lost their eyesight from use of a contaminated indomethacin ophthalmic solution compounded in Pittsburg, PA.

⁴ At the time, USP had an informational General Chapter on sterile compounding, <1206> *Sterile Drug Products for Home Use*. ASHP had published *Guideline for Sterile Compounding* in 2000. General Chapter <797> was subsequently revised twice, with the last revision published on June 1, 2019.