

Baxa Corporation

**Patient Safety and Peak Performance
Through Pharmacy Training**

Technical Paper

The history of sterile compounding in pharmacy practice and the role of training in pharmacy compliance and practice excellence.



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Executive Summary

Incidences of patient morbidity and mortality associated with improperly prepared or contaminated sterile preparations have prompted the FDA to consider regulating or even banning pharmacy compounding.¹ The first official, enforceable sterile preparation compounding requirement in the United States took effect on January 1, 2004, when United States Pharmacopeia published USP Chapter <797>. This Chapter is now the US standard for pre-administration manipulations of compounded sterile preparations (CSPs), which includes compounding, transportation, and storage. <797> focuses on protecting patients and therefore applies not only to pharmacies but to *all sites* where CSPs are compounded and to *all personnel* who compound sterile preparations, *regardless of practice setting or profession*.²

The following article discusses the history of sterile compounding in pharmacy practice, current state, and the need for a purpose-built facility that provides practical, hands-on training in pharmacy preparation and regulatory compliance in order to achieve the level of patient safety and performance excellence required in today's pharmacy environments.

History

Compounding is an integral part of today's pharmacy practice. However, this has not always been the case. As the pharmaceutical industry expanded during the early to mid-20th century, the need to perform pharmaceutical compounding became less important as the pharmaceutical industry provided many different dosage forms for most of the drugs available; including oral solids, oral liquids, parenterals, topicals, suppositories and so on.³ Therefore, the role of the USP, which once set standards for drug products prescribed by physicians and prepared (compounded) by pharmacists, changed from that of setting practice standards for pharmacists to setting industry standards for manufactured drug products.

During the 1960's and 1970's, intravenous (IV) admixture services were incorporated into hospital pharmacy departments from nursing services. Then, compounding primarily consisted of manipulating commercially available dosage forms.⁴ Operations were low risk, and few patients experienced problems with the final sterile preparations. Pharmacists believed they were fulfilling their responsibility to ensure CSP sterility, safety, and efficacy.⁵ Pharmacies grew complacent about aseptic preparation of IV products, and the USP and NF, formerly required textbooks and reference books in colleges of pharmacy, were removed from the curriculum.⁶ Though much of their content continued to set standards of practice for the dispensing pharmacy, the books no longer reflected information used in contemporary pharmacy practice.⁷

During the 1980's and 1990's, the increasing demand from home health care, total parenteral nutrition, hospice care (in particular, pain management) combined with pharmaceutical manufacturers decreasing the number of available dosage forms led to an increasing number of compounded prescriptions.⁸ In addition, many physicians prescribed therapeutic agents or

¹ Trissel LA. An Update on USP Chapter <797>: The New National Standard for Sterile Preparation. 2005. pg., 1.

² Trissel, pg., 2.

³ Allen LV. Rationale for a Pharmacists' Pharmacopeia. U.S. Pharmacopeia leaflet. 2004:1-2.

⁴ Ibid.

⁵ Kastango ES. *USP<797>: Making the Case for Increasing Environmental Controls in Pharmaceutical Compounding*. Infusion. 2005; 11(4), Supplemental:3.

⁶ Kastango ES and DeMarco S. Pharmacy Cleanroom Project Management Considerations: An Experience-Based Perspective. IJPC. 2001; 5(3): 221.

⁷ Allen, pg 1.

⁸ Ibid.

alternative dosage forms that were not commercially available and therefore, required compounding.⁹

Aseptic knowledge and skills, however, had not kept up with marketplace demand and were not being taught in schools of pharmacy, with subsequent carryover to standards of practice. This, coupled with the growing complexity of drugs and drug products, made it inevitable that pharmacies would commit errors while preparing and distributing compounded sterile products (CSPs).¹⁰

Assuring CSP Quality

The National Coordinating Committee on Large Volume Parenterals (NCCLVP) was convened to take the first steps toward correcting this deviation from appropriate compounding standards. The committee developed recommended standards of practice for the preparation, labeling, and quality assurance of hospital pharmacy admixture services. The American Society of Health-System Pharmacies (ASHP) later found through two national surveys that these standards were not widely implemented in hospital pharmacies. Few hospital pharmacies were equipped with adequately controlled compounding environments; and environmental monitoring, end-product testing, and process validation was not being conducted to provide critical quality assurance checks on pharmacy-prepared sterile products.¹¹

In 1992, the USP issued a draft recommendation entitled USP <1074>, Dispensing Practices for Sterile Drug Products Intended for Home Use. This was later officially adopted in its final version entitled USP <1206>, Sterile Drug Products for Home Use. The recommendation provided specific practice standards and operating guidelines for CSPs. Unfortunately, this chapter did not receive the attention it deserved for several reasons: 1) newly trained pharmacists during this time were taught only about USP's usefulness in industrial type situations, which led to 2) these pharmacists overlooking USP topics for more clinically relevant topics; and 3) because the chapter title included the words "Home Use," most pharmacists believed this chapter only applied to the home health industry.

In 1993, ASHP issued the Technical Assistance Bulletin, "Quality Assurance for Pharmacy-Prepared Sterile Products." With ASHP's backing, there should have been no question as to which practice setting these standards belonged – all pharmacies that have sterile areas. However, ASHP's 2002 national survey found results similar to their 1995 national survey, demonstrating that the Technical Assistance Bulletin had not produced significant changes in sterile compounding in the 10 years since its publication.¹² These attempts at self-regulation and quality assurance failed to completely eliminate the threat to patient safety caused by inadequate and inconsistent procedures in pharmacy compounding.¹³

It was clear that compliance was going to have to be enforced. USP took decisive action with the publication of USP Chapter <797> Pharmaceutical Compounding – Sterile Products, which took effect January 2004. Chapter <797> is now the US standard for pre-administration manipulations of CSPs, applies to all sites compounding CSPs and affects all personnel who compound sterile preparations, regardless of practice setting or profession.¹⁴ In addition, since USP Chapter <797> compliance is required (general chapters numbered <1> through <999>

⁹ Ibid.

¹⁰ Kastango ES. The Cost of Quality in the Pharmacy. *IJPC*. 2002; 6(6): 404.

¹¹ Ibid., 406.

¹² Kastango ES. The ASHP Discussion Guide on USP Chapter <797>: Compounding Sterile Preparations. 2004. pg., 2.

¹³ Trissel, pg., 1.

¹⁴ Trissel, pg., 2.

are considered requirements as official monographs and standards of the USP/NF), pharmacies may be subject to inspection against these standards by the FDA, State Boards of Pharmacy and accreditation organizations, such as the JCAHO, Accreditation Commission for Health Care, Inc. (ACHC), etc.

Impact of USP Chapter <797>

The introduction of USP Chapter <797> turned the pharmacy world upside down. For nearly two decades prior, the USP/NF had been viewed as a pharmaceutical industry reference not applicable to everyday practice. Without training, pharmacists and students didn't know how to appropriately use the USP/NF in everyday pharmacy practice. Now, the pharmacy community was being told to comply with new standards virtually overnight. As with many standards, the Chapter presented guidance that left specific interpretation and implementation up to the individual pharmacy and its manager(s). Even today, more than two years after <797> was introduced, the pharmacy profession continues to struggle with issues of cleanroom management, staff procedures, facility design, equipment and materials, cleaning, monitoring and documentation; all of which affect the quality of pharmacy-prepared sterile products.

The reality is that USP Chapter <797> wasn't written to make pharmacists' lives difficult. It resulted from the profession's inability to create and implement safe standards on its own. It's a common belief that <797> will be minimized or even eliminated, but because of its patient safety goal, it's here to stay. However, like any radical change, it has the potential to be misinterpreted and thus feared.¹⁵

The major barrier to recognizing the inherent risks in CSPs is a combination of pride, ignorance, and resistance to change. This attitude has to change, as no one is immune to committing errors.¹⁶ Numerous recent studies and media reports have demonstrated that contamination errors occur in even the most professional compounding environments (i.e., FDA-inspected pharmacy compounding centers). And, a small error rate can be very significant when multiplied by a high volume of doses made and patients served.¹⁷

Another reason that many pharmacists / pharmacies have yet to fully comply with USP Chapter <797> is the profound helplessness they feel when reading and interpreting the document. Its 13 sections and more than a dozen pages are overwhelming. Readers often have the misconception that a sophisticated (translation: expensive) cleanroom must be installed and operational before any other improvements are made. In reality most of the problem is everything but the cleanroom. Pharmacies can begin immediately to have a significant impact on the quality of their CSPs by implementing policy and procedure guidelines, training and good aseptic practice.

The Need for Change

ASHP surveys made it clear that attempts at pharmacy self-regulation failed to eliminate the threat to patient safety caused by inadequate and inconsistent procedures in pharmacy compounding.^{18,19} A possible cause for this was elucidated during the ASHP's 2005 House of Delegates session: "... [USP <797>] continues to be cumbersome and hard to plan and

¹⁵ Hurst M. Understanding USP 797 Technical Paper: An Overview of USP General Chapter <797>, Pharmaceutical Compounding – Sterile Preparations. Baxa Corporation. 2004; pg., 2.

¹⁶ Kastango ES. USP <797>: Making the Case for Increasing Environmental Controls in Pharmaceutical Compounding., pg., 3

¹⁷ Ibid., pg., 3.

¹⁸ Kastango ES. The ASHP Discussion Guide on USP Chapter <797>: Compounding Sterile Preparations. 2004. pg., 2.

¹⁹ Trissel, pg., 1.

implement.”²⁰ “Delegates noted the need for ASHP to continue to be engaged with USP and JCAHO on the challenges to practical implementation of the Chapter [USP <797>].”²¹

Pharmacy leaders estimate that only about 50% of Pharmacy Directors have read USP Chapter <797>.²² In addition, the first compliance step, a gap analysis, was a JCAHO requirement with a Jan 1, 2005 deadline.²³ However, only 35.7% of hospital pharmacies were estimated to have completed this assessment of their sterile compounding processes.

Pharmacy OneSource conducted polls in spring and fall of 2005 that showed nearly three fourths of respondents believed that USP <797> compliance was a *difficult to very difficult* undertaking. More than half of the respondents believed that <797> implementation and compliance was currently their biggest challenge.

A subsequent Baxa Corporation survey showed that 60% of respondents were *partially confident to not at all confident* that they could withstand a JCAHO, State Board and/or FDA inspection for USP <797> compliance. More than 95% of the respondents believed that a hands-on USP <797> training center would be *useful or extremely useful*. In fact, collectively, the 84 respondents reported that they would send anywhere from 179 to 316 people to a USP <797> training center.

The short-term need for guidance on USP <797> compliance will continue for the next 4-5 years, as pharmacists realize that it is not going away – evidenced by the revision released for public comment in May 2006. After that, hospital pharmacies will have a continuous need for <797> guidance as new facilities are built and/or remodeled and as new pharmacists graduate and current pharmacists change practice venues.

²⁰2005 RDC Report. Accessed at http://www.ashp.org/aboutashp/PolicyGovernance/HOD/RDC_report.pdf on Aug 24th, 2005.

²¹ Ibid.

²²Conversation with Larry Trissel, Eric Kastango, and Dr. Newton at *Practical Application of General Chapter <797> by USP* workshop at the Hyatt Fisherman’s Wharf Hotel in San Francisco, CA. Aug 5-6, 2005.

²³Objective 4.2 in ASHP Health-System Pharmacy 2015 Initiative: Baseline statistics. *Am J Health-Syst Pharm.* 2005; 62:1393-7.

Practical Pharmacy Training for <797> Compliance

Baxa Corporation has focused its product development efforts on tools that streamline pharmacy operations and improve patient safety. After the release of the USP guidelines for sterile compounding, the company developed training tools and support materials that would enable hospital pharmacies to comply with USP <797> requirements using Baxa hardware and software. However, it was clear that a greater gap needed to be filled in pharmacy training.

In late 2005, the company decided to fund the development of a state-of-the-art, fully USP <797>-compliant cleanroom and training facility that would take the lead in training the pharmacy profession. As a service to its core customers, Baxa promotes hands-on training in high-quality sterile products preparation. Courses are ACPE-accredited, with tuition priced to cover training and material costs.

Opened in the summer 2006, the STAR (Skills Training, Academics and Resources) Center features an 836 ft² positive pressure ISO 7 cleanroom with an ISO 5 workbench; laminar flow hoods, Biological Safety Cabinets and isolators; a 250 ft² negative pressure ISO 7 hazardous drug preparation area; and a 300 ft² instructional gowning area, 288 ft² clean storage area, and a 110 ft² supply intake room. The center teaches the concept of aseptic processing including appropriate material and personnel flow.

STAR Center Participants:

- Learn the facility and environmental requirements for safely compounding CSPs
- Understand proper workflow and material and personnel movement for cleanrooms
- Practice aseptic technique in industry-standard LAFWs and barrier isolators

Pharmacy personnel must take personal and legal responsibility for the quality and accuracy of the compounds they prepare and dispense²⁴. Baxa invested in the Center because it believes that the best way for pharmacists and other professionals to understand and implement state-of-the-art standards of practice is for them to have practical, hands-on experience with expert trainers.²⁵

Finally, while the Center's initial focus is on pharmacy practice — with the hands-on USP <797> training seminar, future courses will take advantage of the STAR Center's unique cleanroom training environment to support a variety of professions and activities. STAR Center management is open to creation of unique curricula to meet identified needs of industry and provider participants. Individuals can email starcenter@baxa.com for more information.

²⁴ American Society of Health-System Pharmacists. ASHP Guideline on Quality Assurance for Pharmacy-Prepared Sterile Products. *Am J Health-Syst Pharm.* 2000; 57: pg., 1.

²⁵ *Ibid*, pg. 1.