Evaluating the Sensitivity of a Media-Fill Challenge Test Under Various Situations as a Reliable Method for Recommended Aseptic Technique Competency Assessment

Journal of Pharmacy Technology
2016, Vol. 32(2) 47–53
© The Author(s) 2015
Reprints and permissions:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/8755122515607537
pharmatech.sagepub.com

Colleen A. Moody^{1,2}, Stephen F. Eckel, PharmD, MHA, BCPS, FASHP, FCCP, FAPhA^{1,2}, and Lindsey B. Amerine, PharmD, MS, BCPS^{1,2}

Abstract

Background: Microbial contamination of compounded medications is a serious concern within hospital pharmacies as it can lead to severe patient injury. The United States Pharmacopeia <797> mandates that pharmacy personnel responsible for preparing compounded sterile preparations must annually demonstrate competency in aseptic technique by performing a media-fill challenge test. **Objective:** The purpose of this study is to evaluate the sensitivity of a commonly used media-fill test through proper and improper compounding techniques. **Methods:** Two aseptically trained pharmacy technicians performed media-fill challenge testing by carrying out 5 separate manipulations 5 times each for a total of 25 trials. Sterile vials, syringes, and intravenous bags were prepared. The first manipulation followed best-practice aseptic technique and sterile compounding procedures. Each of the following 4 manipulations removed one aspect of best-practice aseptic technique. The prepared products were incubated at 20°C to 25°C. A positive result for microbial contamination is indicated by visible turbidity within the vials, syringes, and intravenous bags at the following check points: 24 hours, 72 hours, 7 days, 14 days, 21 days, and >30 days. **Results:** Twenty-five trials, each containing 10 distinct admixtures, resulted in a total of 250 compounded preparations. No single preparation showed signs of turbidity, sedimentation, or visible microbial growth at any of the 6 checkpoints yielding a 0% contamination rate. However, the positive controls inoculated with bacteria did have positive microbial growth results. **Conclusion:** A more sensitive test needs to be developed to provide assurances that all poor aseptic practices are detected in compounding personnel.

Keywords

drug compounding, oncology, sterile technique, sterile products, chemotherapy

Background

The United States Pharmacopeia (USP) and the American Society of Health-System Pharmacists (ASHP) began providing professional mandates and practice assistance to pharmacists and pharmacy technicians responsible for preparing compounded sterile preparations (CSPs) in the early 1990s. The initial guidelines developed included USP <1074>: Dispensing Practices for Sterile Drug Products; USP <1206>: Sterile Products for Home Use; and ASHP Technical Assistance Bulletin: Quality Assurance for Pharmacy-Prepared Sterile Products. However, these did not produce significant changes to sterile compounding practices.¹ The first set of official and enforceable sterile compounding standards and procedures, USP Chapter <797>: Pharmaceutical Compounding—Sterile Preparations, took effect on January 1, 2004, in an effort to improve compliance. The standards set forth in USP <797> apply to all locations and individuals preparing CSPs.¹

USP <797> mandates that pharmacy personnel complete CSP training instructed by experienced staff who have previously demonstrated competency in aseptic technique. Aseptic technique requires that individuals follow best-practice garbing and cleansing procedures and employ the appropriate strategies while compounding sterile products to ensure systematic and deliberate preparation of CSPs in an effort to avoid contamination or environmental and personnel exposure and maintain appropriate and adequate airflow. The use of audiovisual resources and didactic training serve as supplements to hands-on training. Newly hired

¹University of North Carolina (UNC) Hospitals, Chapel Hill, NC, USA

²UNC Eshelman School of Pharmacy, Chapel Hill, NC, USA

Corresponding Author:

Lindsey B. Amerine, University of North Carolina Hospitals, 101 Manning Drive, CB 7600, Chapel Hill, NC 27514, USA.

Email: Lindsey.Amerine@unchealth.unc.edu

personnel must be trained in the cleaning and disinfection practices of compounding areas, appropriate and thorough hand cleansing, and proper technique for garbing in personal protective equipment (PPE). Additionally, personnel must pass a written assessment, observational evaluation, and media-fill challenge test demonstrating competency in aseptic technique. Thereafter, USP <797> mandates personnel complete these tests annually for low- and medium-risk-level compounding and semiannually for high-risk-level compounding.² Specific training, retraining if personnel fail the assessments, and performance evaluations must be documented for any individual involved in the preparation of CSPs in all of the competencies described above.²

The contamination rates for CSPs prepared within International Organization for Standardization (ISO) Class 5 hospital environments while employing proper aseptic technique have been shown to be less than 2.2 contaminated preparations per 1 million total preparations.³ Previous researchers have expressed concern regarding the reliability of this risk level and sensitivity of media-fill challenge testing.⁴ Media-fill challenge testing of compounding personnel can only prove personnel have the ability to compound one or more sterile preparations at a specific point in time. Statistically speaking, ISO recommends that at least 3000 products be compounded to detect with 95% confidence a contamination rate of 0.1% (1:1000), the minimum sterility goal for aseptic compounding.³ Within hospital pharmacies, the total number of sterile preparations compounded by a single technician daily and the media-fill challenge testing systems employed to validate aseptic technique fall well below the recommended value. While all compounding personnel who fail a media-fill challenge test must be retrained and reevaluated, a 0% failure rate for human operators does not represent a realistic and consistently reproducible goal.⁴ In addition, it might put a false sense of safety that overall technique is appropriate when media-fill tests are negative. Of further concern is the improbable, yet commonly reproducible incidence of absolutely no contamination when media-fill challenge tests are performed within an ISO Class 5 environment.^{3,5}

Using a method similar to the testing method utilized in this study, Stucki et al evaluated the role that high-risk manipulations of aseptic technique play in compromising sterility.⁶ Their findings revealed that high-risk manipulations only conferred contamination when the manipulations took place outside of an ISO Class 5 horizontal laminar-airflow hood in an ISO Class 6 clean room environment, and the manipulations producing the most contaminated CSPs were due to contact between the sterile hub of the syringe and either an unsterile object or ungloved fingers.⁶ Stucki et al found that 6% of CSPs prepared in the operating room and 16% of CSPs prepared on a hospital ward conferred contamination versus no contaminated preparations in a hospital cleanroom.⁶ However, holding all other aspects

of the preparation constant, when septa of media-fill challenge vials were intentionally contaminated with a microbe sensitive to alcohol disinfection and commonly found on dry skin, only the products prepared using inappropriate aseptic technique yielded contamination at a rate of 2.3%. All of the preparations, both those employing appropriate and inappropriate aseptic technique, were prepared in an environment without a HEPA filter but with low air microbial contamination.³ In direct contrast to these findings, Trissel and colleagues demonstrated higher rates of contamination for CSPs prepared within a cleanroom (5.2%) than those prepared in a non-cleanroom environment (<0.1%) through 2 independent studies.^{5,7,8}

In addition, it has been determined that contamination rates of untrained and inexperienced compounding operators can be up to 6.9% higher than their respective properly trained and experienced operators.⁹ These findings illustrate that end-product contamination has more to do with aseptic technique accuracy and competency than with engineering controls providing even more of a basis for use of an accountable and accurate sterility test.

Institutional Practice

Our institution compounds all sterile products, nonhazardous and hazardous, in accordance with USP <797> standards. Hazardous drugs are compounded within a biological safety cabinet (BSC) with air quality of ISO Class 5 located within an ISO Class 7 cleanroom environment. Sterile compounding training lasting from 6 to 8 weeks is provided to all pharmacy technicians responsible for preparing nonhazardous and hazardous CSPs. The training program consists of didactic training, audiovisual instructional training, computer-based learning, and practical training targeted toward aseptic technique, cleaning, and disinfecting compounding areas, hand cleansing, and garbing technique. On completion of the training program, technicians must demonstrate competency in all of the aforementioned tasks through written and practical exams utilizing media-fill kits under the mandated engineering controls and PPE recommendations. Thereafter, media-fill testing is assessed at least annually to ensure the sterility of the low- to medium-risk preparations our institution is responsible for compounding.

Our institution's policy on the handling and disposal of hazardous drugs further imposes mandates on the proper preparation and handling of hazardous CSPs. This policy requires that 2 pairs of sterile chemoprotective gloves be worn and closed system transfer devices (CSTDs) used while preparing hazardous CSPs. Additionally, the BSCs are lined with plastic-backed absorbent pads.

The ChemoTEQ Hazardous Substances Containment/Aseptic Technique Validation System: Hazardous Substances Compounding Validation Kit, a type of media-fill challenge testing system, is used to validate aseptic

technique after completion of practical training prior to the technician preparing hazardous CSPs in a “live” position and then annually to ensure competency is maintained. However, while following recommended best practices for preparing CSPs, no pharmacy technician at our institution has ever produced a positive result for microbial contamination during their media-fill challenge assessments. This includes numerous pharmacy technicians with various expertise in aseptic technique. This raises the question of what degree of aseptic technique deficiency is necessary to produce a positive result using the media-fill challenge test and whether the test is sensitive enough to detect poor aseptic technique among pharmacy personnel preparing CSPs without conducting 3000 manipulations per technician.

Purpose

The goal of this study is to determine the sensitivity of a widely used media-fill challenge test, ChemoTEQ, by objectively assessing the results of the test through proper and improper sterile compounding techniques in an effort to ensure that the recommended testing strategy meets the desired goal of assessing individual aseptic technique competency. This study will investigate whether it is possible to introduce a detectable level of microbial contamination to a CSP by changing different parameters and testing conditions since human error due to deficient aseptic technique is the main source of CSP contamination. The purpose behind media-fill challenge testing is to prove that pharmacy personnel are adept at preparing sterile compounds. As such, a media-fill challenge testing system should be able to detect blatant deviations from the accepted standards of aseptic technique and sterile compounding procedures. This study utilized 2 hospital pharmacy technicians each having completed didactic and practical aseptic technique and sterile compounding procedure training and verification as mandated by institutional practices.

Methods

USP Recommendations for Aseptic Techniques

Recommended by USP <797> and the US Food and Drug Administration through the Current Good Manufacturing Practices (CGMPs), media-fill challenge testing is used to assess aseptic technique. USP <797> and the CGMPs outline criteria for appropriate testing conditions, media type selection, incubation environment and length, and contamination evaluation and visual interpretation. Testing must be completed in an environment that is analogous to the challenges and stress level faced under standard operating procedures.^{2,10} The growth media selected must promote growth

of gram-positive and gram-negative bacteria, yeast, and mold. All compounded media preparations should be incubated for no less than 14 days under temperatures ranging from 20°C to 35°C. Media preparations should be visually examined for microbial contamination by personnel with appropriate education, training, and experience in inspecting media preparations. Clear containers should be employed to allow for visual detection of microbial growth.¹⁰

Media-fill kits are available commercially and consist of sterile fluid culture media with the ability to promote the exponential colonization of microbes if contaminated with pathogens that are commonly transmitted by compounding personnel to CSPs.¹¹ A positive result for microbial contamination is indicated by visible turbidity within the vials or bags at the following check points: 24 hours, 72 hours, 7 days, or 14 days. The vials and bags are kept at temperatures of 20°C to 25°C or 30°C to 35°C during the incubation period.²

Study Methodology

Media-fill challenge testing using ChemoTEQ Hazardous Substances Containment/Aseptic Technique Validation System: Hazardous Substances Compounding Validation Kit was conducted to determine potential microbial contamination while preparing hazardous CSPs. This particular media-fill challenge test complies with USP <797> and the FDA recommended CGMPs, as well as one utilized by our institution.^{2,10} The sterile fluid culture media used was double-strength trypticase-soy broth (2X TSB) shown to promote the growth of many common aerobic and facultative anaerobic microorganisms, including *Bacillus subtilis*, *Candida albicans*, and *Aspergillus niger*. The broth also contains a noninhibitory color tracer additive used to verify containment technique of CSP personnel. The ChemoTEQ Kits* were received from the manufacturer with the certificate of performance indicating USP growth performance standards have been met.¹² Additionally, the 2 pharmacy technicians completing the study visually inspected the shipping container for any loss of integrity; the media-fill vials and ampules for breakage, contamination, and discrepancy in color; and the media-fill kit as a whole for an appropriate expiration date. The compounding supplies not included in the ChemoTEQ kits but necessary to complete the study were received through the pharmacy wholesaler. Baxter manufactured the evacuated containers, intravenous (IV) administration sets, dispensing pins, and normal saline. BD manufactured the syringes and needles. MediChoice manufactured the sterile 70% isopropyl alcohol (IPA) and

*ChemoTEQ Hazardous Substances Containment/Aseptic Technique Validation System: Hazardous Substances Compounding Validation Kit. Cumberland, WI: Lab Safety Corporation (Lot Numbers: 0307301301 and 0307171303).

Figure 1. Overview of the media-fill challenge manipulations.

gloves. Hospira manufactured the sterile water for injection (SWFI), and Covidien manufactured the gowns. No issues were identified with any of the compounding products or supplies used to conduct this study.

Sterile vials, syringes, and IV bags were prepared without the use of CSTDs by 2 aseptically trained pharmacy technicians who had previously passed the required competency assessments of our institution. A total of 25 trials were carried out consisting of 5 separate manipulations (Figure 1) performed 5 times each. The trials were carried out within the ISO Class 7 cleanroom of a hospital pharmacy on a weekday during regular operating hours. This arrangement was intended to simulate the challenging and stressful conditions encountered during actual operations as closely as possible. The first manipulation followed best-practice and recommended aseptic technique and sterile compounding procedures, as defined in the appendix, with each of the 4 remaining manipulations removing one aspect of best-practice and

recommended aseptic technique and sterile compounding procedures. Once an aspect was removed, it was not returned to the manipulation. The 5 manipulations were (1) the use of recommended best practices, (2) without the use of sterile 70% IPA in the form of a spray or swab, (3) without the use of gloves (2 pairs of chemoprotective gloves are used to compound hazardous drugs, neither of which were used) along with manipulation 2, (4) within an ISO Class 7 cleanroom without the use of an ISO Class 5 BSC along with manipulations 2 and 3, and (5) after the vials containing the growth medium were stored without easy removal caps, outside of a sterile cleanroom, and in air quality greater than ISO Class 8 along with manipulations 2, 3, and 4. Aside from these manipulations, the 2 technicians followed proper aseptic technique and the operational steps outlined in the appendix to carry out all 5 manipulations.

Each of the 25 trials consisted of 13 transfers and produced 10 media-fill admixtures (1 IV bag, 3 vials, and 6

Table 1. Contamination Rates of the Media-Fill Challenge Preparations.

	Contamination Rate					
	24 Hours	72 Hours	7 Days	14 Days	21 Days	>30 Days
Manipulation 1 (n = 50)	0%	0%	0%	0%	0%	0%
Manipulation 2 (n = 50)	0%	0%	0%	0%	0%	0%
Manipulation 3 (n = 50)	0%	0%	0%	0%	0%	0%
Manipulation 4 (n = 50)	0%	0%	0%	0%	0%	0%
Manipulation 5 (n = 50)	0%	0%	0%	0%	0%	0%

syringes) for a total of 250 compounded products. The 250 final preparations were incubated at temperatures between 20°C and 25°C. A positive result for microbial contamination is indicated by turbidity or nonresoluble sedimentation within the vials, syringes, and IV bags containing the test medium at any checkpoint on or before the 14-day incubation period as defined by the ChemoTEQ system.¹² The vial, syringe, and IV bag compounded preparations were inspected at the following checkpoints: 24 hours, 72 hours, 7 days, 14 days, 21 days, and >30 days.

To serve as a positive control, the vials of 2X TSB from 8 media-fill challenge kits from the same manufacturer and lot numbers used in this study were inoculated with gram-positive and gram-negative bacteria commonly found on the skin and hands: *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. Each bacterium was prepared for inoculation through 6 serial dilutions starting with a 0.5 McFarland standard. Two vials of test media were inoculated each with 0.1 mL from 3 distinct dilutions containing 10^{-4} , 10^{-5} , and 10^{-6} of each microorganism per milliliter. Additionally, one vial of test media was inoculated with 0.1 mL of the original 0.5 McFarland standard containing 10^7 microorganisms per milliliter. These procedures were completed for each of the 4 bacteria being tested for a grand total of 28 contaminated samples. All of the contaminated vials were incubated at temperatures between 20°C and 25°C and inspected for colonization at the same time checkpoints of the compounded, noncontaminated vials. The positive controls were not subjected to the ChemoTEQ process outlined in the appendix. They simply served to demonstrate that the 2X TSB within the undiluted vials of the test kits could in fact grow common gram-positive and gram-negative strains of bacteria at varying concentrations.

Results

The current study was performed to evaluate the sensitivity of a widely used media-fill challenge test in ascertaining the competency of pharmacy personnel in aseptic technique. Each of the 25 trials consisted of the preparation of 10 distinct admixtures. Of the 250 combined preparations across the 5 manipulations, no single preparation contained turbidity, sedi-

mentation, or visible microbial growth at any of the 6 checkpoints (Table 1).

While the 2 technicians performing the 5 manipulations each compounded 125 preparations and were both aseptically trained and validated, they did not carry the same level of experience associated with preparing CSPs. One of the pharmacy technicians had practiced for 19 years, while the other technician had practiced for only 3 months. Although each technician was progressively asked to use specific improper aseptic techniques, all of the other aspects of aseptic technique were held constant. As such, the decision to select technicians with such divergent experience levels was done under the assumption that the more experienced technician should produce fewer contaminated preparations.

In contrast, all of the positive control vials had signs of positive microbial growth demonstrated by unresolvable, visible sediment and turbidity within 48 hours of inoculation. Along with the certificate of performance from the manufacturer, these results verify that the kits were functional and should, therefore, operate appropriately to validate aseptic technique.

Discussion

As noted in the results, modifying or removing various engineering controls, PPEs, or best practice aseptic procedures did not result in any positive media-fill challenges. In addition, when evaluating the media-fill products produced by pharmacy technicians with varying degrees of compounding experience, no differences were detected. These results suggest concern around the sensitivity of a test to determine proper aseptic technique as preparing media-fill CSPs in different scenarios did not produce a failure.

Since no positive results, other than the positive controls, have been detected thus far, further research is needed to evaluate media-fill challenge testing systems manufactured by different companies and develop a more sensitive test to categorize both proper and improper technique. This could include the development of new technologies or changes to the recommendations for aseptic technique validation. Media-fill challenge testing is the most realistic way to assess aseptic technique competence. However, without a test that

delivers accurate and appropriately sensitive results, institutions cannot have confidence that their pharmacy technicians possess and are practicing proper aseptic technique. That concern exists for our institution due to a lack of a positive media-fill challenge product across numerous years of assessing aseptic technique using media-fill challenge tests.

Limitations of this study include the evaluation of only one specific brand of media-fill challenge test and limiting each technician to 125 preparations, instead of preparing 1500 products each for a total of 3000 as statistically recommended by ISO.

Conclusion

In conclusion, evaluation of 250 compounded microbial growth media products prepared by 2 aseptically trained and validated pharmacy technicians employing 5 distinct manipulations of best-practice aseptic technique and sterile compounding procedures yielded a 0% contamination rate. A more sensitive media-fill challenge test needs to be developed to provide assurances that all poor aseptic practices are detected in compounding personnel.

Appendix

Best-Practice Garbing Steps²

1. Remove all cosmetics. Artificial nails are not allowed within the clean room.
2. Remove all jewelry and outer garments.
3. Don shoe covers one at a time. Step over line of demarcation as each shoe cover is donned.
4. Don head cover, facial hair cover, facial mask, and eye shield (eye shield is only necessary when working with hazardous drugs). Check in the mirror to ensure all head and facial hair is covered.
5. Using a fingernail cleaner and warm water, remove debris from beneath the fingernails. Wash hands and arms up to the elbows for at least 30 seconds using soap and warm water being sure to clean the palms, backs of each hand, and webbing between the all fingers and thumb. Dry hands and arms with lint-free disposable towels or an electronic hand dryer.
6. Don non-shedding gown.
7. Cleanse hands with waterless alcohol-based surgical hand scrub and allow hands to dry.
8. Don sterile gloves.

Best-Practice Cleansing Steps

Compounding Environment Preparation. Appropriate and complete aseptic technique also requires that the laminar flow hoods be cleaned with sterile 70% IPA prior to beginning sterile manipulations, anytime a spill occurs, and once all of the manipulations are complete. Hoods devoted to

chemotherapy preparations are first cleaned with cleansers specific to removing chemotherapeutic agents and then with sterile 70% IPA. Cleansing begins along the back panel of a horizontal laminar flow hood, progresses to the side panels, and finally the base panel. The substances used to clean the hood are sprayed directly on the surface of the hood and wiped from left to right avoiding overlap.

Compounding Supply and Personnel Preparation. Prior to preparing each compounded sterile chemotherapeutic product, personnel don a clean pair of sterile outer gloves and spray these gloves with sterile 70% IPA. Anytime their gloves leave the laminar flow hood, they are resprayed with sterile 70% IPA. Additionally, the septa of all admixtures, evacuated containers, and IV bags are wiped or sprayed with 70% IPA prior to puncture.

Operator Procedural Steps¹²

1. Using a 60 mL syringe and a 16-gauge needle, transfer 50 mL of normal saline from the IV bag to the empty evacuated container.
2. Attach the administration set to the bag, prime the tubing, and secure it to prevent leakage.
3. Using a 60 mL syringe and a dispensing pin, remove 50 mL of media from one of the VM-50 vials. Attach a 16-gauge needle to the syringe and transfer the media to the IV bag.
4. Using a 60 mL syringe and a 16-gauge needle, remove 50 mL of media from the other VM-50 vial. Attach a 16-gauge needle to the syringe and transfer the media to the evacuated container.
5. Using a 20 mL syringe and a 19-gauge needle, transfer 10 mL from one of the VM-10AC ampules to the IV bag.
6. Using a 20 mL syringe and a 19-gauge needle, transfer 10 mL from the other VM-10AC ampule to the evacuated container.
7. Using a 30 mL syringe and a 16-gauge needle, obtain 25 mL of SWFI from the 100 mL SWFI vial. Transfer the SWFI to one of the VM-25 vials.
8. Using a 30 mL syringe and a dispensing pin, remove 25 mL of SWFI from the 100 mL SWFI vial. Attach a 16-gauge needle to the syringe and transfer the SWFI to the other VM-25 vial.
9. Using a 19-gauge needle, prepare 3 each 10 mL syringes from the vial diluted in step 7.
10. Using a dispensing pin, prepare 3 each 10 mL syringes from the vial diluted in step 8.
11. Properly label and secure all vials and bags prepared for storage.
12. Incubate all test materials at 20°C to 25°C for 14 days checking the materials for turbidity and nonresoluble sedimentation at 24 hours, 48 hours, 72 hours, 7 days, and 14 days.

Acknowledgment

Richard F. Redding, CPhT, Pharmacy Technician, University of North Carolina Hospitals.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Kastango ES. The ASHP discussion guide for compounding sterile preparations: summary and implementation of USP chapter <797>. http://forums.pharmacyonesource.com/phos/attachments/phos/pharmacy_ops/778/1/USP797DiscGuide_2004.pdf. Accessed May 29, 2013.
2. United States Pharmacopeia and National Formulary. *USP 36-NF 31*. Vol 1. Rockville, MD: United States Pharmacopeia Convention; 2013:361-398.
3. Sigward E, Fourgeaud M, Vazquez R, Guerrault-Moro MN, Brossard D, Crauste-Manciet S. Aseptic simulation test challenged with microorganisms for validation of pharmacy operators. *Am J Health Syst Pharm*. 2012;69:1218-1224.
4. Kastango ES. Challenging our aseptic skills using more-rigorous media-fill tests. *Am J Health Syst Pharm*. 2012;69:1197.
5. Trissel LA, Ogundele AB, Ingram DS, Saenz CA, Gentempo JA. Using medium-fill simulation to establish a benchmark microbiological contamination rate for low-risk-level compounding. *Am J Health Syst Pharm*. 2003;60:1853-1855.
6. Stucki C, Sautter AM, Favet J, Bonnabry P. Microbial contamination of syringes during preparation: the direct influence of environmental cleanliness and risk manipulation on end-product quality. *Am J Health Syst Pharm*. 2009;66:2032-2036.
7. Trissel LA, Gentempo JA, Anderson RW, Lajeunesse JD. Using a medium-fill simulation to evaluate the microbial contamination rate for USP medium-risk-level compounding. *Am J Health Syst Pharm*. 2005;62:285-288.
8. Thomas M, Sanborn MD, Couldry R. I.V. admixture contamination rates: traditional practice sites versus a class 1000 cleanroom. *Am J Health Syst Pharm*. 2005;62:2386-2392.
9. Austin P, Elia M. Improved aseptic technique can reduce variable contamination rates of ward-prepared parenteral doses. *J Hosp Infect*. 2013;83:160-163.
10. US Federal and Drug Administration. Guidance for industry: Sterile drug products produced by aseptic processing—current Good Manufacturing Practice. <http://www.fda.gov/downloads/Drugs/.../Guidances/ucm070342.pdf>. Published September 29, 2004. Accessed December 27, 2014.
11. Trissel LA, Gentempo JA, Saenz LM, Woodard MY, Angeles CH. Effect of two work practice changes on the microbial contamination rates of pharmacy-compounded sterile preparations. *Am J Health Syst Pharm*. 2007;64:837-841.
12. ChemoTEQ [Package insert]. Cumberland, WI: Lab Safety Corporation; 2001.