



How USP Standards Are Regulated

Rich Bucher RPh, JD
Scott Milner PharmD, MBA

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801-823-0923

contact@terluminarx.com

3290 Mayflower Ave Ste 100
Lehi, UT 84043

Vital Role of USP in Pharmacy

In recent discussions with industry experts, the importance of compliance with the United States Pharmacopeia (USP) chapters has been a recurring theme. Often regarded as mere “recommendations” or guidelines for best practices, in reality these chapters actually serve as expectations of what is required .



The Evolution of Pharmacy Compliance

As we delved deeper into compliance, we recognized the disparities in how different states and regulatory bodies experience and approach pharmacy oversight. For example, notably states like Florida, Texas, and California have especially unique scrutiny levels. Florida experiences what appears to be a higher frequency of FDA audits than other states. Also, it is important to note that hospitals or health systems are not exempt from these surveys. These nuances underscore the importance of being well-versed in the specific regulations that apply to your practice location.

Our goal is to equip readers with the knowledge needed to navigate the USP regulatory landscape effectively.

Who Enforces USP?

Over the years as a pharmacist, pharmacy law teacher and consultant, Rich Bucher often noted confusion about USP. Sure, at a high level, we all know that USP Chapters <795>, <797>, and <800> provide essential standards and guidelines that we must follow when compounding or handling hazardous drugs. How are these standards enforced? Who enforces them? The short answer is that federal, and state agencies and independent third-party accrediting bodies, like The Joint Commission, rely on USP standards for guidance on what standards are applicable. However, as health providers, we must understand more.

USP Standards Overview

The USP is a scientific, non-governmental organization that sets quality standards for medicines, food ingredients, and dietary supplements. In the

context of hospital settings, three primary USP chapters are particularly relevant and regulated: USP 795, USP 797, and USP 800.

- **USP 795:** Provides standards for non-sterile compounding, which involves the preparation of medications in a form that does not require sterility but does include proper cleaning. It covers aspects such as the quality of ingredients, compounding processes, documentation, and facility requirements.
- **USP 797:** Focuses on sterile compounding, which involves the preparation of medications that must be free from microbial contamination. It outlines stringent requirements for cleanroom environments, personnel training, and quality assurance processes to ensure that compounded sterile preparations (CSPs) are safe for patient use.
- **USP 800:** Addresses the safe handling of hazardous drugs (HDs) to minimize the risk of exposure to healthcare personnel, patients, and the environment. It includes guidelines on facility design, engineering controls, personal protective equipment (PPE), and work practices. This chapter retains the content required to maintain sterility from USP 797.

Federal Laws/Rules

It is important to understand that both state and federal agencies oversee pharmacies and pharmacy practice. The Supremacy and Commerce Clauses, along with the Doctrine of Preemption, serve as the basis for the federal government's oversight. With respect to compounded human drugs in particular, the Federal Food Drug, and Cosmetic Act (FDCA) and its enforcement by the FDA plays the primary oversight role.

How Does USP Fit In?

Understanding how USP chapters fit into the FDCA and the FDA's enforcement of compounding is helpful. Both the USP and the FDA have clarified that they work closely together. The FDA has multiple delegates in the USP's top leadership body (the USP Convention). USP staff maintain regular contact with FDA leadership in quarterly meetings, and FDA staff serve as liaisons on USP expert committees, meetings, expert panels, and stakeholder forums. Therefore, it is not surprising that the FDCA specifically references USP standards that the FDA relies upon for its inspections and investigations. Examples include USP references in Sections 501(b) (adulterated drugs), 503A (pharmacy compounding), and 503B (outsourcing facility).

FDA Enforcement

FDCA Sections 503A, 503B, and 501 provide the most important regulations and standards that impact FDA oversight of drug preparation and compounding. For example, the FDA might inspect a pharmacy that considers itself a compounding pharmacy under Section 503A and determine that it fails to meet the specific USP <797> standards referenced under this section.

Alternatively, the FDA might decide that the compounding pharmacy fails to meet the traditional compounding criteria in 503A and is thus subject to the much more rigorous current good manufacturing practices (cGMP)s of 503B.

As another example, the FDA might inspect a pharmacy relying on the USP <797> immediate-use provisions but determine that it produces adulterated, contaminated, or injurious products under Section 501(a). Alternatively, it might decide that the pharmacy is improperly relying on the immediate-use provision and determine that it is subject to complete USP standards under 503B and applicable cGMP criteria.



Introduction: Accreditation

Accreditation bodies such as The Joint Commission (JCO) and the Accreditation Commission for Health Care (ACHC) are tasked with evaluating hospitals' compliance with CMS standards, which includes adherence to USP requirements. These organizations conduct thorough surveys to assess whether hospitals meet the requirements, focusing on critical areas such as sterile compounding, handling hazardous drugs, and environmental controls. The surveys conducted by JCO and ACHC are pivotal in ensuring that hospitals maintain high standards of care and continuously improve their practices.

Joint Commission (JCO) Survey Process

Introduction to JCO

The JCO is an independent, non-profit organization that accredits and certifies healthcare organizations and programs in the United States. JCO's mission is to continuously improve healthcare for the public by evaluating healthcare organizations and inspiring them to excel in providing safe and effective care. Accreditation by JCO is recognized nationwide as a symbol of quality that reflects an organization's commitment to meeting specific performance standards.



Survey Preparation

Hospitals must be well-prepared for a JCO survey, which typically involves several months of preparation. This preparation includes conducting internal audits, maintaining, and training staff on the latest USP standards, and ensuring that all documentation is up-to-date and readily accessible. Hospitals often form committees or task forces to oversee the preparation process and address any areas of concern before the survey begins. Pharmacy usually participates in these preparations, in conjunction with hospital or health system quality leadership. I have observed the evolution of engagement with JCO surveyors that started superficially in my early years, with increasing time spent interviewing those involved in sterile compounding.

Survey Process

The JCO survey process is thorough and multifaceted, designed to assess every aspect of a hospital's operations about USP standards.

1. **Initial Assessment:** The survey begins with an initial assessment, where JCO evaluators review the hospital's policies, procedures, and previous compliance records. This assessment helps JCO determine the areas that will require the most focus during the on-site survey.
2. **On-Site Survey:** During the on-site survey, JCO surveyors visit the hospital to conduct a comprehensive evaluation. This process includes interviews with staff, facility tours, and an in-depth review of documentation. Surveyors pay close attention to how the hospital handles compounding, especially sterile compounding, to ensure compliance with USP 797 and USP 800 standards.

3. **Key Areas of Focus:** JCO surveyors focus on several key areas during their evaluation:

- **Compounding Practices:** The surveyors assess whether the hospital's compounding practices align with USP standards. This includes evaluating the cleanroom environment, staff competency, and quality assurance protocols. Having the correct documentation promptly becomes essential. Documentation includes required competencies of all team members involved in compounding practices.
- **Hazardous Drug Handling:** Compliance with USP 800 is critical for patients AND employees, and JCO surveyors review how the hospital handles hazardous drugs, from receiving and storing to compounding and administering. Proper PPE for the protections of patients AND employees are evaluated.
- **Environmental Controls:** The environmental controls within compounding areas are scrutinized to ensure that they meet the necessary standards for air quality, pressure differentials, and temperature control.

4. **Tracer Methodology:** One of the unique aspects of the JCO survey is the use of tracer methodology. This approach involves following the care process for specific patients from the point of entry to the hospital through to discharge. Pharmacy team members can be pulled into any review of standards and be asked to describe how pharmacy contributes to positive patient outcomes.

Surveyors may review USP standards from questions arising from a patient tracer, or direct review of how policies and procedures align with observed practices and interviewing staff.

Survey Outcome

At the conclusion of the survey, JCO provides the hospital with a detailed report outlining their findings. This report includes any citations for non-compliance, recommendations for improvement, and, if necessary, a timeline for addressing deficiencies. Hospitals are required to submit a plan of correction to JCO, detailing how they will resolve any issues identified during the survey. JCO may also conduct follow-up surveys to ensure that corrective actions have been implemented effectively.

In our time working around these surveys, JCO surveyors have increased their awareness of the USP standards, including increasing the amount of time spent in the pharmacy overall. There may still be a “surveyor roulette” related to the depth of experience in pharmacy-related topics, but the integration of USP standards continues to expand.

If you have only worked in hospital systems, you may not be familiar with the next group below who have an increased focus on home health, hospice, and ambulatory programs. As health systems have increased ambulatory offerings JCO has also expanded their “conditions of participation” to include more content geared towards specialty pharmacies, and home infusion elements being published in July 2019.

ACHC Survey Process

Introduction to ACHC

The Accreditation Commission for Health Care (ACHC) is a non-profit organization that provides accreditation services to a variety of healthcare providers, including hospitals. In my experience, ACHC has not been as common with hospital accreditation in the western states I have practiced in and an increased focus on home health, hospice and other ambulatory programs that benefit from accreditation. ACHC’s mission is to promote excellence in patient care and operational efficiency through a collaborative and consultative approach to accreditation. ACHC accreditation is recognized as a mark of quality and commitment to compliance with industry standards, including those set by USP. In fact, in my background with ACHC surveyors in the home infusion setting, I quickly found their surveys (all before the 2019 and 2023 updated standards) were far more detailed in content and review of our pharmacy practices.

Survey Preparation

Preparation for an ACHC survey is similar to that for a JCO survey, with hospitals conducting internal reviews, training staff, and ensuring that their policies and procedures are aligned with USP standards. ACHC offers resources and support to hospitals during the preparation phase, helping them understand the accreditation process and the specific requirements they will be evaluated against.

Survey Process

The ACHC survey process is designed to be thorough yet collaborative, with a focus on helping hospitals improve their compliance and patient care practices.

1. **Pre-Survey Preparation:** ACHC's approach to surveying is highly customized, taking into account the specific needs and challenges of the hospital/home infusion teams. Before the on-site survey, ACHC surveyors work with the hospital to understand its unique circumstances and to identify areas where the survey will focus.
2. **On-Site Survey:** During the on-site survey, ACHC surveyors conduct a comprehensive evaluation of the hospital's facilities, processes, and documentation. This includes interviews with staff, facility tours, and a detailed review of how the hospital complies with USP standards. ACHC places a strong emphasis on collaboration, often working with hospital staff to identify practical solutions to compliance challenges.
3. **Key Areas of Focus:** Similar to JCO, ACHC surveyors focus on key areas related to USP compliance:
 - **Compounding Practices:** ACHC evaluates the hospital's compounding practices, ensuring that they meet the standards outlined in USP 795, USP 797, and USP 800. Surveyors assess the physical environment, staff competencies, and quality assurance measures.
 - **Hazardous Drug Handling:** Compliance with USP 800 is a significant focus, with ACHC surveyors reviewing how the pharmacy/hospital manages hazardous drugs throughout the movement from entering the facility, compounding, transportation/storage, administration and disposal of waste.
 - **Risk Assessment:** ACHC places a particular emphasis on risk management, encouraging hospitals to proactively identify and mitigate risks associated with compounding and handling hazardous drugs.

Survey Outcome

ACHC's survey process culminates in a comprehensive report that outlines the findings of the on-site evaluation. This report includes any areas of non-compliance, along with recommendations for improvement. ACHC adopts a consultative approach, often working with hospitals to develop practical strategies for addressing deficiencies. Accredited facilities are required to

submit a plan of correction, and ACHC may conduct follow-up surveys to ensure that improvements have been made.

Comparative Analysis: JCO vs. ACHC Surveys

Both JCO and ACHC are respected accreditation bodies that survey hospitals against USP standards, but they approach the process in slightly different ways. While JCO's survey process is rigorous and focuses heavily on compliance through the use of tracer methodology, ACHC's approach is more collaborative, with a strong emphasis on risk management and continuous improvement. We want to emphasize their approaches may feel similar from afar, but it is clear that compounding standards are increasingly gathering attention during the surveys we have participated in. Despite these differences, both organizations share the common goal of ensuring that hospitals adhere to USP standards to protect patient safety and improve care quality.

Strategies for Success

To overcome these challenges, hospitals can adopt several strategies:

- **Best Practices for Compliance:** Hospitals should implement best practices in compounding, hazardous drug handling, and environmental controls. This includes regular staff training, routine internal audits, and the use of advanced technologies to track, monitor, and maintain compliance. As updates are issued, work to address them early to avoid being caught trying to implement after your survey window hits. There may be grace from a surveyor, but dragging your feet will not be a survivable strategy.
- **Staff Training and Education:** Ongoing training and education are critical to ensuring that staff are knowledgeable about USP standards and competent in their application. Pharmacy teams are finding traditional hospital education platforms difficult to update, and bringing them in-house to a pharmacy-managed platform is becoming more common.
- **Continuous Quality Improvement:** Hospitals should adopt a culture of continuous quality improvement, regularly reviewing and refining their processes to enhance compliance and patient safety. It is essential to have the right checklists in place to ensure risk is minimized, but also cloud-based solutions that provide redundant methods for reporting allowing deeper and more meaningful improvements to be implemented. Find a platform that can be adjusted with your improvement timelines.

Understanding State Licensing for Pharmacies That Compound in Relation to USP Guidelines

In addition to the FDA and accrediting bodies, the state board of pharmacies are tasked with ensuring the practice of pharmacy protects patients. These surveyors are also becoming more expert in the chapters and their content, and spending more time reviewing policies and procedures, but also interviewing team members involved in the work.

While I have worked in hospital areas most of my career, compounding pharmacies play a crucial role in the healthcare system by providing customized medications tailored to individual patient needs. However, the enforcement and interpretation of these guidelines can vary significantly from state to state, influenced by state laws and regulations. Those not licensed to require historic FDA inspections can still find themselves seeing FDA surveyors walk in the door and have reason to stay until they are satisfied with the results. This can be confirmed in the 483's publicly available where the FDA acknowledges they may not be a 503b facility, but the compounding practices can be subject to FDA scrutiny

The Differences of State Enforcement of USP Guidelines in Compounding Pharmacies

With the rise of compounding pharmacies blatantly advertising for GLP-1 “me-too” compounded medications across our country, its also important to note there may be increased scrutiny of these pharmacies even if they have very proper compounding methods hard coded in their business model. I will not address any of those here.



Florida: A Flexible Approach with Strong Oversight

Regulatory Environment. Florida is known for its supportive yet carefully regulated environment for compounding pharmacies. The state's Board of Pharmacy has adopted USP <795> and <797> as the minimum standards for

compounding but allows some flexibility in how pharmacies implement these guidelines. This flexibility is evident in the state's allowance for office-use compounding, where pharmacies can prepare medications in advance for use by healthcare providers in their offices without a patient-specific prescription.

Office-Use Compounding. Florida's regulations permit compounding pharmacies to prepare and distribute medications to healthcare providers for office use, a practice that is prohibited in some other states like California. This regulation enables Florida pharmacies to serve a broader range of clients, including doctors and clinics, thereby increasing their market reach and service offerings.

Inspection and Compliance. Florida's Board of Pharmacy conducts regular inspections of compounding pharmacies, with a focus on compliance with USP standards, including <795>, <797>, and <800>. While the state provides a supportive environment for pharmacies, it also maintains rigorous oversight to ensure patient safety. Inspections typically evaluate adherence to these standards, including facility cleanliness, personnel training, and documentation practices.

Impact on Pharmacy Operations. The relatively flexible regulatory environment in Florida allows compounding pharmacies to innovate and expand their services. However, the state's inspection process ensures that this flexibility does not come at the expense of patient safety. Pharmacies in Florida must strike a balance between leveraging regulatory flexibility and maintaining strict adherence to USP guidelines.

Texas: A Supportive Yet Stringent Regulatory Framework

Regulatory Environment. Texas also offers a supportive environment for compounding pharmacies but with a more stringent regulatory framework compared to Florida. The Texas State Board of Pharmacy strictly enforces USP <795>, <797>, and <800> guidelines, with additional state-specific requirements that enhance patient safety.

Office-Use Compounding. Similar to Florida, Texas allows compounding for office use, but with stricter guidelines regarding labeling, distribution, and documentation. Texas pharmacies must ensure that all compounded medications meet the state's safety standards, which are often more stringent than the minimum requirements set by the USP.

Oversight and Compliance: Texas has a strong oversight mechanism, with frequent inspections by the state Board of Pharmacy. These inspections focus on compliance with USP <795>, <797>, and <800>, ***as well as state-specific regulations*** that govern compounding practices. Texas requires pharmacies to have robust policies and procedures in place to ensure that all aspects of compounding meet regulatory standards.

Pharmacy Technician Support: Texas law permits certified pharmacy technicians to have a greater role in the compounding process under the supervision of a licensed pharmacist. This support structure allows pharmacies to manage their workload more effectively, ensuring that they can meet demand while maintaining compliance with USP guidelines.

Impact on Pharmacy Operations: The stringent regulatory framework in Texas ensures high standards of safety and quality in compounding pharmacies. While the state allows for office-use compounding, the additional regulatory requirements and oversight make it imperative for pharmacies to maintain meticulous records and procedures. This environment supports the growth of compounding pharmacies while ensuring that patient safety remains the top priority.

California: Stringent Regulations and Rigorous Enforcement

Regulatory Environment: California is known for having one of the most stringent regulatory environments for compounding pharmacies in the United States. The California State Board of Pharmacy has adopted USP <795>, <797>, and <800> as foundational guidelines but has implemented additional state-specific regulations that often exceed federal requirements.

I have seen a handful of 503B pharmacies come and go, and typically the instability follows when the California BOP issues concerns in the business or compounding practices.

Prohibition on Office-Use Compounding: Unlike Florida and Texas, California does not allow traditional compounding pharmacies to prepare medications for office use. All compounded medications must be patient-specific, which limits the flexibility of compounding pharmacies in the state. This prohibition reflects California's emphasis on patient safety and its concern about the potential risks associated with non-patient-specific compounding.

Inspection and Compliance: California conducts frequent and rigorous inspections of compounding pharmacies, focusing on adherence to both USP guidelines and state-specific regulations. The state is known for its strict enforcement of compounding laws, with significant penalties for non-compliance. Inspections in California are comprehensive, including detailed assessments of facility conditions, personnel training, and compounding processes.

USP <800> Compliance: California's adherence to USP <800> is particularly stringent, with rigorous requirements for handling hazardous drugs. This includes strict protocols for the use of personal protective equipment, facility design, and environmental controls. California pharmacies must demonstrate full compliance with these standards during inspections.

Continuing Education Requirements: California mandates additional continuing education for pharmacists involved in compounding. This includes a mandatory one-hour compounding credit as part of the overall continuing education requirements for pharmacists. This requirement ensures that pharmacists stay updated on the latest compounding practices and regulatory changes, further enhancing patient safety.

Impact on Pharmacy Operations: The stringent regulatory environment in California creates a challenging landscape for compounding pharmacies. The prohibition on office-use compounding limits the range of services that pharmacies can offer, potentially reducing their market reach. Additionally, the rigorous inspection and enforcement regime requires pharmacies to maintain exceptionally high standards of practice. While these regulations may pose operational challenges, they also ensure that compounded medications in California meet the highest safety standards.

Other State Examples

We want to be clear there are other state board of pharmacy that have extra requirements that pharmacy leaders have to be aware in managing their compliance. Oregon has a self-inspection expectation that is completed each year. In talking with leaders in Oregon, this requires a lot of preparation and

review, and can cause some heartburn as they are required to complete it and sign off annually.

The requirement for the *Annual Self-Inspection* is found in the Oregon Administrative Rules (OAR), specifically under the rules governing the Oregon Board of Pharmacy. These forms are required to be kept for 3 years (as of the writing of this article, it may be updated).

Idaho is an example of a less restrictive approach. Idaho pharmacy rules and regulations don't have a long list of extra requirements, rather they point to the USP requirements as they are updated in the chapters. In alignment with USP 795 for non-sterile preparations, USP 797 for sterile preparations, and other relevant chapters of the USP-NF, pharmacies must establish comprehensive policies and procedures. These policies must address critical aspects of compounding, including appropriate packaging, handling, and storage; accuracy in calculations and measurements; verification of ingredient identity and quality; accurate labeling; and establishing beyond-use dating. Additionally, pharmacies are required to implement auditing processes for deficiencies, maintain environmental quality control, and adhere to safe limits for strength, pH, bacterial endotoxins, and particulate matter.

While your pharmacy practice may be compliant today with current standards by those who routinely survey your operations, but it is clear the development of these standards require engagement to ensure proper compliance.

Conclusion

The USP standards for sterile compounding compliance require diligence in crafting policies and procedures that include detailing staff expectations for ordering, receiving, compounding, and even disposal. Cleanroom requirements of how to maintain sterility, requirements of the environment, beyond use dates (BUD) that correlate to the compounding environments can be called into question by surveyors from the federal, state and accrediting agencies. The most effective way to make sure all elements are covered is by implementing checklists that follow the outlined expectations. Performing the documentation of these tasks can be made simple with an electronic solution. This enables real time understanding of how you and your team is doing, and prevents unnecessary heartburn when surveys occur.

We would like to work with you in your compliance journey!

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