The revised USP Chapter <797> became available on USP’s website (www.usp.org/USPNF/pf/generalChapter797.html) on December 3, 2007, and is scheduled to become official on June 1, 2008. While minor tweaks may be made to grammar and sentence structure, the content and substance of the chapter will not change in the foreseeable future. Although compliance with <797> has never been avoidable, per se, it is now more important than ever.

As pharmacists and technicians, we have an obligation to comply with all applicable local, state, and federal regulations that govern our practice; USP Chapter <797> is considered part of the Federal Food, Drug, and Cosmetic Act and almost every state board of pharmacy has some overarching requirement for compliance with this act. But our obligation to meet these standards should be driven by patient safety, first and foremost. Furthermore, the revised <797> has been through an extensive revision process and has been reviewed by several expert groups. It is a synthesis of evidence-based science and best practices and provides the health care community with a set of community standards to adhere to when providing compounded sterile preparations (CSPs). It is expected that harm and death can be avoided by applying the minimum quality and practice standards detailed in the chapter. The following article outlines some of the most significant areas of changes within the revised USP Chapter <797> and can get you started on understanding your compliance requirements. However, there is no substitute for a thorough reading of the chapter; as pharmacists, we are obligated to familiarize ourselves with primary source material, instead of relying solely on the interpretations offered by secondary sources.

Allergen Extract CSPs
One of the first significant areas of change within the updated chapter is its recognition of and quantified requirements for patient-specific allergen extract CSPs. When the specific criteria listed in <797> are met, highly preserved allergen extract CSPs are exempt from the personnel, environment, and storage requirements of the chapter. This decision was based on extensive input from AAOA/JCAAI and other experts, in addition to the results of a published retrospective patient-impact study that showed zero infections in a sampling of 26,795 injections.

Hazardous Drugs
The revisions also incorporate recommendations from the NIOSH Alert on hazardous drugs. To protect operators and provide asepsis, personnel are required to wear appropriate PPE and can use the appropriate ISO Class 5 devices, i.e. biologi-
To protect operators and provide asepsis, the revised chapter recommends the use of appropriate ISO Class 5 devices, such as biological safety cabinets or compounding aseptic isolators (CAIs). CAIs must be placed in a negative-pressure room when not in an ISO Class 7 area.

Facility Design and Engineering Controls

<797> now clearly articulates the requirements for physical plant design, outlining detailed requirements for air quality, frequency of air exchanges, pressure differentials, and the like. Unidirectional airflow must be provided by all primary engineering controls, i.e. CAIs, CACIs, BSCs, and laminar airflow workstations (LAFWs). Cleanrooms for nonhazardous and nonradioactive CSPs must be supplied with HEPA-filtered air that enters from the ceiling and may be returned via low, wall-mounted vents, which are efficient in the removal of airborne particulate contamination. Low wall returns should be well distributed throughout the room and, ideally, have adjustable louvers or dampers.

The direct compounding area should experience no less than 30 air changes per hour (ACPH), with up to 15 ACPH coming from the cleanroom supply. In other words, your primary engineering control can “borrow” 15 ACPH from the surrounding cleanroom. This new allowance should ultimately save hospitals money as they design <797>-compliant compounding complexes. CAIs and CACIs proven to isolate – in other words, maintain ISO Class 5 air quality – when located in worse-than-ISO Class 7 air can be used outside of the cleanroom environment. If used in this manner, the isolator must be tested to the guidelines outlined in the CETA Compounding Isolator Testing Guide (CAG-002-2006). Pharmacies must hold their certifiers accountable to these guidelines for engineering controls, as there may be significant variances between certifiers’ work practices. The only way to ensure your engineering controls are performing correctly is to hold your certifier accountable to a known set of industry standards, such as those presented in CAG-002-2006.

When reading the chapter, you will note that guidance has been added regarding room segregation and the placement of devices not essential to compounding, such as refrigerators and printers. There are also additional personnel requirements related to food, drink, unpacking of supplies, and demarcation designation, among others.

First Air

Good aseptic technique requires the use of first air – air exiting the HEPA filter in a unidirectional stream that is virtually free of particulate contaminants. The revisions to <797> require that all critical manipulations must be carried out in unobstructed first air, in order to provide a contaminant-free direct compounding area. Proper product placement and process movement with respect to air supply and discharges will provide a contaminant-free compounding area.

Gowning and Gloving

The changes to <797>’s personnel gowning and gloving requirements are harmonized with the CDC’s guidelines for hand hygiene. The USP’s Sterile Compounding Expert Committee received a tremendous amount of feedback from world-renowned experts in the area of infection control, cleaning, and disinfection, and the section of the chapter related to personnel reflects their guidance. The revised chapter requires the use of sterile gloves, frequently disinfected with sterile 70% IPA, during compounding activities. Although it is likely to have a financial implication on pharmacy operations, this requirement is backed up by evidence-based science. For example, sterile alcohol though more costly than 70% IPA, is devoid of spores – unlike normal 70% IPA.

It is crucial that, regardless of cost or inconvenience, we comply with the sterile glove and alcohol requirement, as people are the greatest source of contamination in the cleanroom. In fact, human hands harbor an average of 100,000 organisms.
per square millimeter. The use of sterile gloves and alcohol for hand sanitization can reduce the impact humans – the particle generators that we are – have on a controlled environment.

In this vein, it is important to understand that using a CAI or CACI does not obviate the need for sterile gloves during compounding activities. It is strongly recommended that you contact your CAI/CACI manufacturer to determine how best to outfit their isolator with sterile gloves.

Environmental Monitoring
Historically, USP Chapter <797> called for a pharmaceutical-manufacturing model of environmental monitoring, requiring routine air, surface, and fingertip sampling in various locations, but now the chapter follows more of an infection-control model. Recognizing that people are the biggest source of contamination, surface and fingertip sampling are tied to specific, employee-related events, such as initial training, media fill verification, and the ongoing annual or semi-annual training and certification of compounding personnel (depending on risk level). In tandem with the required facility air sampling, the new environmental monitoring requirements should allow you to maintain a state of control in your compounding environments, provided those environments are certified as functioning properly.

The revised requirements for environmental monitoring include:

- Viable, volumetric air sampling must occur at least every six months.
- Gravimetric methods (i.e., the use of plates or paddles) are not permitted for air sampling.
- Personnel fingertip sampling must occur during initial training, as part of the media fill process, and as part of the personnel competency assessment that takes place annually for low- and medium-risk compounding operations and semi-annually for high-risk compounding operations.
- Surface sampling via contact plates and swabs must occur periodically and at the end of the compounding day.

Full details on the new requirements for environmental monitoring, including fur-
Personnel Training and Evaluation Requirements
The training and competency assessment requirements of the new chapter, as they apply to your operations, are largely dictated by the type of compounding activities performed by your organization. If you prepare a significant volume of chemotherapy, for instance, you need to ensure your people understand containment and the use of primary engineering controls, the use of personal protective equipment (PPE), and the like. For high-risk compounding, the chapter offers specific language regarding the verification of the sterility and accuracy of final preparations, including the use of filters and methods of terminal sterilization (i.e., autoclaves and dry-hear ovens).

The current chapter provides no clear curriculum for compounding training, but there are a number of available educational resources that can aid pharmacists in their efforts to train and assess the competency of their compounding staff. USP <797> does require that personnel receive annual (for low- and medium-risk compounding) or semi-annual (for high-risk compounding) didactic training, with an added requirement for a written test. Additionally, all personnel must undergo a skills assessment, using observational audit tools, and successfully complete aseptic media fill testing. The chapter also provides sample observational competency-assessment checklists to guide the supervisor’s evaluative process. Of course, it is important to remember that adults learn better via kinetic, hands-on training. Consider offering this to your staff members, in addition to the required didactic training.

Sterility Testing and Sterilization
To achieve compliance with USP <797>'s sterility testing requirements, you must follow the requirements of USP <71>. There are two methods for sterility testing: direct inoculation and membrane filtration. While direct inoculation is easier and cheaper, membrane filtration is necessary for high-risk level CSPs. Furthermore, all sterilization methods employed by your facility must be verified to achieve sterility. All sterility filters are subject to integrity testing, i.e. bubble point tests. Furthermore, the revised chapter provides prescriptive guidance for steam and dry-heat sterilization, as well as depyrogenation.

In purchasing products for sterility testing and sterilization, or any other compounding-related product for that matter, be wary of claims of “USP <797> compliance.” USP writes standards that regulators enforce; no body for deeming a product “compliant” exists within USP. As such, it falls upon the pharmacist to determine the accuracy of such statements. Perform the necessary due diligence during your product research before accepting a product’s claim of USP <797> compliance.

Documentation
First and foremost, pharmacists need to follow their state board of pharmacy regulations regarding the documentation of compounding activities. Some states provide very specific guidance in this area. While I am loath to use this example, should your hospital face a lawsuit related to CSP contamination, you should have the documentation to prove that quality standards were adhered to throughout your processes. At the very least, you should keep a detailed log of your compounding activities, detailing the batch numbers, lot numbers, and expiration dates of your CSPs and the components used to prepare them. If nothing else, this list will serve you well in tracking down CSPs affected by an internal or external product recall.

Closing Remarks
As health care professionals, pharmacists are obligated to “first, do no harm.” With this in mind, it should be our professional responsibility to adhere to the evidence-based guidelines set forth in the updated USP Chapter <797>. We cannot forget a patient will receive our compounded preparation. The practice of pharmacy has evolved significantly in the past 20 to 30 years, and our standards have changed to reflect that. While some of our traditional compounding practices are still very appropriate, others need to evolve. We have to advance our understanding of the science of compounding and embrace change in order to promote patient safety.

While it is valuable to consult reliable outside sources of information, there is no substitute for a thorough understanding of the primary source material — the revised USP Chapter <797> itself. The original chapter, published in 2004, was said by some to not be a clear primary source of information, but the USP’s Sterile Compounding Expert Committee has received significant feedback that this latest version is a robust primary source that provides clear direction, guidance, and assistance in achieving compliance. By studying the new chapter and incorporating its guidelines into your facility and daily practices, you can be confident that you are taking a significant step toward patient safety.

Eric S. Kastango, RPh, MBA, FASHP, is the president, CEO, and owner of ClinicalIQ, LLC, a provider of customized process and educational strategies for the pharmaceutical, medical device, and health care industries. A member of USP’s Sterile Compounding Expert Committee, he has practiced in the field of both hospital and home care pharmacy since 1980.