AANA’s Professional Practice Division has received several member inquiries questioning the application of United States Pharmacopeia General Chapter <797>, Pharmaceutical Compounding – Sterile Preparations (“Chapter <797>”) to anesthesia practice. We partnered with Eric S. Kastango, MBA, RPh, FASHP, a pharmacy consultant specializing in USP Chapter <797> and a member of the United States Pharmacopeia’s Sterile Compounding Expert Committee, to answer your questions regarding Chapter <797> and sterile compounding techniques.

Chapter <797> is not law, but is a synthesis of accepted evidence-based science and best practices from the contamination and infection control industry that provides healthcare providers with a set of minimum practice and quality standards when delivering compounded sterile preparations (CSPs). Persons who perform sterile compounding include pharmacists and pharmacy technicians, nurses, anesthesia professionals, and physicians.

Language in Chapter <797> emphasizes the important role that compounding personnel and aseptic technique plays in preventing inadvertent contamination of CSPs during preparation. The Introduction to Chapter <797> states, “It is generally acknowledged that direct or physical contact of critical sites (e.g., vial septa, syringe and needle hubs, and injection ports) of CSPs with contaminants, especially microbial sources, poses the greatest probability of risk to patients.” Unfortunately, not all compounding personnel realize that they may pose various levels of risk to the patient when preparing a CSP. In addition to the commonly recognized risk of medication error, microbial contamination (i.e., non-sterility) remains a serious threat to patients. Touch contamination by compounding personnel poses the highest risk of microbial contaminations of CSPs.

While most compounding occurs in the pharmacy, if adopted by your facility, Chapter <797>’s guidelines may also apply to nurses, nurse anesthetists and physicians who prepare sterile preparations. In other words, to the extent your institution or your institution’s pharmacy has implemented policies requiring compliance with Chapter <797>, your anesthesia department must comply with those policies. In addition, and regardless of whether your institution formally requires compliance with Chapter <797>, anesthesia professionals must always use proper aseptic technique when preparing sterile preparations.
United States Pharmacopeia and USP Chapter <797>

The United States Pharmacopeia is an independent organization which acts as the official standards-setting authority for all prescription and over-the-counter medicines, dietary supplements and other healthcare products manufactured and sold in the United States. It was chartered by the United States Congress in 1863. As part of its activities, the United States Pharmacopeia publishes the United States Pharmacopeia – National Formulary (the “USP” or “USP-NF”), a book containing the standards for medicines approved for prescriptions, including key information on composition, prescribing, dispensing, and administration of medicines. With the exception of Chapter <797>, the USP applies to drug manufacturers and is generally used by drug manufacturers and, more recently, pharmacies.

Chapter <797> of the USP regarding pharmaceutical compounding was first published on January 1, 2004. Enforceable national standards for sterile compounding did not previously exist, and the purpose of Chapter <797> was to combat patient morbidity and mortality associated with improperly prepared or contaminated sterile preparations. Chapter <797> has become the national pharmacy standard for pre-administration manipulations of CSPs, which include biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals. Chapter <797> was written to apply not only to pharmacies, but to all sites where CSPs are compounded, including hospitals, clinics, physician offices and other healthcare facilities.

Chapter <797> categorizes CSPs as either low-risk level, medium risk-level, or high-risk level and sets forth preparation standards for each category. Risk levels are assigned according to the corresponding probability of contaminating a CSP with microbial contamination (e.g., microbial organisms, spores, endotoxins) and/or chemical and physical contamination (e.g., foreign chemicals, physical matter).

Under Chapter <797>, with one exception (the “immediate use provision”), all CSPs must be compounded with aseptic manipulations entirely within ISO Class 5 or better air quality environment. ISO Class 5 is a universally accepted classification of air cleanliness in controlled environments, and requires use of a containment hood or compounding aseptic isolator based on the level of environmental pollutants in the air. Operating rooms and even bone marrow transplant units rarely, if ever, meet this air classification level.

Chapter <797> lists examples of low-risk level compounding as:

(i) Single-volume transfers of sterile dosage forms from ampuls, bottles, bags, and vials using sterile syringes with sterile needles, other administration devices, and other sterile containers, and

(ii) Simple aseptic measuring and transferring with not more than three packages of manufactured sterile products, including an infusion or diluent solution to compound drug admixtures and nutritional solutions.
In other words, low-risk level CSPs include any single drug drawn into a syringe for direct injection (e.g., atropine, fentanyl, phenylephrine, or vecuronium) and up to two drugs in a small volume parenteral minibag (e.g., cefazolin).

According to Mr. Kastango, Chapter 797’s preparation standards for low-risk level CSPs can be summarized as follows:

* Visual confirmation that compounding personnel are properly donning and wearing appropriate items and types of protective garments, (e.g., hair net, beard cover, face mask, nonsterile gown or frock, sterile gloves and shoe covers.

* Routine disinfection of critical sites (e.g., injection ports, vial septa, and ampul necks) with sterile 70% isopropyl alcohol, and disinfection of environmental surfaces with EPA-approved germicidal detergents which are consistent with current CDC guidelines.

* Semi-annual air quality testing (nonviable and viable particles via impaction air sampler) of both the primary (e.g., laminar airflow workbenches) and secondary engineering controls (clean rooms) which correlates with recertification schedules. This also applies to commissioning of these primary and secondary engineering controls.

* The aseptic technique of compounding personnel is verified through simulated compounding activities using a microbial growth media (e.g., trypticase soy broth) annually along with gloved fingertip sampling to ensure that compounding personnel are maintaining aseptic technique as part of an ongoing competency assessment and training plan.

* Review of all orders and packages of ingredients to ensure that the correct identity and amounts of ingredients were compounded.

* Visual inspection of CSPs to ensure the absence of particulate matter in solutions, the absence of leakage from vials and bags, and the accuracy and thoroughness of labeling.

Low-risk level CSPs commonly used in anesthesia practice include but are not limited to phenylephrine, atropine, and regional anesthetic medications. Under Chapter 797, low-risk level CSPs prepared in accordance with the above-listed preparation standards may be stored for up to 48 hours at controlled room temperatures, 14 days at cold temperatures (2°-8° C), and 45 days frozen, unless manufacturers’ recommendations provide otherwise.

Medium-risk level compounding involves the transfer of volumes of several medications (more than 3) into an infusion device or sterile container and typically occurs in the pharmacy or under the pharmacist’s direction. Quality assurance
procedures for medium-risk level CSPs include all the above-listed criteria for low-risk level CSPs, as well as a more challenging media-fill test passed at least annually.

High risk-level compounding occurs when nonsterile components (e.g., talc or alum) are compounded and administered to patients. Any type of aseptic transfer of solutions directly into the patient or into infusates that will be infused by the patient can be a source of extrinsic contamination or error. High-risk level compounding also requires adherence to the above-listed safety precautions, as well as even more involved semi-annual media-fill testing.

Under Chapter <797>, the only exception to the above-listed preparation standards for CSPs is set forth in a relatively new provision designed to exempt emergency medications from those preparation standards detailed in the chapter. The “immediate-use” provision is intended for situations in which there is a need for emergency or immediate patient administration of a low-risk level CSP. According to Chapter <797>, such situations may include

- cardiopulmonary resuscitation,
- emergency room treatment,
- preparation of diagnostic agents, or
- critical therapy where the preparation of the CSP under the preparation standards otherwise required for low-risk level CSPs would subject the patient to additional risk due to the delay.

Certain low-risk level anesthesia medications may qualify for this immediate-use exception if a delay in their preparation would subject the patient to additional risk. Medium-risk level and high-risk level CSPs may not be prepared as immediate-use CSPs, and immediate-use CSPs are not intended for storage or batch compounding.

In order for providers to take advantage of the immediate-use exception for low-risk level preparations, the following criteria for immediate-use CSPs must be met:

1. The compounding process involves simple transfer of not more than three commercially manufactured packages of sterile nonhazardous products or diagnostic radiopharmaceutical products from the manufacturers’ original containers and not more than two entries into any one container or package (e.g., bag, vial) of sterile infusion solution or administration container/device. (emphasis added)

2. Unless required from the preparation, the compounding procedure is a continuous process not to exceed 1 hour.
3. During preparation, aseptic technique is followed and, if not immediately administered, the finished CSP is under continuous supervision to minimize the potential for contact with nonsterile surfaces, introduction of particulate matter or biological fluids, mix-ups with other CSPs, and direct contact of outside surfaces.

4. Administration begins not later than 1 hour following the start of the preparation of the CSP.

5. Unless immediately and completely administered by the person who prepared it or immediate and complete administration is witnessed by another preparer, the CSP shall bear a label listing patient identification information, the names and amounts of all ingredients, the name or initials of the person who prepared the CSP, and the exact 1-hour beyond-use date and time.

6. If administration has not begun within 1 hour following the start of preparing the CSP, the CSP shall be promptly, properly and safely discarded.

   Again, where preparation of a CSP according to low-risk level requirements would subject a patient to additional risk due to the delay, healthcare providers may prepare low-risk level medications and solutions outside of an ISO Class 5 environment, provided the immediate-use provision criteria are met.

   Of the six immediate-use criteria, the requirement that administration begin within one hour of the CSP’s preparation may be the most challenging to meet for anesthesia providers due to daily work flow issues. According to Chapter <797>, it would not be appropriate to prepare multiple medication syringes in the operating room environment at the beginning of the day for later use on patients throughout the day.

   Chapter <797> is silent on the maximum number of hours an immediate-use CSP may be used, provided administration has begun within one hour of the start of preparation. In our opinion, if a practitioner has begun administration of an immediate-use CSP within the one hour requirement, it would be acceptable to continue using that CSP for the same patient for the duration of the procedure for which it was prepared. The CRNA need not dispose of an immediate-use CSPs simply because administration of the immediate-use CSP has not been completed within one hour from the start of its preparation. CRNAs should remain mindful, however, of the continued risk posed to patients due to repeated touch contamination that may occur through repeated dosing of an immediate-use CSP past the one hour timeframe.

   In addition, while preparation of low-risk level CSPs outside of an ISO Class 5 environment may be appropriate in certain circumstances under the immediate-use exception, Mr. Kastango advises that USP Chapter <797> prefers all CSPs be prepared in accordance with at least the preparation standards for low-risk level CSPs whenever
possible. Mr. Kastango believes that it is not the intent of the United States Pharmacopeia that the immediate-use exception be used to exempt common medications and solutions from the safety precautions established for compounding sterile preparations. Instead the immediate-use exception should be reserved for odd doses and uncommon emergency situations where medications and solutions cannot be prepared in an ISO Class 5 environment in accordance with the preparation standards for low-risk level CSPs.

A strict interpretation of Chapter <797> may require common anesthesia medications used for planned cases to be prepared in an ISO Class 5 environment in accordance with the preparation standards for low-risk level CSPs. Thus, in facilities that have elected to comply with <Chapter 797>, anesthesia professionals may find that medications that had previously been routinely prepared at the bedside by anesthesia professionals are now being prepared by the pharmacy or being purchased pre-filled and pre-labeled from the manufacturers.

Enforceability of Chapter 797

As stated above, USP Chapter <797> is not law, but is an accepted guideline for best practices for compounding sterile preparations. With the exception of Chapter <797>, the USP-NF applies to drug manufacturers and is enforceable by the United States Food and Drug Administration (FDA) under authority granted by Congress in the Federal Food, Drug and Cosmetic Act. USP Chapter <797> is unique among the general chapters in the USP-NF because it applies to practitioners and not drug manufacturers. Practitioners, such as pharmacists, physicians, nurses and nurse anesthetists, are not regulated by the FDA, but by their state licensing board and various state laws. Thus, while compounded preparations prepared by practitioners may still be adulterated or misbranded under the Federal Food, Drug, and Cosmetic Act, individual practice and facility policy and procedures do not fall under the federal law and are generally controlled by state law and practice acts.

On this point, the United States Pharmacopeia writes:

Regardless of the recognition of General Chapter <797> in law, the chapter represents a best practice for compounding sterile preparations. Even in the absence of a legal requirement to comply with the chapter, practitioners might chose to review the chapter’s requirements, assess its applicability to their practice, and change their practices and procedures as they deem necessary. These actions may help to protect both practitioner and patient, and may assist the practitioner in maintaining compliance with practice standards.15

Though not law, Chapter <797> may ultimately apply indirectly to anesthesia practice, such as in states where the board of pharmacy requires compliance in all pharmacies, or in situations where an institution has voluntarily adopted a facility-wide policy requiring compliance with Chapter <797>. In addition, accrediting bodies may directly or indirectly require compliance with Chapter <797>.
For example, The Joint Commission’s standards concerning medication preparation are consistent with the immediate-use exception in Chapter <797>. Standard MM.05.01.07 requires that hospitals safely prepare medications. Element of Performance 1 for Standard MM.05.01.07 provides as follows: “A pharmacist, or pharmacy staff under the supervision of a pharmacist, compounds or admixes all compounded sterile preparations except in urgent situations in which a delay could harm the patient or when the product’s stability is short.” The same requirement applies to Joint Commission-accredited critical access hospitals and ambulatory surgery centers if an on-site pharmacy is available. To our knowledge, AANA members are not experiencing problems with this standard during Joint Commission surveys.

The Joint Commission does not directly require its accredited facilities to comply with Chapter <797> (unless local or state laws and regulations require compliance) and does not survey specifically for compliance with Chapter <797>. However, The Joint Commission’s Leadership standards do require facilities to consult current knowledge and information in designing services and processes, which would include an organization’s process for medication management. In addition, the Joint Commission’s Standard MM.08.01.01 for hospitals specifically require hospitals to evaluate their medication management system and to identify opportunities for improvement. In addition to data collection and analysis, hospitals are expected to review “the literature and other external sources for new technologies and best practices” when evaluating their medication management system. (Element of Performance 5, MM.08.01.01.)

On this point, The Joint Commission advised as follows in an April 2006 article in its Perspectives publication:

The Joint Commission requires, as part of standard MM.8.10 [now MM.08.01.01], that organizations evaluate literature for new technologies and successful practices relevant to improving their medication management system. The Joint Commission considers USP 797 a valuable set of guidelines – contemporary consensus-based safe practices – that describe a best practice for establishing safe processes in compounding sterile medications. USP 797 guidelines, while more specific than Joint Commission standards about sterile medication preparation and infection control, can help organizations comply with applicable Joint Commission standards.

This language has led many Joint Commission-accredited organizations to consider policies requiring full compliance with Chapter <797>.

**Implications for Anesthesia**

As stated above, if adopted by institutional policy, Chapter <797>’s guidelines may apply to nurses, nurse anesthetists and physicians who prepare sterile preparations. Many hospital pharmacies, in order to comply with Chapter <797>, are having their pharmacies prepare common anesthesia medications or are outsourcing to medication preparation companies who can provide a wide selection of ready-to-use...
medications commonly used during surgery and anesthesia. Anesthesia professionals in hospitals and other facilities that have adopted Chapter <797> should work closely with the pharmacy to ensure that all opportunities to ensure safe and effective patient care and medication delivery are explored. Regardless of a facility’s approach to Chapter <797>, anesthesia professionals, as with all healthcare providers, should always take care to use proper aseptic technique when preparing sterile preparations.

* Although Eric S. Kastango is a member of the USP Sterile Compounding Expert Committee, he is writing in his individual capacity and not as a member of the Committee or as a USP representative. The views and opinions presented are entirely his own. They do not necessarily reflect the views of USP, and nor should they be construed as an official explanation or interpretation of Chapter <797>.

References:


8. Trissel LA, Ogundele AB, Ingram DS, Saenz CA, Gentempo, JA. Using medium-fill simulation to establish a benchmark microbiological


