UNIVERSITY OF WISCONSIN-MADISON SCHOOL OF PHARMACY STUDENT WRITING CLUB:

# The Importance of USP <797>: Teaching Proper Aseptic Technique and Implementation of Standard Operating Procedures

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Compounded medications—medications that are combined, mixed, or have altered ingredients to tailor the medication to the needs of an individual patient—are estimated to make up 1% to 3% of all prescriptions, despite a lack of tracking of their exact volume.[1,2] Although compounded medications are a small portion of the overall number of dispensed prescriptions, the impact of an error in compounding one of these medications can result in dramatic consequences. In 2012, contaminated preparations of a preservative-free methylprednisolone acetate injection prepared in a compounding pharmacy caused a meningitis outbreak in 20 states.[3] Fourteen thousand people were exposed to the contaminated injections, resulting in 751 cases of fungal meningitis, other infections, and strokes, and 64 deaths, making this one of the largest healthcare-related outbreaks in the United States. In fact, over the past 40 years, there have been a significant number of cases of contaminated compounded products that have caused various adverse events, including infections, blindness, and deaths.[4] Great advances have been made since the development of compounding guidelines, and survey data from 2007 reveal that 96% of pharmacy schools provided some didactic and laboratory instruction about sterile compounding.[5] However, variation in the depth of this education among schools of pharmacy and space for interpretation within the guidelines poses a risk for compounding errors. In this article, we aim to emphasize the importance of the aseptic technique and explore its strengths and weaknesses, to highlight the importance of sterile-compounding education in both pharmacies and pharmacy schools.

## USP <797>

The United States Pharmacopeia (USP) is an independent, nonprofit organization whose founding purpose was to devise standards for the quality and safety of medicines to protect the health of the public.[6] That mission is still the driving force for USP today. For sterile compounded preparations (CSPs), USP <797> is the governing chapter. One important element of this document is its thorough breakdown of several sections, especially CSP microbial contamination risk levels, which provides an in-depth assessment and examples of corresponding aseptic manipulations.[7] Another notable feature is its mention of rigorous testing methods for ensuring compounders are performing aseptic technique adequately. For example, USP <797> mentions using media fill tests as the method for evaluating the quality of aseptic manipulation skills of personnel, and requires that the test is performed under the most challenging or stressful conditions by the personnel being evaluated.[7] Additionally, a recent revision to USP <797> in 2018 included biannual testing of sterile techniques, as opposed to only annual testing, using the media-fill tests in addition to yearly testing of core competencies through either written exam, observed demonstration, or both.

However, an ostensible gap in USP <797> is its level of ambiguity, where it explains what must be done for proper aseptic technique but not how it must be done, which means it is up to the best judgment, interpretation, and training experience of compounders. Furthermore, other areas of ambiguity rely on the instruction of more experienced personnel rather than thoroughly written out techniques. For example, USP <797> mentions under its "Responsibility of Compounding Personnel" heading that all CSPs are to be prepared sterilely and with minimal introduction of particulate matter, and refers to both compounders and compounding supervisors as the parties responsible for ensuring this goal is met.[7] However, despite the extensive duties of the compounding personnel, compounders must rely on direct measurement and judgment of the compounding supervisor, or unspecified appropriate information sources as a means to fulfilling these requirements. This further raises the question of how aseptic technique is facilitated by personnel beyond the compounder.

Aseptic technique is a practice used by healthcare professionals where its purpose is to prevent the contamination of sterile compounded medications with microbial pathogens, bacterial endotoxins, and unintended chemical and physical contaminants.[7] The set of rules governing aseptic technique minimize the risk of causing infection; bodily harm via chemical contaminants or physical particles; or death to patients being administered compounded sterile preparations, surgical operations using sterile equipment, or exposure to medical tools designed to enter the body.[7,8] Healthcare professions who apply aseptic technique include pharmacists, pharmacy technicians, physicians, nurses, and a multitude of others whose position is to handle sterile medications or equipment.

In pharmacy practice, aseptic technique is important for producing sterilely compounded medications. However, when it comes to the oversight of these products, what responsibilities does the pharmacist

take? Patricia C. Keinle, a pharmacist and leading medication safety expert at Cardinal Health, argued in 2020 that the role of the pharmacist in sterile compounding is patient safety and being aware of risks associated with compromised sterile preparations.[9] Pharmacists can work with other pharmacy personnel to help see that sterile preparations are being compounded using the safest and most effective techniques and processes.

Proper aseptic technique leads to fewer incidences of contamination, as indicated by Austin and Elia in their 2013 study that compared a pharmacy operator with more training in aseptic technique to nurses who have less instruction in this area.[10] When tasked with preparing parenteral intravenous dose syringes, the pharmacy operator outperformed the nurses by making more syringes, faster, and with much less contamination. This emphasized the importance of using proper aseptic technique when preparing intravenous doses, because doing so leads to fewer occurrences of contamination. In 2002, van Grafhorst et al. further represented the impacts of aseptic technique by seeing it from another perspective.[11] This study compared syringes made by pharmacy technicians under standard aseptic conditions to intensive care unit nurses practicing under ICU standard procedures. It was found that the deficiency of proper aseptic technique and the lack of an aseptic environment led to high rates of contamination with Gram-positive bacteria. Both incidents suggest that using proper aseptic technique promotes fewer occurrences of contamination and yields safer compounded products.

## Hospital/Clinic

Any community pharmacy, institutional pharmacy, specialty pharmacy, etc. has the creative ability to develop an aseptic compounding procedure. What's more, these compounding sites need to follow USP <797> to the best of their ability, despite the guideline being largely open to interpretation. A standard operating procedure (SOP) is one way aseptic technique and USP <797> can be organized and customized to fit each pharmacy's specific practices and needs. Standard operating procedures are beneficial to the success of aseptic compounding and have the potential to benefit different pharmacy settings. One important idea is that aseptic compounding is a skill that should be continuously improved upon by using standard operating procedures to promote the advancement of safety and efficacy.[12] Standardized training programs have the ability to properly train staff while reducing variability among staff members.

Aurora Health Care (AHC), located in eastern Wisconsin, performs sterile compounding at 15 of its 16 hospitals and 22 specialized cancer-care clinics.[12] Before 2016, AHC did not have a standardized process for sterile compounding, leading to different procedures, techniques, knowledge, and skills that varied among sites. AHC worked to fix this by identifying super users at each site, who attended an in-person, one-day refresher course focusing on key concepts related to USP <797> and <800>. Before the training, there was a pre-intervention stage that assessed super users' current knowledge of aseptic technique. The assessments included a written sterile-compounding knowledge-based exam; a media-fill challenge test; and a rubric-based observation assessment of aseptic technique, done in conjunction with the media-fill challenge test. After the pre-intervention assessments, trainees participated in a one-day refresher training intervention, which included a one-hour online review of related calculations, a 30-minute online review of beyond-use date (BUD) assignment, and a live training course focused on aseptic technique and major knowledge-based concepts within USP Chapter <797>.

A main focus of this training was to instill standardized knowledge across all sites.[12] After all training had been completed, a post-intervention assessment was conducted that included the same assessments given in the pre-intervention. Trainees passed if they received a score of 80% or higher for the knowledge-based exam, and if their media-fill test was negative for contamination. Overall, there was a statistically significant improvement on all assessments that were included in the pre- and post-intervention (written exam scores $P < 0.0001$; written exam pass rates $P < 0.0001$; aseptic technique observations pass rates $P < 0.0001$; media fill with aseptic technique evaluation for matched pair only $P < 0.0002$). These statistically significant results demonstrated an increased retention of sterile-compounding knowledge and better performance of aseptic compounding, leading to reduced microbial contamination. After the course, the super users brought their valuable knowledge back to their sites, to distribute the information and perform evaluations of other personnel who perform sterile compounding. From this study, a new sterile-compounding training program was developed. It incorporated a refresher training course, online learning modules, and repeated evaluations.

## Schools of Pharmacy

Pharmacy school is one place where future pharmacists can learn sterile compounding, and the manner of teaching has evolved over time. In late 2016, a survey was sent to 139 schools of pharmacy across the United States to gain information about their compounded sterile products curriculum.[13] This study was an update to one completed by Hellums et al. in 2007.[5] The survey measured elements of course structure, compounding environment, and compounding experience.[13] In the ten years between surveys, there was a significant increase in schools teaching beyond use dating and incorporating a laboratory aspect to teach aseptic technique. After passing written competencies, sterile compounding is generally guided by technique and skill more than knowledge. Implementing experiences to practice the concepts learned in lecture reinforces those teachings. Learning and practicing proper aseptic compounding processes in pharmacy school creates a foundational experience students will take into their careers. Students may also receive further guidance at their workplace when sterile compounding plays a role in their practice.

## Rural Areas

Smaller critical access hospitals (CAHs) have needs for sterile compounding as well. When these products are needed, it is essential to follow USP standards. Crawford et al. surveyed 40 rural hospitals in Illinois to determine compliance with USP <797>, the availability of sterile compounding practices, and where the compounding is done.[14] Results showed that 75% of the hospitals surveyed were in compliance with USP <797>, while 17.5% were unsure of their compliance status; the remaining hospitals did not respond.

Furthermore, the most common areas for sterile compounding in the CAHs were in a glove box (47.8%); in a laminar flow hood in a clean room (30.4%); and in a laminar-airflow hood in a separate I.V. room (17.4%). The glove box affords a sterile environment about the size of a desk for staff to prepare medications in places where space may be limited. Data from this survey demonstrates that there is ample room to implement SOPs to ensure practices are up to date with USP <797> at rural hospitals despite challenges they may face.

## Conclusion

While SOPs create a standardized process, that uniformity only extends to the specific institution for which it was developed. Furthermore, there is great variability among institutions with respect to available resources and sterile compounding volume, so a one-size-fits-all approach is not appropriate. Regardless of the details of implementation, the crucial factor in developing high-quality aseptic technique is the implementation of an SOP itself, along with the administrative support needed to create and maintain it. Additionally, rules are best learned and retained when they are continuously reinforced.[15] Therefore, it is important that sterile compounding be integrated into pharmacy school curriculum. Students who learn aseptic technique early in their careers can implement these standards into their future pharmacy practice, and work to prevent future healthcare outbreaks and consequences for patients.

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