

PRACTICE PEARL

USP <797> Monitoring Guidelines:

Standards for Pharmacy Practice

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Although most pharmaceuticals are mass-produced to meet supply and demand needs, certain medications need to be custom-prepared when they are needed to meet requirements for light, temperature, chemical stability, sterility, etc. Sterility is essential for compounded medications intended for parenteral or sterile routes of administration to ensure medication safety. Safe compounding practices for sterile medications are important to prevent harm to patients from products that are contaminated, are the wrong strength, or are of poor quality. Pharmacists play a key role in developing and initiating safe medication practices to ensure that drug products indicated for sterile administration are prepared according to good compounding practices and that they meet standards of sterility, purity, quality, identity, and strength. They can set up and monitor compounding practices and develop competency checklists, such as that shown in the Table,¹ to help ensure best practices for sterile compounding.

A key development in ensuring safe compounding practices was the United States Pharmacopeia's final release in 2008 of Chapter <797> (USP <797>) Pharmaceutical Compounding—Sterile Preparations, as a set of required standards for the compounding of sterile medications.¹ It is considered an official minimum standard for compounding sterile medications and is enforceable by the FDA, state boards of pharmacy, and other regulatory agencies.² As such, USP <797> mandates procedures and processes for sterile drug compounding of pharmaceuticals in a cleanroom environment and establishes the International Organization of Standards (ISO) requirements for acceptable cleanroom airborne particulate concentrations and assessment procedures. The maintenance of sterility and overall freedom from contamination of a compounded sterile preparation (CSP) depends on environmental quality control specifications, cleanroom monitoring and aseptic sterilization techniques, and appropriate personnel training. This review discusses the components of a program that hospitals need to establish to meet the USP <797> standards and

describes the role of pharmacists in ensuring that these standards are met.

Environmental Quality And Control

Environmental conditions dictate the amount of exposure of the CSP to the immediate environment during processing. Therefore, it is important for conditions to ensure a certain level of quality and control. Total particle counts are designated according to each ISO classification. All certification records are to be maintained and reviewed by a supervising or designated employee to ensure that the controlled environment complies with requirements for air cleanliness, room pressures, and air changes per hour. Recertification should be done every 6 months, with environmental sampling under certain conditions, such as when new facilities are commissioned and certified, facilities are recertified, facilities and equipment are serviced, problems are identified with end products or staff techniques, and infections occur, with the source possibly linked to a CSP or inappropriate compounding practices. One way for hospitals to approach compliance with the USP <797> guideline is by renegotiating their current contract with the vendor to include biannual viable air monitoring, rather than purchasing a personal air sampler and conducting their own tests.

Pressure differential is another important parameter that must be monitored and recorded at least during daily work shifts or by a continuous recording device. The pressure between ISO class 7 and the general pharmacy should not be less than 5 Pascal (Pa). Also, the airflow between the buffer area and ante area where low- and medium-risk CSPs are prepared should be maintained at a minimum velocity of 0.2 m per second.

If the cleanroom has been constructed to prepare medium-risk products only but occasionally receives orders for high-risk sterile products, the hospital may want to consider formulary changes or searching for an outside vendor that has the capability to provide high-risk sterile products in a timely manner.

It is acceptable for institutions that prepare a low volume of hazardous sterile preparations (chemotherapy) without a negative pressure room to use a compounding aseptic containment isolator or biological safety cabinet along with a closed-system transfer device. These institutions must have 2 levels of containment to prepare hazardous product in a non-negative pressure area.

Cleanroom Monitoring and Aseptic Sterilization Techniques

Proper cleaning procedures are essential for sterile compounding. The surfaces and air quality that can come in contact with the materials used to compound must be free of any pathogens or debris that can compromise the integrity of the final product.

In an ISO class 5 area, cleaning and disinfecting before any compounding begins should be done with sterile water and nonshedding wipes (eg, composed of synthetic microfibers) and/or followed by wiping with residue-free disinfecting agents, such as sterile 70% isopropyl alcohol. The recommended frequency for cleaning the ISO class 5 area should be at the onset of each shift; before each batch, if there is a known surface contamination; after spills; and every 30 minutes following previous disinfection during ongoing compounding activities.

In ISO class 7 buffer areas, ISO class 8 ante areas and segregated compounding areas, cleaning and disinfecting should be done daily. When necessary, clearing of dust and debris from storage sites for compounding supplies should be done with caution to preserve air quality. Other daily tasks include cleaning counters, work surfaces, and floors with cleaning and disinfecting agents and a nonshedding mop. Walls, ceilings, and storage shelving should be cleaned monthly according to American Society of Health-System Pharmacists (ASHP) recommendations.³

One way to ensure cleanliness and a sterile environment within a cleanroom is to request that environmental management services (EMS) assign staff trained in cleaning operating suites and other highly sensitive areas

to clean the IV cleanrooms. Also, creating log sheets for EMS staff to initial when they have completed their daily and monthly cleaning, in addition to pharmacy staff cleaning, will help keep track of these procedures.

Personnel Testing

According to USP <797>, compounding personnel are responsible for maintaining quality control over the products they compound by practicing proper aseptic techniques and perfecting the skills necessary to ensure that CSPs are correctly identified, measured, diluted, mixed, purified, sterilized, packaged, sealed, labeled, stored, dispensed, and distributed.¹ Personnel who are to handle CSPs are required to undergo adequate training and pass written competency assessments and media-fill tests of aseptic manipulative skills. For initial training, it is recommended that personnel watch the ASHP video, "Quality Assurance for Pharmacy-Prepared Sterile Products," and then undergo an assessment. For personnel who compound low- and medium-risk CSPs, testing must be done at least annually; for those who compound high-risk CSPs, testing should be semiannual.

Maintaining appropriate cleanliness also is important for personnel. They must be able to demonstrate how to clean all internal components of the IV cleanroom hood using the proper technique and products. They also must demonstrate that they are able to correctly select appropriate syringe/needle sizes and be aware not to touch the syringe tip, plunger, or barrel. All items must be placed in the hood before compounding is started, and a distance of 6 inches must be kept from the edge to avoid any obstruction of air flow. CSP labeling requirements such as name and identification number, ingredient names, amounts, strengths, concentrations, expiration dates, administration regimens, auxiliary labels, and storage requirements all are basic guidelines personnel should be aware of when compounding.

Garbing and gloving competency needs to be documented, assessed, and maintained. Evaluation involves visual observation. Proper technique involves removing all jewelry, wearing appropriate clean attire, and thoroughly washing hands and arms up to the elbows.

For glove fingerprint sampling, sterile contact agar plates in which successful completion equals zero colony-forming units should be used to evaluate garbing and hand-washing techniques for all compounding risk levels. This should be done no less than 3 times prior to the worker initially being allowed to compound. After the initial assessment, it

should be performed again once a year for low- and medium-risk levels or semi-annually for high-risk levels.

Aseptic manipulation competency evaluation media-fill testing should be done during media-fill test procedures. Testing should reflect the most challenging/stressful conditions that will be encountered during preparation. An initial media-fill test should be conducted and then additional testing should be done annually for low- and medium-risk levels, and semiannually for high-risk levels.

Garbing, hand hygiene, environmental cleaning and disinfecting performed by compounding staff should be visually evaluated for competency and the results should be documented. Periodic surface sampling of defined ISO-classified areas

should be conducted at the completion of a compounding shift, and the results should be maintained and recorded in the pharmacy. Evaluations should be done during initial training of personnel, after completion of any media-fill test procedure, and when staff changes.

One way to ensure that personnel training meets these standards is by designating a technician and a pharmacist to be accountable for tracking and monitoring all quality assurance recommendations associated with USP <797>, such as maintaining staff competency, performance improvement projects, and environmental quality assurance logs.

Conclusion

Pharmacists are in a prime position

to ensure that USP <797> standards are adhered to for sterile drug compounding in health-system facilities. Their skills in pharmacotherapy help to ensure safe compounding practices to enforce the USP <797> environmental and competency standards required of pharmacy and hospital personnel. Pharmacist oversight of this area to ensure compliance and best standards of practice in sterile drug compounding, administration, and storage will promote patient safety.

References

1. The United States Pharmacopeial Convention. USP Chapter 797 Pharmaceutical Compounding – Sterile Preparations. In USP 31/NF 26;2008. Rockville, MD.

2. Traynor K. JCAHO Offers Guidance, Timeline of USP 797 Compliance. 2004. <http://www.ashp.org/import/news/HealthSystemPharmacyNews/newsarticle.aspx?id=1684>. Accessed January 26, 2011.
3. American Society of Health-System Pharmacists in collaboration with Baxter Healthcare Corporation. The ASHP Discussion Guide on USP Chapter 797 for Compounding Sterile Preparations. http://www.ashp.org/s_ashp/docs/files/HACC_797guide.pdf. Accessed March 28, 2011.
4. Huynh T, Jalundhwala Y, Subramaniam V. Hazardous drugs—maintaining standards of safe pharmacy practice. *Pharmacy Practice News*. 2010;37(12):4-6.

This article was written by the authors in their private capacity. No official support or endorsement by the VA is intended or should be inferred.

Table. Pharmacy Competency Checklists for Meeting USP <797> Standards for Sterile Compounding

Standard Area	Task/Test	Expectations (USP <797>; USP 33/NF 28; 2010)	Frequency (USP <797>; USP 33/NF 28; 2010)	Date/Time Completed
Environmental Quality and Control	Total particle counts	<ul style="list-style-type: none"> • ISO class 5, 7, and 8 classified areas and any of the PECs • All certification records shall be maintained/reviewed by a supervising or designated employee 	<ul style="list-style-type: none"> • Every 6 mo for recertifications and whenever any alteration/relocation is done to the environment/equipment 	
	Pressure differential monitoring	<ul style="list-style-type: none"> • Pressure from ISO class 7 to pharmacy shall be >5 Pa • Airflow between buffer and ante area where low- and medium-risk CSPs are prepared shall be a minimum velocity of 0.2 m/sec 	<ul style="list-style-type: none"> • Recorded every shift (minimum at least daily) or by continuous recording device 	
	Temperature and humidity monitoring	<ul style="list-style-type: none"> • Provide a temperature and relative humidity sensor in each buffer room to monitor these 2 environmental parameters 	<ul style="list-style-type: none"> • Continuous monitoring • Temperature ≤68° F (20° C) • Relative humidity range between 30% and 60% 	
	Viable air sampling with appropriate growth media	<ul style="list-style-type: none"> • Performed at locations prone to contamination, with impaction preferred for volumetric air collection 	<ul style="list-style-type: none"> • Every 6 mo as part of the recertification of facilities/equipment 	
Cleaning	ISO class 5 primary engineering control (LAFW, BSC, CAI, CACI)	<ul style="list-style-type: none"> • Cleaning and disinfecting all areas before compounding using recommended disinfectants and materials 	<ul style="list-style-type: none"> • At onset of each shift, before batches, after spills or surface contamination, every 30 min during compounding activities 	
	Counters/work surfaces/floors	<ul style="list-style-type: none"> • Appropriate cleaning and disinfecting agents 	<ul style="list-style-type: none"> • Daily 	
	Walls/ceilings/storage shelving	<ul style="list-style-type: none"> • Appropriate cleaning and disinfecting agents 	<ul style="list-style-type: none"> • Monthly 	
Personnel Testing	Initial training/demonstration: didactic training, written test, observational skill assessment, and media-fill testing	<ul style="list-style-type: none"> • All personnel should view the ASHP video “Quality Assurance for Pharmacy-Prepared Sterile Products” and take assessment, demonstrate appropriate cleaning, manipulation and placement of materials and components within IV cleanroom hood, and be familiar with CSP labeling requirements 	<ul style="list-style-type: none"> • Prior to being allowed to prepare CSPs and during regular interval assessments 	
	Glove fingerprint sampling	<ul style="list-style-type: none"> • Sterile contact agar plates shall be used to evaluate competency of garbing and hand-washing techniques • Successful completion = zero CFU 	<ul style="list-style-type: none"> • Complete 3 successful tests before compounding CSPs for human use, then: <ul style="list-style-type: none"> -Annually (low- and medium-risk CSPs) or -Semiannually (high-risk CSPs) 	
	Garbing and gloving competency evaluation	<ul style="list-style-type: none"> • Observe performing appropriate hand hygiene and garbing procedures (remove all jewelry, wear appropriate attire, and cleanse hands/arms/elbows) 	<ul style="list-style-type: none"> • Regular visual observation to be documented, maintained, and assessed 	
	Aseptic manipulation competency evaluation media-fill testing	<ul style="list-style-type: none"> • Performed during media-fill test procedures that represent the most challenging/stressful conditions after successful completion of garbing and gloving competency • Maintain records of evaluation 	<ul style="list-style-type: none"> • Before compounding sterile products, then: <ul style="list-style-type: none"> -Annually (low- and medium-risk CSPs) -Semiannually (high-risk CSPs) 	
	Cleaning and disinfecting competency evaluation	<ul style="list-style-type: none"> • Visual observation shall be documented and maintained for long-term assessment 	<ul style="list-style-type: none"> • Initial training on cleaning procedures • Changes in staff • Completion of any media-fill test procedure 	
	Surface cleaning and disinfecting	<ul style="list-style-type: none"> • Surface sampling performed in all ISO classified areas 	<ul style="list-style-type: none"> • Performed periodically (results as CFU/surface area unit) 	

ASHP, American Society of Health-System Pharmacists; BSC, biological safety cabinet; CACI, compounding aseptic containment isolator; CAI, compounding aseptic isolator; CFU, colony-forming units; CSP, compounded sterile preparation; ISO, International Organization of Standards; LAFW, laminar air-flow workbench; PECs, primary engineering controls. Based on reference 1.