

# DRUG TOPICS

## Get ready for new sterile compounding regulations

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### HOME CARE

#### Get ready for new sterile compounding regulations

Pharmacists who compound sterile products need to become familiar with U. S. Pharmacopeia Chapter 797-Pharmaceutical Compounding Sterile Preparations Regulations. The regulations, which become effective Jan. 1, 2004, replace USP Chapter 1206, Sterile Drug Products For Home Use.

The regulations involve sweeping changes from those prior guidelines, according to Eric S. Kastango, R.Ph., MBA, FASHP, president/CEO of Clinical IQ LLC. He recently held an audio conference for members of the National Home Infusion Association (NHIA), entitled Meeting the Future Challenges in Sterile Product Compounding.

"The significance of USP 797 is that chapters that have numbers less than 1,000 can be enforced by the state boards of pharmacy and can be used by the Food & Drug Administration to cite when sterile preparations are contaminated and adulterated. The FDA has the authority to exercise any enforcement actions in the practice of pharmacy in the event of a patient injury or death due to contaminated product," said Kastango. He provided the following landmark cases involving patient injuries or death that resulted from contaminated products:

- In May 2001, a pharmacy in Walnut Creek, Calif., prepared batches of betamethasone and distributed them to a surgical center. The medication was contaminated with *Serratia* bacteria. Over a two-week period, 38 people received spinal injections of the contaminated betamethasone. Five people developed *Serratia* meningitis infections. Three of those patients died as a result of the infection.
- In June 2001, California Contra Costa County health officials and California State Board of Pharmacy inspectors conducted an inspection of a specialty compounding facility. They observed the following: technicians wearing long-sleeved sweaters and jewelry while compounding, poor hand washing technique, failure to wear gloves, the compounding area was not properly segregated—there were open cans of cat food and a tropical fish tank was bubbling and sputtering in the area. They found several environmental locations that contained *Serratia* bacteria.
- In the spring of 2002, a pharmacy in Spartanburg, S.C., prepared and dispensed batches of methylprednisolone to pain management clinics. These batches were contaminated with a fungus known as *Exophiala*. One patient died and four others were hospitalized and treated for a fungal infection.

According to Kastango, the South Carolina Board of Pharmacy found improper performance of an

autoclave, no written procedures, no testing for sterility or appropriate checking of quality indicators as well as clean room practices that failed to measure up to those outlined in ASHP guidelines for pharmacy-prepared sterile products. "The problem is not as widespread as everybody says it is, but we have fundamental challenges and fundamental inconsistencies among practice settings. USP is trying to address these inconsistencies," he said.

Kastango highlighted the critical elements of USP 797, which include the following:

- Compounding conditions. "If you're making sterile products, you must have an ISO Class 8 room, which is a Class 100,000 clean room," said Kastango.
- A quality assurance (QA) program.
- Outcomes monitoring. Kastango said there is concern that compounding operations shipping to several locations don't monitor which patients are receiving the product. This occurred in the South Carolina case. Distribution of the product was so widespread that there was no way to monitor the outcome of the patients to understand how they were responding to the drug and/or the ability to track down the product once an issue was identified, he explained. When the owner of the pharmacy refused to issue a recall, the FDA announced a nationwide recall of every product prepared by this pharmacy.
- Reports and documents. The following questions must be answered: Does the facility have batch records? Are lot numbers being recorded? What components were used in the documented procedures?
- Patient and caregiver training. Nurses and pharmacists who provide care to patients at home need to teach patients how to use and properly store the compounded product.
- Packaging, handling, and transport. Temperature-sensitive products should be handled properly. Products delivered overnight shouldn't sit out under the blazing sun over the weekend. Frozen drugs shouldn't be permitted to defrost. "It is important that products stored at controlled temperatures are not exposed to temperature excursions that could affect their stability," said Kastango.
- Storage and beyond-use dating. *Beyond-use dating* is a new term in USP 797 that means expiration date.
- Finished product release checks and test. To make sure the finished product was prepared correctly, tests must be conducted. They include visual inspections, reviewing the label, and putting injection port seals on the product. Emphasizing that USP 797 doesn't state what an acceptable finished product release check and test is, Kastango said, "We look to the literature and we use good common and professional sense."
- Compounded Sterile Preparation (CSP) work environment. *CSP* is a new acronym appearing in USP 797.
- Equipment. USP 797 details equipment requirements that compounding operations should be using to measure and deliver preparations including parenteral nutrition.
- Aseptic technique processing. "Anybody who makes anything aseptically has to have his or her aseptic technique validated. Pharmacists do not inherently learn good aseptic technique in pharmacy schools. It is an acquired skill and has to be practiced," said Kastango.
- Environmental control and monitoring program. This program includes ensuring a clean environment that is working as intended. "It's important to know the hood is class 100 all the time, that technicians or pharmacists are properly cleaning and sanitizing it, that the air-conditioning system is providing proper temperature and relative humidity and is maintaining proper pressure and providing proper air flow," said Kastango.

- Sterility testing. Kastango said sterility testing is one of the more volatile areas in USP 797. "People say sterility testing has inconsistencies. That's why we have to look at validation procedures. How do you know your process is validated and how do you know you can aseptically prepare that preparation in the hood?"
- Compounding conditions. These include where and how compounded preparations are prepared and what types of components are used, Kastango explained. "Nonsterile or high-risk products have very different requirements from sterile because with nonsterile, you are starting with nonsterile ingredients and the compounding conditions have a great impact on the sterility of the product."
- QA practices. Do you have a routine disinfecting and cleaning procedure? How do you test your environment?
- Visual inspection of CSP. Are you watching your compounders mix? Do they have proper techniques? Are they following policies and procedures?

Kastango advised pharmacists to take the following measures in order to meet the new regulations:

- Compare their current operations with the USP 797 requirements. Identify deficiencies. Develop an action plan to address any deficiencies. Determine risk versus benefit in order to comply.
- Review current operations against state board of pharmacy regulations relative to CSPs to identify possible areas of noncompliance or deficiencies.
- Contact your state board of pharmacy to see how it interprets USP 797 and how it is planning to enforce the requirements.

To obtain a copy of USP 797 in its current form (still with revision marks and edits), contact Lynn Lang at [lfl@usp.org](mailto:lfl@usp.org) or fax (301) 816-8299.

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## History of guidelines involving sterile product compounding preparation

- In 1993, ASHP published its Technical Assistance Bulletin on Quality Assurance for Pharmacy-Prepared Sterile Products.
- In 1996, ASHP conducted a national survey of quality assurance for pharmacy-prepared sterile products. It indicated that few pharmacies were equipped with adequately controlled compounding environments and many pharmacists were not performing critical QA checks by means of environmental monitoring, end product testing, and process validation.
- Effective June 15, 1998, New Jersey became one of the first states to mandate detailed physical plant requirements for all pharmacies preparing sterile drug products.
- In 2000, ASHP revised and published ASHP Guidelines on Quality Assurance for Pharmacy-Prepared Sterile Products.

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