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**trust**

# Proposed Resolution 9

## **Compounding**

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Resolution white paper developed  
by USP staff, with input from the  
Council of the Convention

# Proposed Resolution 9

## Compounding



USP will continue to collaborate with stakeholders on standards to help ensure the quality of compounded drug preparations. New and revised standards will be developed utilizing data, scientific evidence, and input from recognized healthcare professionals.

### Summary

USP defines the practice of compounding involves combining, admixing, diluting, pooling, or otherwise altering a drug product or drug substance to create therapies tailored to meet the unique or specific needs of individual patients. Compounding remains an important and necessary practice that provides specialized formulations for individual patients when commercially available medicines may not be appropriate. In the United States, compounding is regulated by federal and state laws and regulations. USP provides public standards to help ensure the quality of compounded drug preparations, including monographs for bulk drug

substances and other ingredients, monographs for compounded preparations, and general chapters to aid in the preparation of compounded medicines and the handling of hazardous drugs in healthcare settings. USP monographs and general chapters are part of the *U.S. Pharmacopeia–National Formulary (USP–NF)*. This Resolution proposes that USP will strengthen its collaboration with practitioners, academia, industry, and regulators to ensure that its standards for the quality of compounded preparations reflect best practices and current science while preserving patient access.

## Background

USP has a long history of setting standards for compounding, starting in 1820 with the first edition of the *United States Pharmacopeia*, which contained 217 formulas for making medicines. Today, compounding continues to play an important role by providing medications tailored to individual patients' needs. Millions of prescriptions are compounded by pharmacists, nurses, and doctors each year in the United States to meet the unique needs of patients. All stakeholders and personnel involved in compounding should have a clear understanding of the risks inherent in compounding. In addition, incorporation of established USP standards into everyday practice is essential for patient safety.

USP considers that compounding is accomplished by combining, admixing, diluting, pooling, or otherwise altering a drug product or bulk drug substance to create therapies tailored to the unique or specific needs of patients. Compounding plays a critical role in situations where the strength or dosage of a medicine needs to be customized. Another important function of compounding is reformulating a drug to exclude an unwanted, nonessential ingredient (e.g., lactose or a dye to which the patient is allergic). In still other cases, compounding is used to alter the physical form or route of administration of the medication for patients with certain limitations or disabilities, such as those who have difficulty swallowing oral medication.

USP sets standards for compounding that include general chapters, compounded preparation monographs, and monographs for components that may be used in compounded preparations (see box on page 3). General chapters include those such as <795> and <797> for nonsterile and sterile compounding, or <825> for compounding of radiopharmaceuticals. USP has more than 200 compounded preparation monographs that were developed based on the following criteria:<sup>1</sup>

- Medications with the highest public health impact (i.e., those that affect major population groups, disease states, and access needs)
- Medications essential for treating pediatric and geriatric patients where there are unmet needs
- Medications that need to be formulated to avoid allergic reactions and to be suitable for patients with specific genetic anomalies
- Medications for currently unmet clinical and therapeutic needs

## Quality Framework for Compounded Medicines

USP standards are recognized in various provisions of the Federal Food, Drug, and Cosmetic (FD&C) Act and in state laws, regulations, and policies. Specific to human drug compounding, USP standards are recognized in Section 503A of the FD&C Act, as added by the Food

# USP Standards for Compounding

## → Monographs for Bulk Drug Substances and Other Ingredients:

These provide standards for the identity, quality, purity, strength, packaging, and labeling of bulk substances and other ingredients that may be used in compounded preparations.

## → Compounded Preparation Monographs:

These contain formulations and quality standards for specific preparations. Compounded preparation monographs assist practitioners in compounding formulations for which there is no suitable commercially available product and provide standards to ensure the quality of these medicines.

## → General Chapters:

These serve as overviews and outline information, procedures, or analytical methods that apply across multiple products or settings (e.g., compounding). General chapters aid in the preparation of compounded medicines and the handling of hazardous drugs in healthcare settings.

and Drug Administration Modernization Act of 1997, which states that, among other things, to qualify for the exemptions under section 503A, a compounder using bulk drug substances must comply with the standards of an applicable *USP-NF* monograph, if a monograph exists, and the USP chapter(s) on pharmacy compounding.

In 2013, Congress enacted the Drug Quality and Security Act (DQSA) to clarify FDA's authority over human drug compounding and to reaffirm that USP standards for compounded medicines apply under Section 503A. Following enactment of the DQSA, FDA provided further clarification of its views on the application of USP standards to pharmacy compounding through an FDA Guidance: Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act.<sup>2,3</sup> This guidance states that compounded preparations made by a licensed pharmacist or physician can qualify for exemptions from new drug approval requirements, current good manufacturing practice requirements, and the requirement to label drug products with adequate directions for use, if, among other things, they are compounded in compliance with the USP chapters on pharmacy compounding and, if bulk drug substances are used, such substances and ingredients comply with the standards of an applicable *USP-NF* monograph, if one exists.

State pharmacy regulatory bodies generally are responsible for the day-to-day oversight of the practice of pharmacy. FDA may conduct oversight in certain instances. Almost all states have laws, regulations, or policies specific to compounding.<sup>4</sup>

Although it has no role in enforcement, USP is committed to continuing to work with stakeholders and state and federal regulators to encourage the use of public standards to help ensure the quality of compounded drug preparations.

### **USP Efforts to Ensure Quality in Compounding**

USP supports collaborative efforts to advance safe compounding. These efforts include discussions among stakeholders, including state and federal policymakers, to support quality compounding.

USP compounding standards describe widely acknowledged, scientifically based procedures and practices and facilitate consistency and quality in the

medicines prepared for patients. New and revised standards represent many years of deliberation and stakeholder engagement in the form of public comments and their review, roundtables, workshops, public face-to-face meetings, and open, public microphone sessions. USP actively seeks diverse input and participation from pharmacists, practitioners, representatives of healthcare organizations, academicians, industry, patients, federal and state regulators, and many others.

USP develops standards based on public health needs. Such needs can be identified by any stakeholder and are evaluated by the relevant Expert Committees who consider risks to patient safety and access in determining whether a quality standard is warranted. For example, through stakeholder engagement, USP has learned of the request for standards specific to veterinary practitioners, who treat a range of species and practice in varied settings and environments.<sup>5</sup> USP has also received public input requesting development of resources for assigning and extending beyond-use dates for compounded preparations.<sup>6</sup> Based on stakeholder input, USP experts expanded provisions in USP <795> and <797> to develop a public standard aimed at minimizing the potential risk of exposure to hazardous drugs. The result of these efforts is USP <800>, a general chapter that applies to hazardous drug handling during nonsterile and sterile compounding, and that contains principles that stakeholders may choose to apply across healthcare settings more generally.

With evolving work practices and new technologies, USP will consider public input on safe practices and monitoring tools to ensure safety. As a science-based, solution-oriented organization, USP is uniquely positioned to convene stakeholders and is committed to increase engagement with a diverse group of stakeholders to ensure the multifaceted issues relative to compounded drug preparation are well understood and addressed to the extent possible. Additionally, revised monographs and general chapters reflect advancements in science and clinical practice, rephrasing and reorganization to promote clarity, and input from the public.<sup>7</sup> In the next USP cycle, the relevant Expert Committees will evaluate all stakeholder input and determine whether standards, tools, and other resources may be able to address these public health needs. USP will continue to support the implementation of new or revised standards, using education programs, practical tools, and innovative solutions.

## Alignment with USP Mission

USP is working to ensure continued rigor in the development of quality standards for compounding while maintaining patient access to medicines. USP engages with stakeholders to advance compounding quality, promote patient safety, and respond to evolving public health needs. Key elements of USP's strategy support efforts to build awareness and encourage use of compounding quality standards. Through its education and training programs as well as domestic stakeholder engagement activities, USP can help strengthen practitioner awareness of appropriate circumstances and

settings for compounded drug preparations, including how to consistently follow procedures that promote patient safety.<sup>8</sup> Additionally, USP will monitor relevant advancements in science as well as patient safety issues related to compounding to inform the development and revision of standards.<sup>9</sup>

## Resource Assessment

*Refocus of resources currently in place.*

Significant staff efforts from across the USP organization are underway and will continue in this area.

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## References and Notes

<sup>1</sup> USP. Compounded Preparation Monographs (CPMs). Available from: <https://www.usp.org/compounding/compounded-preparation-monographs>.

<sup>2</sup> FDA. Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act Guidance. Available from: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pharmacy-compounding-human-drug-products-under-section-503a-federal-food-drug-and-cosmetic-act>.

<sup>3</sup> USP. Recognition of USP Compounding Standards. Available from: <https://www.usp.org/compounding/legal-considerations>.

<sup>4</sup> U.S. Government Accountability Office. Drug Compounding: FDA Has Taken Steps to Implement Compounding Law, but Some States and Stakeholders Reported Challenges; Report to Congressional Committees, GAO-17-64; 2016 Nov 17. Available from: <https://www.gao.gov/assets/690/681096.pdf>.

<sup>5</sup> Adapted from a Resolution proposal submitted by Dharati Szymanski, American Veterinary Medical Association.

<sup>6</sup> Adapted from Resolution proposals submitted by Ronna Hauser, National Community Pharmacists Association, and Michael Ganio, American Society of Health-System Pharmacists.

<sup>7</sup> Adapted from a Resolution proposal submitted by Mark Neuenschwander, THRIV Coalition for IV Accuracy.

<sup>8</sup> Pew Charitable Trusts. Best practices for state oversight of drug compounding. Washington, DC: 2016 Mar. Available from: [http://www.pewtrusts.org/-/media/assets/2016/02/best\\_practices\\_for\\_state\\_oversight\\_of\\_drug\\_compounding.pdf](http://www.pewtrusts.org/-/media/assets/2016/02/best_practices_for_state_oversight_of_drug_compounding.pdf).

<sup>9</sup> Kienle P, Federico F. Pharmacy impact on quality and outcomes: new era for measuring value. Paper presented at 15th Annual ASHP Conference for Leaders in Health-System Pharmacy; Chicago, IL: 2010 Oct 17–18.