



Preface to the Sixth Edition

Much has happened at both the state and national levels in pharmacy compounding since the fifth edition was published. The Preface to this sixth edition covers several different topics of current interest directly affecting the future of compounding and patient access to individualized compounded medications.

Regulation and Standards

Many years ago, certain items of clothing came out labeled with the slogan “One Size Fits All.” Well . . . they didn’t and they still don’t! Specifically, we are addressing the “one size fits all” approach of *United States Pharmacopeia (USP)* Chapters <795>, <797>, and <800>. Much of the content in these chapters is unreasonable for certain pharmacies to achieve, and the result is that some pharmacies are discontinuing compounding, thus limiting the availability of important medications to patients.

We have different “levels,” or “categories,” in many aspects of our society: different types of automobile drivers licenses and pilots licenses, different speed limits for different areas, even different glues or adhesives for different purposes. We are accustomed to a tiered approach (e.g., credit card limits), different requirements to be licensed or registered (e.g., general and specialty practice physicians, general and specialty practice nurses), different categories of the same basic item (e.g., computers, washing machines, cars), and even television viewing alternatives (e.g., antenna, cable, streaming services). Businesses comply with applicable standards and adjust their equipment and inventory to accommodate the different amount of activity they have and/or expect.

If one looks at the details in the *USP* chapters, they do not allow for different “levels” of compounding, that is, the compounder who does only 5 per day, 10 per day, or 500 per day; everyone is treated the same, and this is irrational and inappropriate. A compounder doing 1–5 compounds per day does not have the same risk exposure as one doing 100 or more compounded prescriptions per day. Also, there are many factors involved, including the types of formulations, drug sources, and so on. The way things are going now, only pharmacies in larger cities will be able to meet the standards. Larger hospital pharmacies may not have an issue because they can increase their budget to address the issues, but this is not reasonable or practical for many smaller or even many mid-size hospitals because a number of them are closing.

There is no question that each facility size needs standards, but they do not have to be the same because the risk exposures are different. In fact, if one looks at the different sections

of *USP* Chapters <795>, <797>, and <800>, standards can be easily modified to accommodate different levels/volumes of compounding for nonsterile, sterile, and hazardous drugs.

The United States Pharmacopeial Convention (*USP*) standards are supposedly “science based”; however, these three chapters do not meet that criterion because many of the aspects of the chapters are strictly “opinion and idealistic standards” that are not science or risk based. This is especially evident in the sections on beyond-use dating, and in fact, two different appeals on *USP* <795> and <797> have been filed with *USP* by groups of compounders challenging the standards. The first-level appeal was rejected by *USP* and the second-level, more serious, appeal is still under consideration.

The primary route for relief is for individual state boards of pharmacy to prepare their own standards for compounding nonsterile and sterile drugs and for handling hazardous drugs, as many have already done. Also, because pharmacies are all subject to National Institute for Occupational Safety and Health, Occupational Safety and Health Administration, and Environmental Protection Agency, there appears to be no need for *USP* Chapter <800>. State boards of pharmacy have an awesome responsibility to protect the public in various aspects of pharmaceuticals availability, distribution, and utilization. An important aspect of this responsibility is to aid in providing patient access to needed compounded medications; this can be assisted by state boards of pharmacy developing/modifying and implementing their own standards for nonsterile and sterile compounding and handling hazardous drugs.

One size does not fit all, and there must be appropriate categories or levels with reasonable standards so that all pharmacies can be compliant.

Patient Satisfaction with Compounded Medications

An interesting study, “Patient Experiences with Compounded Medications,”¹ stated the following conclusion:

Respondents used compounded prescriptions for hormone replacement therapy, pain treatment and a variety of medical conditions. Compounded prescriptions were used primarily to replace other medications due to treatment failure or intolerable side effects. Respondents were satisfied with all aspects of compounded prescription therapy with the exception of out-of-pocket cost. The prescriber’s recommendation was the single most important factor in a patient choosing to use compounded prescriptions and in choosing a compounding pharmacy.

Compounded preparations contribute to patient well-being, health, and ability to function and lead productive lives, and they even save lives. There is no question that pharmaceutical compounding is a vital service performed by pharmacists.

U.S. Food and Drug Administration Implementation of the Drug Quality and Security Act

U.S. Food and Drug Administration (FDA) continues to overextend its authority into compounding, resulting in pushback by some pharmacy organizations. The following issues were discussed at an FDA Drug Quality and Security Act (DQSA, H.R. 3204) Implementation Subcommittee Hearing in January 2018:

1. State board of pharmacy oversight of pharmacy compounding is appropriate and critical.

2. Office-use compounding is important for proper patient care in doctor's offices.
3. Outsourcing facilities are limited in what they can provide in office-use medications.
4. In the memorandum of understanding, "distribute" and "dispense" are two different activities, but FDA considers them the same when they are not the same.
5. Section 503A pharmacies should not be inspected using Current Good Manufacturing Practice standards that are intended for pharmaceutical manufacturing facilities.
6. Changes in the FDA Pharmacy Compounding Advisory Committee composition and activities should be made to be more representative of pharmaceutical compounding.
7. Compounding with "dietary supplements" should be allowed.
8. FDA has caused concern by using guidance for industry documents to implement and enforce DQSA instead of using notice-and-comment rulemaking pursuant to the Administrative Procedure Act (5 U.S.C. §§ 551–559).

FDA continues to overextend their authority in the implementation of the DQSA despite pushback from pharmacy organizations.

Drug Waste and Expired Drugs

Disposal of expired and partially used chemicals and drug products is a constant problem. This is partially due to products in the market at one dose and price, and patients are not "one size fits all." Alternatives include requiring manufacturers to provide drugs in a reasonable set of size options, selecting appropriate vial sizes for each individual patient, or requiring the manufacturer to refund the cost of any leftover drug. Proposed resolutions that have also been discussed include dose rounding, drug vial optimization, dose capping, using overfill to reduce waste, patient scheduling, creating a virtual marketplace for excess drug, and inventory management. There are a number of changes in the federal regulations for the management of hazardous waste pharmaceuticals, and these are incorporated into Chapter 3 of this edition.

State Boards of Pharmacy

State boards of pharmacy have the authority to establish their own pharmacy professional practice regulations for pharmacy, and the adoption of professional practice standards contained in *USP* Chapters <795>, <797>, <800>, and so forth, is optional. It appears that many of the state boards of pharmacy are writing their own or rewriting the *USP* practice standards for their individual states, while some adopt them by reference.

Education of Pharmacy Students

Pharmacy students' interest in compounding continues to grow. With some published articles related to pharmacy education and student interest, some colleges of pharmacy are implementing and upgrading their compounding courses and laboratories. This is a positive sign.

Clinical Pharmaceuticals Applications in Pharmaceutical Compounding

Clinical pharmaceuticals is becoming more prevalent in compounding and is used to solve many chemical, physical, and clinical problems in medication therapy. Clinical pharmaceuticals involves the application of this unique knowledge base in pharmaceutical sciences

to clinical situations in order to solve some clinical problems. Clinical pharmaceuticals also incorporates the issues of compatibility and incompatibility.

The COVID-19 Pandemic of 2020

Pharmacists involvement in the COVID-19 epidemic of 2020 is described, including compounding (1) oral liquids for children and the elderly, (2) antiviral injections, (3) IV admixtures, (4) hand and surface sanitizers, (5) testing, and (6) routine provision of pharmaceuticals related to patient care. The efforts of the FDA in working with compounders with more flexibility and addressing drug shortages by compounding is discussed, along with some presented formulations.

New in This Edition

There are general updates in all chapters with current information and current laws and regulations, with significant additions to Chapter 25 (parenterals). Chapter 19, on emulsions, has been expanded and now also includes microemulsions along with example formulas. Also, three new chapters were developed and added, including:

- Chapter 34, Three-Dimensional Printing and Compounding
- Chapter 35, Self-Emulsifying Lipids and Hot Melt Extrusion Formulations
- Chapter 36, Clinical Pharmaceuticals and Pharmaceutical Compounding (includes drug incompatibilities [nonsterile and sterile])

Looking at the Future

Compounding pharmacy has made great strides both in quality and in utilization of new technology to meet patients' individualized needs. In the future, we will undoubtedly see requirements for more documentation and verification of compounding processes, as well as enhanced regulations for compounding personnel safety as well as patient safety. This is a normal part of the growth of a needed and valued profession, and one that will be embraced.

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References

1. McPherson T, Fontane P, Bilger R. Patient experiences with compounded medications. *J Am Pharm Assoc.* 2019;59(5):670–7. <https://doi.org/10.1016/j.japh.2019.05.005>.