

Baxa Corporation

Understanding USP 797

Technical Paper

An Overview of USP General Chapter <797>

Pharmaceutical Compounding – Sterile Preparations

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Introduction

USP Chapter 797¹, enacted January 1, 2004, presents the first enforceable standards for sterile compounding. Following years of patient safety recommendations and professional guidelines, the intent of USP 797 is to set forth the procedural and practical requirements for safe compounding of sterile preparations. The Chapter's requirements are applicable in all practice settings where sterile preparations are compounded, raising concern among many facilities regarding the cost and difficulty of compliance. That concern has resulted in numerous symposia and journal articles attempting to bring clarity to the requirements.

One article, "USP Chapter 797: Establishing a practice standard for compounding sterile preparations in pharmacy"² published in the September 15, 2004 issue of the *American Journal of Health-System Pharmacists* provides an excellent historical framework for understanding how USP 797 came about. In addition, the article summarizes the Chapter's major topics and offers 38 references to complete the story. Copies of this article, and many other excellent resource and reference materials are available at the American Society for Health-System Pharmacists' (ASHP) Web site. There, the ASHP Compounding Resource Center³ brings together information on publications, educational seminars, compliance tools and references regarding USP 797.

While understanding the historical background is important, most hospital pharmacists just want to comply with the basic requirements and get on with the business of patient care. This brief paper is intended to help pharmacies get started in that direction. It also discusses USP 797 from a couple of unique angles not necessarily considered in the initial literature published on the subject.

Getting Into the Flow of USP 797

First, it's important to appreciate that USP 797 was written to improve the compounding of sterile products. But, like any change, it has the potential to be misinterpreted, and thus feared. The biggest misconception about USP 797 seems to be that a sophisticated "cleanroom" is required. This "requirement" has been interpreted in many different ways, and is explained in more detail below. For the most part, USP 797 contains many procedural, training and quality assurance requirements that are not unreasonable for a quality IV operation.

In time, USP 797 will be implemented as the US standard for sterile compounding, with ASHP and other industry guidelines following its lead. Once the initial concerns over the cost and difficulty in meeting 797's requirements have passed, patients and staff alike will be better off as a result. Baxa products can be outstanding quality partners in this journey. Our goal is to enable pharmacies to learn how to use Baxa products in compliance with USP 797.

The US Pharmacopoeia

The USP (US Pharmacopoeia) is a private organization formed in 1820. Current members include many members of accredited schools of medicine and pharmacy, state medical and pharmacy associations, government agencies, consumer organizations and other prestigious health organizations.

The standards developed by USP are important for several reasons:

1. The Food, Drug and Cosmetic Act (and thus the FDA) recognizes the USP/NF (National Formulary) as the official compendia of US drug standards. There are hundreds of USP drug standards and all standards numbered less than 1,000 are enforceable by either individual State Boards of Pharmacy, or the FDA. The FDA does not routinely inspect individual pharmacies but may intervene in the case of injuries, a death, or a complaint.
2. USP/NF standards are often used as evidence of national standards in lawsuits.
3. The JCAHO (Joint Commission for Accreditation of Healthcare Organizations) has adopted these standards for use after July 1, 2004. JCAHO accreditation is the most universally recognized standard of US healthcare system quality. JCAHO accreditation is required for reimbursement through the national Medicare program and almost all state Medicaid (welfare) programs.
4. Many State Boards of Pharmacy are adopting USP 797 for their pharmacy inspections.

USP Chapter 797 was published in the 2004 edition of the *United States Pharmacopeia 27 – National Formulary 22 (USP-NF)*. Copies of the chapter may be purchased through ASHP⁴ or USP⁵.

USP: What It Is

Pharmacy rumors abound about USP 797. Clarification on some of the most important topics is below. First, USP 797 is a number of things:

1. *Long*. It's 18 pages, including 13 using single spacing and a small text font. That's a lot of information to read, but the concepts are not complicated.
2. *Paperwork and process intensive*. Virtually every significant step of the sterile compounding process is covered in detail. Once again, the major topics are summarized in the September 2004 American Journal of Health-System Pharmacy article.
3. *Intended to upgrade pharmacy admixture processes to reasonable precautions*. While some pharmacists may disagree with a number of the requirements, the overall tone is proactive, scientific, comprehensive and effective. There is nothing in USP 797 that a pharmacy cannot implement with a "reasonable" amount of time and resources.

4. *Specifies increasing controls based on risk.* CSPs (compounded sterile products) are classified into low, medium and high risk categories. Most CSPs prepared with/for Baxa products are in the low and medium risk categories.

USP: What It Isn't

But USP 797 is *not* some of the things that it's rumored to be:

1. *USP 797 does not require **sophisticated** cleanrooms to be installed.*

What the guideline **does** require is environmental controls – specifically, a separate area for compounding that meets a defined level of cleanliness, and monitoring to ensure that control is maintained. A brief explanation of standards clarifies the actual USP 797 cleanroom requirements. First, there are six levels of ISO (International Organization for Standardization) cleanrooms from ISO Class 3 to ISO Class 8. Three of these are:

ISO Class 3 – equivalent to the former Class 1 designation, allows a maximum of one particle (over 0.5 microns in size for all classes) per cubic foot. This cleanliness level is suitable for the ultimate cleanroom application such as microchip manufacturing, but is not required for pharmaceutical manufacturing or sterile compounding.

ISO Class 5 – (formerly Class 100), allows a maximum of 100 particles per cubic foot; which is the level for the typical laminar airflow hood that is required by USP 797 for the actual mixing area. Mixing IVs in a hood is nothing new in US pharmacies.

ISO Class 8 – (formerly Class 100,000), allows a maximum of 100,000 particles per cubic foot. This level is required for an IV preparation area/IV room.

There are other issues recommended in the Chapter, such as an ante room for dressing, etc. but the Class 100,000 mixing area is the primary environmental control requirement. Implementing the most basic steps of straightening up an IV room, coupled with a positive pressure air system, will result in a room with less than 10,000 particles per cubic foot. Getting an IV room to less than 100,000 particles per cubic foot is achievable by following the simple USP 797 physical facility suggestions.

The first step is getting a baseline on your existing facility to determine what remediation steps, or facility and procedural redesign, will be required to meet the environmental controls above. The net result of the USP 797 guidelines is that sterile mixing take place in a properly maintained laminar airflow hood (ISO Class 5) situated in a relatively clean room (ISO Class 8). For most pharmacies, this is neither difficult or unreasonable. In some cases, individual interpretations of this requirement have made it seem more onerous.

2. *USP 797 is NOT a radical departure from what most admixture programs are already doing.* There are basic steps in quality sterile compounding that many inpatient pharmacies have unfortunately not had the time, or interest, to implement. Regulatory agencies such as the FDA and State

Boards of Pharmacy have long recognized this need. USP 797 simply puts the requirements in a format that inspectors can check against.

3. *USP 797 cannot be fully met by outsourcing.* Legitimate first doses are not covered by USP 797 and other doses can be outsourced. But almost any pharmacy will still need to make many doses such as those subject to change, short-expiration drugs, some antineoplastics etc. that are not candidates for outsourcing. Other expensive and specialized drugs may be hard to outsource, also. Sterile compounding activities can be minimized through an outsource arrangement, but not entirely eliminated. This means that nearly all hospital pharmacies will still have to meet the requirements of USP 797.
4. *Isolators alone will not ensure compliance with USP 797.* Using an isolator for sterile compounding handles only part of the requirements for USP 797. Issues such as process validation, training, expiration setting, product quality maintenance after the CSP leaves the pharmacy, caregiver training, patient monitoring, QA program, etc. remain the same as for products compounded in standard laminar flow hoods. The special requirements for cleaning the isolator itself and for cleaning materials entering the isolator make this a demanding alternative to standard pharmacy flow hoods. Additionally, many users find isolators physically difficult to work in and inappropriate for medium-to-large institution workloads.

What's Next?

Compliance with USP 797 will be achieved through the completion of steps on a timeline that stretches out to January 2008. The requirements allow pharmacies to plan appropriately for compliance, understanding that changes of this magnitude will not be accomplished overnight. JCAHO surveyors began surveying facilities for compliance with Chapter 797 on July 1, 2004. Many of the requirements are equivalent to current elements of performance of the 2004 Joint Commission standards. Current compliance to these will be evaluated and scored in JCAHO reviews. Other areas of Chapter 797 will be evaluated but not scored.

The October 2004 issue of *Joint Commission Perspectives* listed the five items that the USP 797 advisory group recommends that organizations focus on for compliance. This list, repeated below, recognizes that the task of developing a comprehensive plan for USP 797 compliance is a daunting one. While all components of the Chapter must be addressed for compliance, these priority activities will allow organizations to make the most significant progress towards achieving its goal of improving the quality of sterile compounded products.

1. *Personnel training and evaluation (that is, competence assessment)*
2. *Beyond-use dating and labeling*
3. *Verification of automated compounding devices*
4. *Finished preparation release checks and tests*
5. *Aseptic technique*

USP 797 represents a profound change for the profession of pharmacy. The key is using aseptic technique with the right equipment in an environment that's appropriate. Baxa is working on a number of consultive strategies and tools to help our customers meet the compliance challenges of USP 797 as easily as possible. The company is committed to providing the right equipment, along with the training and assessment tools, to meet patient safety and sterile compounding requirements.

Key Compliance Dates and Activities

Summarized below are the key dates and activities for USP 797 compliance. Please refer to full document for details.

Pharmacies should have basic policies for aseptic technique, finished product testing, patient monitoring, and adverse drug reaction (ADR) reporting in place currently. Immediate attention should be paid to high-risk level product sterility.

That said, the most urgent initial task for USP 797 compliance is the completion of a *gap analysis*. This document details the current state of the pharmacy against the end state, or compliance with USP 797, to identify the differences or gaps. From that analysis, an action plan can be formed to prioritize the gaps and develop options for compliance.

January 2005 – The Gap analysis and an initial action plan for each section must be completed by January 1, with interim measures for personnel performance training and testing set up. This is the first major milestone for most organizations. Action plans are expected to have realistic timeframes for completion, with the understanding that full compliance will not be accomplished quickly.

Several templates available for performing this gap analysis. The *International Journal of Pharmaceutical Compounding* offers a reasonably priced gap analysis template on CD.⁷ Two additional options are available through the ASHP. The first, the 797 Compliance Advisor is an industry-sponsored tool that offers downloadable checklists.⁸ The second is a more comprehensive, Web-based tool that takes users through the step-by-step questions to complete the analysis.⁹ Check the sources at the end of this paper for Web links to these templates.

July 2005 – Renovation plans for physical site must be completed. Equipment and personnel training, and all operational policies and procedures and the quality assurance plan should be in writing. Standard operating procedures (SOPs) for personnel and equipment need to be in place and operational.

January 2006 – Formal quality assurance plan should be in place and operational.

January 2008 – Physical site changes should be complete, with sterile compounding fully compliant with USP 797.

Sources Cited

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