

A Practical Guide to Aseptic Technique Verification: Policies and Procedures that Meet USP Chapter <797> Requirements

By Eric S. Kastango, RPh, MBA, FASHP

ENSURING THAT PERSONNEL MAINTAIN GOOD ASEPTIC TECHNIQUE DURING all phases of the compounding process is critical to the sterility of the final CSPs (compounded sterile preparations). Good aseptic technique requires that personnel be properly trained through a didactic review of the principles of contamination control, and that they successfully demonstrate knowledge and skill through written and aseptic technique verification tests. Training will create a sense of importance, vigilance, and employee responsibility that helps to establish a culture of quality.

Verifying an Employee's Aseptic Technique

Media-fill testing involving the manipulation of a suitable growth media (tryptic soy broth) represents one of the most objective methods of evaluating an employee's knowledge and skill in asepsis. A media-fill or process-simulation test mimics an actual and entire compounding procedure, using a suitable growth medium, such as tryptic soy broth (TSB), in place of the typical ingredients to prepare a finished compounded preparation. According to USP Chapter <797>, media-fill testing also represents the most challenging or stressful conditions actually encountered by the personnel being evaluated when they prepare a compounded sterile preparation. In addition to verifying an individual's ability, process-simulation testing can also be used to evaluate and identify the capabilities and weakness of aseptic compounding procedures that could contribute to the inaccuracy and/or contamination of the compounded sterile preparation. Using the Parenteral Drug Association's Technical Report No. 22 (published in 1996) as a basis, a properly designed process-simulation test will be able to:

- Demonstrate the capability of the aseptic procedures to produce sterile, pharmacy-compounded preparations
- Qualify, certify, and validate the aseptic technique of all pharmacy compounding personnel. (Anyone who prepares compounded sterile preparations, whether pharmacists or technicians, must be aseptically verified.)
- Meet the verification and sterility-testing requirements for compounded sterile preparations, as detailed in USP Chapter <797>

Verification of aseptic technique and aseptic procedures is based on this concept: When a growth medium is contaminated during the compounding process, it will support the growth of microorganisms introduced by the operator. A suitable growth medium must be used (i.e., soybean casein digest media or TSB) to support the types of microbes typically found in operator-contaminated sterile preparations. TSB is a good "all-purpose" growth medium that will support the growth of a large variety of pathogenic microorganisms. Any TSB purchased from a vendor should have with it a certificate of analysis (COA) and a growth promotion certificate. A COA certifies the contents of the solution and the growth promotion certificate certifies that the medium will be able to support the growth of microorganisms like staph, E. Coli, and others.

The amount and frequency of media-fill runs is a controversial topic. Currently, USP Chapter <797> does not specify the number of media-fill units required to verify an employee's aseptic technique. The only stipulation is that it has to occur at least once a year for low- and medium-risk compounding and at least twice a year for high-risk compounding. It is important to consider the volume of compounded sterile products (CSPs)



Q.I. Medical's PATT (Personal Aseptic Technique Test) kits use the media-fill challenge method described in USP Chapter <797>.

being prepared for each compounding procedure, the number of patients that could receive CSPs prepared from the same batch, the complexity of the compounding procedure, the equipment being used, and the physical environment where the compounding is being conducted.

Best practices (as adopted from those performed by pharmaceutical manufacturers) involve verification procedures that are conducted over three consecutive batches or days. The initial media-fill verification could be performed daily for three days, testing the operator's technique for consistency and reproducibility and eliminating results skewed by chance or by the Hawthorne Effect. The Hawthorne

Effect is an initial improvement in a process caused by the obtrusive observation of that process. The effect was first noticed in the Hawthorne plant of Western Electric. Production increased not as a consequence of actual changes in working conditions introduced by the plant's management, but because management demonstrated interest in such improvements.

It may be reasonable to consider additional (quarterly) media-fill runs. Whatever the frequency, number, and results of media-fill units (MFUs) performed, the results must be documented. This documentation becomes an integral part of the pharmacy aseptic QA program. Media fills should not be performed during normal production, but rather immediately after daily production activity under worst-case conditions when microbial bioburden is at the highest level (at the end of a busy day). The suitable growth media (TSB) should not be used while sterile products are being prepared because of the potential for cross-contamination and dispensing errors (such as cases in which media-fill units are accidentally labeled and sent to patients for infusion). Aseptic technique verification kits, as well as their individual components, can be purchased and used to verify the aseptic ability of compounding personnel, as well as the effectiveness of certain procedures and/or compounding devices.

Aseptic Technique Verification Kits

Some aseptic technique verification kits are limited only to the use of

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ampules, vials, and syringes. Although these kits produce a valid representation of aseptic technique for ampule- and vial-transfer activities, many do not include aseptic manipulations performed in most pharmacy operations. Other methods may be required to mimic the range of activities performed in pharmacies that compound sterile solutions. Ideally, a media-fill procedure should incorporate all of the typical and multiple manipulations performed by both people and devices. This may include using syringes, ampules, vials, media-fill bags, transfer tubing, and empty

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bags for the administration of intravenous medication, and the use and sterilization of nonsterile tryptic soy powder to mimic the compounding of a sterile preparation from powder (narcotics and/or anesthesia formulations like morphine, baclofen, buvipicaine, fentanyl, and any combination thereof). A media-fill procedure should also be performed to simulate the preparation of parenteral nutrition using an automated compounding device.

Growth media (bulk bottles of solution and nonsterile powders) and media test kits can be obtained from vendors such as

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bioMérieux and Lab Safety Corporation (Valiteq). It is important to note that any purchased media must have a certificate of analysis and meet the requirements of USP's Growth Promotion Standard.

Sample Media-Fill Procedure

One MFU can be prepared by the following method, which might simulate a medium-risk batch-compounding procedure:

- Use a 20-gauge needle (not a filter needle) attached to a 5-ml syringe to withdraw 1 ml of sterile, preservative-free water from a glass ampule and inject the water into each of two TSB bags.
- Make five additional and separate 1-ml withdrawals from a vial of sterile, preservative-free water and inject the water into each TSB bag, five separate times.
- Transfer the contents of both TSB bags via a Y-type transfer set into an empty bag used for the administration of intravenous medications.
- Clamp the tubing of the transfer set, crimp the tubing to seal it, cut the tubing, and incubate the bag for 7 days at room temperature and then for 7 days in an incubator at a temperature between 30°C and 35°C.

The directions for use of the manufacturers of media-fill test kits must be carefully followed. However, the MFU must be incubated according to the following guidelines from USP <797>: seven days at room temperature, followed by seven days at a temperature between 30°C and 35°C, or 14 days at room temperature (25°C to 35°C). There are media fill kits on the market that incorrectly say that the media only needs to be incubated for seven to 10 days, which is less than the required 14-day period published in USP. The reason that the incubation period is



The Valiteq RL-2 Validation Kit from Lab Safety Corporation simulates a wide range of compounding challenges, utilizing a variety of packaging systems and tools.

Photo courtesy of Lab Safety Corporation

so critical is that microbial contamination is not visible when viewed with the naked eye until 1,000,000 (1x10⁶) CFUs have formed. The incubation period is crucial and has been designed to ensure that one viable microbial-colony-forming unit would replicate to greater than 10⁶ CFUs.

Ideally, MFUs should be read daily, but they must be read on day seven (the last day of room temperature incubation) and day 14 (the last day of incubator incubation). Cloudiness or turbidity indicates a media-positive (contaminated) bag. The information needs to be documented on a media-fill log and retained in the employee's training file. Personnel should not be permitted to compound sterile preparation for use by patients until they can successfully pre-

pare MFUs that exhibit no microbial growth.

Summary

Implementing an aseptic technique verification policy and procedure is not only required by USP Chapter <797>, but it also provides objective and measurable confirmation that an employee is capable of aseptically preparing a compounded sterile preparation. It can be a method to get employees to embrace the necessary changes required by <797> and to take greater pride in the critical work they do to ensure patient safety. **R&P**

Through his New Jersey-based consulting company, Clinical IQ, Eric Kastango, RPh, MBA, FASHP, provides expertise in aseptic processing, medical-device manufacturing, and the implementation of extemporaneous compounding-quality systems. He is also a pharmacy surveyor for the Accreditation Commission for Health Care, Inc.

Additional Reading and Resources:

- Parenteral Drug Association www.pda.org
- Halls NA. Practicalities of Setting Acceptance Criteria for Media Fill Trials. *J Pharm Sci Tech.* 54; May/June 2000: 247-252.
- Kastango ES. In: EC Buchanan, PJ Schneider, eds., *Compounding Sterile Preparations, 2nd edition.* Bethesda, Md: ASHP; 2004: Chap 20—End-Preparation Evaluation.
- Kastango ES. In: EC Buchanan, PJ Schneider, eds., *Compounding Sterile Preparations, 2nd edition.* Bethesda, Md: ASHP; 2004: Chap 20—Process Validation.
- Kastango, ES, Douglass, K. Quality Assurance for Sterile Products. *Int J Pharm Compd.* 2001; 5: 246-253.
- Kawamura K and Abe H. Consideration of Media Fill Tests for Evaluation and Control of Aseptic Processes: a statistical approach to quality criteria. *J Pharm Sci Tech.* 56; Sept/Oct 2002: 235-241.

Where to find it:

- bioMérieux
Circle reader service #23 or
visit www.biomerieux-usa.com
- Lab Safety Corporation
Circle reader service #82 or
www.valiteq.com
- Q.I. Medical
Circle reader service #85 or
www.qimedical.com