

## USP Chapter 797: Compounding Sterile Preparations Q and A

### *What is the history of compounded sterile preparation (CSP) practice guidelines?*

Pharmacists have a critically important role in preparing compounded sterile preparations (CSPs) for patients and for ensuring the sterility, safety, and efficacy of these preparations. Practice guidelines were published over 30 years ago establishing initial practice standards.<sup>1,2</sup> In the early 1990s, the American Society of Health-System Pharmacists (ASHP), United States Pharmacopeia, and National Association of Board of Pharmacy also issued practice recommendations regarding CSPs. However, it appears that some of the basic and fundamental principles of contamination control, aseptic processing, content accuracy, and quality assurance are not being met, and many institutions have not been in full compliance with these guidelines.

USP Chapter 797: Compounding Sterile Preparations was published on January 1, 2004.<sup>3</sup> It details the procedures and requirements with which pharmacists and other health professionals must comply when they compound sterile preparations. Each chapter of USP is assigned a number which appears in brackets along with the chapter name. Chapters 1-999 are requirements and official monographs and standards of USP. Thus, Chapter 797 is considered a requirement and pharmacies may be inspected for compliance with these standards by state boards of pharmacy, the FDA, and accreditation organizations such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO).

### *Have specific areas of concern been identified with USP Chapter 797?*

In the ASHP Discussion Guide on USP Chapter 797 developed by the American Society of Health-System Pharmacists (ASHP and Baxter Healthcare), several areas of concern are highlighted:<sup>4</sup>

- **Applicability in All Healthcare Settings:** proper compounding procedures are not unique to the practice setting where sterile preparations are compounded. USP 797 requirements must be met in all healthcare settings that compound sterile preparations and by all disciplines associated with these settings
- **Risk Levels Criteria:** a risk level checklist (Table 1) has been developed to assist pharmacists in assessing various factors in determining actual risk for preparations being compounded. The most important factor in determining risk level is sound professional judgment based on knowledge of aseptic compounding principles
- **Environmental Quality Controls:** the appropriate combination of cleanrooms, ante rooms, and laminar airflow workbenches to achieve desired cleanliness levels based on risk classification needs to be determined
- **Process and Preparation Quality Controls:** pharmacists and technicians must understand that compounding processes and personnel who perform the compounding have an impact on the quality assurance of the final sterile preparation. These controls are the cornerstone in ensuring CSP sterility and accuracy.

- **Sterility and Beyond-Use-Dating:** Two factors are critically important in establishing beyond-use-dating: the first is the chemical stability of the chemical entity in solution; the second factor is the sterility of the CSP. The assignment of risk levels and operating principles outlined in Chapter 797 serves to prevent microbial contamination
- **Staff Training, Competency, and Performance:** pharmacists and technicians are being asked to do more with less every day. This vicious cycle takes a great toll on one of the most crucial aspects of ensuring sterility and accuracy of CSPs: formal training and periodic competency assessment.

### ***Have critical elements for compliance to USP Chapter 797 been identified?***

Considering the many areas of concern, the following critical elements for compliance with USP Chapter 797 have been identified: <sup>4,5</sup>

- Determine the pharmacy's compounding risk level (low, medium, high) of different preparations using the risk-level assessment checklist, Chapter 797, and professional judgment,
- Perform a gap analysis by comparing Chapter 797 requirements line-by-line with pharmacy operational procedures and facilities,
- Develop an action plan for compliance based on the prioritized gap analysis,
- Communicate the results of the gap analysis and action plan with the pharmacy staff and the administrators and executives of the organization,
- Implement operational changes and revise policies and procedures for CSPs and then address changes needed for facility and equipment compliance,
- Communicate the demonstrated improvements in patient care with staff,
- Evaluate the use of alternative products and reassess workload demands for all compounding sites, and
- Document all measures of quality performance and communicate improvements in compliance with staff, administration, and accreditation organizations

These elements represent the basic components of any quality improvement program.

### ***How well are pharmacists prepared for USP Chapter 797?***

Currently, many pharmacy departments have not performed appropriate gap analyses and have not completed a comprehensive compliance plan with timelines. Thus, they are in jeopardy of not being in full compliance with USP Chapter 797. The following are potential reasons for the lack of preparedness:

- **Pharmacist Awareness and Understanding:** Even though many pharmacists have heard of USP Chapter 797 and reviewed brief communications on the subject, they are not fully aware of the comprehensive requirements and the risks and ramifications of noncompliance.
- **Enforceability:** Pharmacists may feel that at present these guidelines are not really enforceable. As mentioned, in actual practice today, institutions being

- surveyed must have a compliance plan completed. This must include a “gap analysis” and a timeline for full compliance.
- **Leadership:** The focus of leadership regarding Chapter 797 in pharmacy departments varies widely. If the leader does not have a complete appreciation of the importance of Chapter 797 or does not have an organized plan for compliance within an appropriate timeline, this lack of focus and preparation impacts the staff. It may appear that the department as a whole is not committed to meeting the guidelines.
  - **Resources:** Significant resources (e.g. capital monies for cleanrooms and human resources to ensure adequate staffing) may be required to ensure full compliance with USP Chapter 797. Many health systems are struggling financially and directors of pharmacy are already under pressure to stay within a given budget. They may not feel that the time is right to push for additional resources in that USP Chapter 797 may not be fully enforceable at present.

### ***Are USP Chapter 797 requirements really enforceable?***

At present, as long as an institution has an approved action plan with realistic time frames, it is not likely to be cited for noncompliance. If, however, an institution does not adhere to the plan and timeline upon re-review by JACHO or other accrediting bodies at the next visit, they will be cited for noncompliance which may affect their accreditation status. The general sense is that by 2008 at the latest, all requirements (including those that may require facility changes, construction, or staffing changes to ensure compliance) must be fully met. Pharmacists are also encouraged to contact their respective board of pharmacy for information on state enforcement criteria and current activities. The FDA is exercising enforcement discretion during routine inspections but will intervene when patient injury associated with CSPs have occurred.

### ***Are compliance tools and educational opportunities available?***

The best approach to complying with Chapter 797 is to be very familiar with the detail of all requirements. There are several tools available to assist pharmacy in conducting a gap analysis. The ASHP offers a Web-based Chapter 797 compliance advisor and risk assessment-gap analysis tool ([www.ashp.org/SterileCpd/797guide.pdf](http://www.ashp.org/SterileCpd/797guide.pdf)), and the International Journal of Pharmaceutical Compounding has developed a similar tool. Tools such as this can provide the foundation for an action plan that details the activities and resources needed to comply with USP Chapter 797 requirements.

It is also clear that there are significant gaps in knowledge and perception with pharmacy administrators and pharmacists relating to USP chapter 797. A multi-pronged educational approach is still needed to overcome these deficiencies. CE-based programs are readily accessible educational approaches which can be accessed by key pharmacy administrators and pharmacists. For example, University Pharmacotherapy Associates (UPA) offers a web-based CE offering that addresses important aspects of USP Chapter 797 (UPA-LLC.COM). The critical outcome of such programs would be an enhanced appreciation for the scope, practice specifics, accreditation ramifications (enforceability), and a template for effective planning and execution of a compliance plan.

## **Are there other opportunities to facilitate compliance and can a specific example be cited?**

There may also be CSPs where a complicated, labor-intensive, time-consuming plan for compliance may be obviated. When faced with a therapeutic situation which requires a lower dose of a drug than is commercially available, pharmacists have traditionally prepared dosage aliquots. A pertinent example of the application of Chapter 797 requirements in actual practice today revolves around the use of fibrinolytic drugs for central venous access device thrombosis (CVAD). Aliquotting was initially necessitated with t-PA for conditions such as central venous access device (CVAD) thrombosis since only 50 mg and 100 mg vials were initially available. Today, other fibrinolytics such as r-PA must be aliquotted to use them in CVAD thrombosis. Procedures have been developed for aliquotting, freezing, storing, thawing, and determining beyond-use dating for these preparations. However, batch aliquotting of fibrinolytics is a medium-risk compounding activity according to USP Chapter 797. If aliquotting of a fibrinolytic such as r-PA is considered, the need to ensure sterility and validation of aseptic procedures, the question of stability with freezing, beyond-use dating, and the need for appropriate labeling and compliance with USP Chapter 797 remain important issues. A practical consideration today is that t-PA is commercially available in a 2 mg unit-of-use vial (Cathflo™ Activase®). Additionally, the overall economics of the situation do not strongly support aliquotting of these agents. Thus, a labor-intensive, risk-laden process to aliquot fibrinolytics in this situation is unnecessary today. As a result, this CSP medium-risk activity could be totally averted and time and attention focused on compliance to USP Chapter 797 with other vitally important CSPs.

## **Will Pharmacists meet the challenge of USP Chapter 797?**

Pharmacists have a covenant with each and every patient to ensure the effective and safe use of CSPs. The challenge of being in full compliance with the requirements of USP Chapter 797 may be somewhat overwhelming for pharmacists and pharmacy departments. The detailed, fairly complicated requirements may seem to be unattainable. As mentioned, the potential expense associated with ensuring compliance may be quite significant for many health systems. Nevertheless, the pharmacist and pharmacy department are basically responsible for developing, implementing, and monitoring quality systems for CSPs via an organized plan and process. Practice guidelines for CSPs have evolved significantly with the requirements of USP Chapter 797. A comprehensive assessment of the elements of compliance must be performed in devising an effective compliance plan which will ensure success in meeting the challenge.

## References

1. National Coordinating Committee on Large Volume Parenterals. Recommended methods for compounding intravenous admixture in hospitals. *Am J Hosp Pharm.* 1975;32:261-270.
2. National Coordinating Committee on Large Volume Parenterals. Recommended system for surveillance and reporting of problems with large volume parenterals in hospitals. *Am J Hosp Pharm.* 1975;34:1251-3.
3. Pharmaceutical considerations – sterile preparations (general information chapter 797). In: *The United States Pharmacopeia, 26<sup>th</sup> rev., and the National Formulary, 22<sup>nd</sup> ed.* Rockville, MD: The United States Pharmacopeial Convention;2004:2350-70.
4. American Society of Health-System Pharmacists. ASHP Discussion Guide for compounding sterile preparations: summary and implementation of USP chapter 797. [www.ashp.org/SterileCpd/797guide.pdf](http://www.ashp.org/SterileCpd/797guide.pdf) (2004 Dec).
5. Kastango ES. Blueprint for implementing USP chapter 797 for compounding sterile preparations. *Am J Health-System Pharm.* 2005;62:1271-88.

**Table 1**

<b>Compounding Activity</b>	<b>Location</b>	<b>USP &lt;797&gt;Risk Level Determination</b>
Reconstitution of several vials of lyophilized powder with a specific volume of sterile diluent for transfer to a small-volume minibag or large-volume parenteral solution <i>one at a time</i>	In the pharmacy using appropriate engineering controls (ISO Class 5 hood in and ISO Class 8 cleanroom)	Low-Risk Level
Reconstitution of several vials of lyophilized powder with a specific volume of sterile diluent; the resulting solution is then aggregated into an evacuated bottle for transfer to several small-volume minibags or large-volume parenteral solutions	In the pharmacy using appropriate engineering controls (ISO Class 5 hood in and ISO Class 8 cleanroom)	Medium-Risk Level
Reconstitution of a single vial of lyophilized powder with a specific volume of sterile diluent for transfer to a small-volume minibag or large-volume parenteral solution	Nursing station, ambulatory care center or at the patient bedside without any engineering controls	High-Risk Level