From: Paul Davis
Subject: Sterile Gloves & Alcohol
To: "'W Benjamin Fry'"
Date: Tuesday, February 2, 2010, 11:32 AM

Ben -

After the last TSBP meeting you asked me to do a 'straw poll' on what our members thought about the sterile gloves and alcohol issue.

I did that and should have gotten back to you sooner.

Attached are their comments, which I will try to reflect during the Board meeting -

The 'issue' appears to be totally cost and the lack of proven superiority over non-sterile gloves and alcohol.

They make the point that, as soon as you open the gloves they are not sterile anymore. One article says that the rate of contamination with non-sterile gloves vs. sterile gloves was 0.96% vs. 0.34%, which is large in a sense, but still <1%.

I can add to that that the TSBP task force that studied the update for the sterile compounding rules did not include a recommendation for this in their report to the Board.

Beyond that we don't have a lot to offer to the dialogue on this issue.

Thanks for asking and for considering these notes.

Paul

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The point that Paul made about the sterile gloves is what I have been arguing since the USP 797 revision was completed. In addition, the bottle of sterile alcohol is no longer sterile after the initial opening of the bottle. I have read that some institutions are buying the sterile alcohol by the gallon and then pouring the solution into smaller bottles.....again, it is not sterile once the bottle is opened.

I don't know the cost differences, but I assume they are significantly higher. I am also not sure how many different sizes of gloves we would have to carry.

Here is the originating article and the rate of contamination with non-sterile chemotherapy gloves with isopropyl alcohol compared to sterile gloves was 0.96% vs. 0.34% respectively, since both are < 1% you could probably argue the cost difference (not discussed in the article).

It's a cost issue. I originally opposed the sterile glove requirement with the 797 revision citing cost and lack of documentation that it would impact patient care and money could probably be better spent elsewhere, but my comments didn't change their minds in the 797 update.
I was surprised it didn't make it into the rules since it is in 797 and I can't see opposing it as an organization. One good thing is that as sterile alcohol is more widely used, the cost might come down and might have already, I don't know as I didn't jump on the bandwagon to use sterile gloves or sterile alcohol in my cleanroom. We figured it already costs > $10 in supplies if we use our cleanroom just once in a day so what's a little more money? Glove costs are supposed to be going up, so it is another "unfunded mandate", but something we'll just have to live with.
I think if your particle counts are too high and you get lots of growth from your critter checks, than sterile alcohol and gloves would make sense as one way to decrease your particle and critter counts.
I'm not in support of it, rather I'm neutral and ready to live with it.

Key items: 1) no side-by-side study has determined any benefit to sterile over non-sterile and 2) USP relied on infection control, microbiology and CDC “experts”. This same group advices our ORs.

Bottom line – hard to know who is correct versus a group “over-trying” here. Eric Kastango has a bully pulpit and he is not afraid to use it.
ASHP has been after getting higher standards for IV preparation for years and with USP797, they have done that – pharmacy now prepared most/if not all of the IV admixture products rather than some good % being prepared on the nursing unit (e.g., pitocin for L&D, epidurals, etc.)

Unless some government type of person / entity steps in – the use of sterile gloves and sterile alcohol will be (eventually) a done deal.

http://www.pharmacyonesource.com/images/simplifi797/Q&A.pdf

Q9. I work in a small hospital and cost containment is a very big issue. I have read studies that compare sterility between using sterile gloves wiped intermittently with sterile IPA vs. regular gloves that were not wiped at all during preparation of CSP's. Are there any studies using either sterile or non-sterile gloves intermittently wiped with regular IPA. We currently use nonsterile gloves, but we wipe intermittently with regular IPA and we have not had any problems. Why is sterile IPA specifically used?
A9. I understand the concern about cost. I am not aware of any studies that looked at the scenarios you posed. If we agree that contamination most likely comes for touch contamination, all materials that come in direct contact with the critical site within the direct compounding area must be sterile. As such, sterile gloves and sterile alcohol for those activities occurring within the DCA is called for. Nonsterile alcohol is not sporicidal and spores/bacillus is a concern when we prepare CSPs. The USP Sterile Compounding Committee had an expert advisory panel (of infection control, microbiology and CDC experts) advise us that sterile gloves and sterile alcohol were required.

http://www.usp.org/pdf/EN/USPNF/2008-07-18_USP_31_2S_Commentary_Chapter_797.pdf

incorporated.
Comment: The chapter emphasizes the need for high standards but continues to recommend non-sterile alcohol as a disinfectant without discussion or reference to the efficacy of alcohol. One commenter recommends requiring the use of sterile alcohol, requiring all disinfectants to be sterile, identifying a number of examples of disinfectants, and listing FDA recommendations. Another commenter questions whether sterile alcohol must be used, and whether it presents a significant advantage to the use of regular 70% isopropyl alcohol (IPA). Use of sterile 70% IPA is not cost effective for the healthcare facility and patients. Another commenter suggested that sterile alcohol must be used in order to disinfect a suitable environment for compounding a sterile preparation, and that the use of non-sterile disinfectant should not be considered.
Response: The SCC adopted the use of sterile 70% IPA in the chapter after considering published data and recommendations from multiple commenters including the advisory panel formed to review the section. Sterile 70% IPA must be used to disinfect sterile gloves intermittently, vial stoppers, ampul necks, and injection ports on containers. The SCC felt that since a sterile glove is required to minimize bio-burden, the use of sterile 70% IPA will help enhance the bio-burden reduction effort. SCC discussed the use of sporicidal agents, but decided against them because of their drying time of one or more hours, deposition of residues, and chemical reactivity were strong disadvantages.
Comment: A commenter questioned why the SCC requires sterile gloves.
Response: The SCC adopted the use of sterile gloves in the chapter after considering published data and recommendations from multiple commenters, and the advisory panel formed to review the section in addition to the existence of evidenced-based science in community standard of practice. The greatest risk of contamination is from touch, so by using sterile gloves this bio-burden is minimized.

I have put out a call to individuals that may be of great help to us here. The issues countering the use of sterile alcohol and gloves you mentioned are valid, but not necessarily what will sway the TSBP. We need actual data and/or the discussion to poke holes in the data that USP used to make their rulings of 'sterile'. My old comrades at MD Anderson may have that data – I have forwarded the message to them so they can respond (Joe Gentempo is the primary point of contact who actually performed the studies that Larry Trissel originally published that caused the sway to 'sterile' in the first place).

Personally, as someone who has been teaching this and working with experts in sterile compounding for many years, I am not at all compelled with the 'sterile' argument. Honestly, there are several things in 797 I am not compelled to agree with either, but, as you said – that is the current standard. I do know that USP is looking for the next committee members and chairs for 2010-15…I have thought about putting my name in the hat, but unsure that I possess the skill set needed. I would expect that several items will be up for discussion and possibly amended with the new committee. I'll keep you posted on any data I can gather on this current task.

Is sterile alcohol readily available? At one time that was an issue. How is the sterility proven?

Our hospital doesn't do any sterile compounding, due to 797, so I am out of the loop on that.

Another question I have is about sterile chemo prep pads. I haven't been able to find these. I don't want to bring that up to board, but it seems silly to have "sterile" gloves and alcohol and then put a "non-sterile" chemo prep pad in the hood.

Effect of two work practice changes on the microbial contamination rates of pharmacy-compounded sterile preparations

LAWRENCE A. TRISSEL, JOSEPH A. GENTEMPO, LISA M. SAENZ, MONICA Y. WOODARD, AND CAROL H. ANGELES

Purpose. Using a multiple-step testing medium-risk-level compounding test procedure, the evaluation of two work-practice changes to determine if the changes could effectively reduce the potential for contamination occurrence was conducted.

Summary. Along with training and evaluation of aseptic sterile compounding techniques, each individual pharmacist and pharmacy technician at M. D. Anderson Cancer Center must successfully demonstrate aseptic preparation competency annually by performing the complicated multistep aseptic transfers of growth medium with no resulting growth of microorganisms. The multistep aseptic transfers are designed to simulate manual compounding of the most complicated medium-risk-level preparations anticipated as specified in the *United States Pharmacopeia*'s chapter 797. An evaluation of two modest and simple work-practice changes was conducted: The use of bare hands and nonsterile gloves with only initial disinfection with 70% isopropyl alcohol (IPA) during years 1 and 2 (group A) was compared with the use of nonsterile chemotherapy gloves with initial and repeated disinfection with IPA for year 3 (group B) and the use of sterile gloves with initial and repeated disinfection with IPA for year 4 (group C). The process involved multiple discrete manipulations, including reconstitution of dry-growth medium; transfers of growth medium from vials and ampules using syringes, needles, a dispensing pin, and a filter straw; and transfers to an empty plastic i.v. bag. For groups B and C, significant reductions in contaminated samples were found compared with group A.

Conclusion. The use of protective chemotherapy gloves that were repeatedly disinfected with IPA decreased the contamination rate of pharmacy-compounded sterile preparations.

Index terms: Alcohols, isopropyl; Compounding; Contamination; Disinfectants; Gloves; Pharmacy; Sterile products

Am J Health-Syst Pharm. 2007; 64:837-41

The adoption of *United States Pharmacopeia* (*USP*) chapter 797, Pharmaceutical Compounding—Sterile Preparations,[1] set a new national standard for quality assurance measures in compounding sterile preparations. The new *USP* standard came in the wake of a series of injuries and deaths around the United States from contaminated doses.[2-4] Consequently, pharmacies in hospitals and in other settings and regulatory bodies are reappraising the quality of sterile compounding efforts.

Many home care pharmacies were originally established and built with quality assurance measures that met or exceeded the current *USP* standards, even before those standards existed. These high-quality aseptic compounding operations led the way, proving that a higher level of quality assurance was technically feasible and financially achievable. The higher level practices of these pharmacies led to *USP* chapter 1206, Sterile Products for Home Use,[5] and the ASHP Guidelines on Quality Assurance for Pharmacy-Prepared Sterile Products,[6] which provided guidance for quality assurance and quality assessment that were intended to represent an acceptable quality standard

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and a level of aseptic compounding care that patients have a right to expect from those who prepare their sterile medications.

Much of the effort and angst of pharmacists who have undertaken improvement of their quality assurance process tend to be focused on environmental engineering controls, such as cleanrooms, laminar-airflow workbenches, and compounding aseptic isolators. Perhaps this is because the environmental controls are technically challenging and involve expense. However, there also appears to be an unwarranted tendency to act as if any medication prepared in one of these devices is automatically sterile without regard to other factors. This has been termed the "magic box" fallacy. Unfortunately, these clean-air, controlled environmental devices are not magic boxes, and other concerns can negate any beneficial effect from the engineering controls. Indeed, an overconcern with facilities and engineering controls may prove to be a distraction from the most important and potentially least expensive actions that pharmacists can take: the improvement of human work practices in the preparation of sterile dosage forms.

Previously, we have reported the results of using media-fill simulations to evaluate the potential low- and medium-risk-level contamination rates in our institution.[7,8] In the evaluation of low-risk-level compounding,[7] relatively little potential for contamination was observed, which is consistent with other studies.[9,10] However, the medium-risk-level simulation resulted in an astonishing 5.2% contamination rate among 539 individual evaluations, which the authors viewed as wholly unacceptable.[8] This contamination rate occurred even though the media-fill compounding simulation was performed in an International Organization for Standardization (ISO) class 5 (class 100) clean-air environment with a proper aseptic technique.

For the media-fill evaluations of aseptic technique at M. D. Anderson Cancer Center, each individual received training and coaching in proper hand washing and sanitizing, proper gowning and gloving, and proper aseptic manipulations. Even so, we believe that the principal source of this contamination resulted from inadvertent and unrecognized touch contamination during the preparation procedure. Our practice during this two-year period of routinely compounding using bare hands or nonsterile, chemotherapy-protective gloves along with unavoidable human error in sample manipulations appeared to be contributing to this unacceptably high contamination rate.

Therefore, using the same complicated multiple-step testing medium-risk-level compounding procedure that was used previously for the aseptic technique evaluations,[8] we undertook further evaluations of two modest and simple work-practice changes to determine if these simple changes could effectively reduce the potential for contamination occurrence.

Methods

The division of pharmacy at this institution provides sterile compounding training to employees, including a 20-hour didactic training course to all pharmacists and a 40-hour didactic course to technicians who may be involved with sterile preparation. In addition to the didactic course, a practical evaluation is performed on all individuals that involves a complicated multistep series of aseptic transfers so that each individual demonstrates adequate competency in aseptic technique. The didactic training and practical evaluation must be completed successfully before any individual can initiate actual sterile preparation for patient administration.

In addition to the initial training and evaluation, each individual pharmacist and pharmacy technician must successfully demonstrate aseptic preparation competency annually by performing the complicated multistep aseptic transfers of growth medium with no resulting growth of microorganisms. The multistep aseptic transfers are designed to simulate manual compounding of the most complicated medium-risk-level preparations anticipated as specified in *USP*'s chapter 797.[11]

The use of bare hands and nonsterile gloves with only initial disinfection with 70% isopropyl alcohol (IPA) during years 1 and 2 (group A)[8] was compared with the use of nonsterile chemotherapy gloves[a] with initial and repeated disinfection with IPA for year 3 (group B) and the use of sterile gloves[b] with initial and repeated disinfection with IPA for year 4 (group C). Except for these changes, all other aspects of the aseptic technique evaluations remained the same as for group A,[8] including the nonsterile chemotherapy protective gloves.[a] Many of the individuals being tested during this four-year period had extensive experience in sterile preparation and had participated in the testing for a number of years, although many others had more limited experience. The results of evaluation groups B and C were then compared with the previously obtained results of the evaluations in group A.

Before beginning the test, each individual removed all finger, hand, and wrist jewelry and watches; donned shoe covers[c] and hair covers[c]; thoroughly cleaned their hands, nail areas, and arms with antimicrobial detergent and water; and donned gowns.[d] During years 1 and 2 (group A), the gloves that were used were latex free, powder free, nonsterile, and chemotherapy protective.[a] These gloves were not disinfected during the multistep test procedure. During year 3 testing (group B), the same latex-free, powder-free, nonsterile chemotherapy protective gloves[a] were used but were disinfected frequently and repeatedly by wiping the gloves, espe-

cially the fingertips, with sterile pads saturated with IPA before the start of the test and after every manipulative step in the multiple-step procedure. The gloves were considered to be and were handled as nonsterile containment devices to prevent contamination from the shedding of skin organisms in the critical compounding area and to provide protection to the compounding personnel from exposure to chemotherapy drugs. Individuals were reminded and encouraged to avoid touch contamination throughout all of the testing. During year 4 testing (group C), the effect of using latex-free, powder-free, sterile, chemoprotective gloves[b] with frequent and repeated IPA disinfection was evaluated. Sterile gloves do not remain sterile during the compounding process because of the necessity of touching nonsterile items and surfaces. Consequently, the gloves, especially the fingertips, were disinfected after every manipulative step in the multiple-step procedure in which anything that was nonsterile was touched.

No facemasks were used because the vertical laminar-airflow biological safety cabinets[e] were equipped with transparent face shields. The biological safety cabinets had all been certified to meet ISO class 5 air quality on a routine twice-yearly schedule. The biological safety cabinets, which had the blowers running for at least 60 minutes before testing began, were located in a cleanroom or in a pharmacy satellite area separated from the general environment; they were cleaned thoroughly on all surfaces with IPA before each evaluation. In addition, as for the previous testing in years 1 and 2, the exteriors of all nonsterile materials entering the ISO 5 compounding environment, such as media vials, were disinfected with IPA before the start of compounding manipulations.

The sterile growth medium and process used were the Valiteq Aseptic Technique Validation System.[f] The process involved multiple discrete manipulations, including reconstitution of dry-growth medium; transfers of growth medium from vials and ampules using syringes, needles, a dispensing pin, and a filter straw; and transfers to an empty plastic i.v. bag (appendix). Each of these manipulations is routinely required of the aseptic compounding personnel. All of the materials and devices were sterile when purchased. Each individual who is tested must perform all of the steps without contaminating the sterile growth medium. An instructor or coach is present to remind the individual of the steps to be performed, to advise on issues of proper technique, and to evaluate the appropriateness of the technique that the individual then uses. The complicated nature of the evaluation steps were used to simulate *USP* chapter 797 medium-risk-level compounding and is the same as the procedure used in evaluations in previous years.

The final product to test was 100 mL of growth medium packaged in a plastic bag. The bags were stored according to the growth medium manufacturer's recommendation with incubation at 25–35 °C over 14 days and observed for growth of organisms. When growth occurs, the growth medium appears cloudy or turbid or has discrete colonies and shows sedimentation. Successful completion of the test is defined as the growth medium in the plastic bag remaining a uniform, clear, light-amber solution. If growth does occur, the individual must repeat the aseptic technique testing until a satisfactory result of no observed growth is achieved.

The chi-square test[12,13] was used to compare possible differences in contamination rates between years 1 and 2 (group A) and years 3 (group B) and 4 (group C). If the null hypothesis was rejected, the Bonferroni correction[14] was used to determine significant differences, defined as $p < 0.05$.[12,15] Fisher's exact test[12,13] was used to compare the results of groups B and C for the use of sterile versus nonsterile gloves with frequent IPA disinfection.

Results

For groups B and C, significant reductions in contaminated samples were found compared with group A, which exhibited 28 contaminations out of 539 individual tests ($p = 0.000018$). Compared with group A, using nonsterile chemotherapy gloves with repeated IPA disinfection (group B) resulted in 3 positive growth samples among 311 individual aseptic technique tests for a contamination rate of 0.96% ($p = 0.0029$). When sterile chemotherapy gloves were used along with repeated disinfecting with IPA (group C), the contamination rate was lower still with only 1 positive growth sample among 296 individual aseptic technique tests for a contamination rate of 0.34% ($p = 0.0005$). These reduced contamination rates can be contrasted to group A for years 1 and 2 and its unacceptable 5.2% rate. The apparent difference between groups B and C was not statistically significant ($p = 0.3367$), possibly because of the low number of contaminated samples. Even so, this result suggests that a contamination below 1% can be achieved if initially sterile protective gloves are used.

Group A testing also revealed that pharmacists and technicians who worked directly and regularly in sterile preparation had the worst record, exhibiting a contamination rate of about 6.3%; pharmacists who did not work regularly in sterile preparation exhibited a lower rate of contamination of 3.9%.[8] This may have resulted from familiarity of those individuals with aseptic compounding leading to less rigorous aseptic practices.[8] In the testing of groups B and C, all four contaminated samples among 607 total tests were prepared by pharmacists who work directly and regularly in sterile preparation, further supporting that speculation.

Discussion

There is no doubt that these occurrences of microbial contamination are a failure of one or more elements of contamination control. Perhaps it was an inadvertent error in aseptic technique or an unavoidable and unrecognized transfer of microorganisms with no aseptic technique error involved. In either case, the most likely source of the contaminated samples is touch contamination. However, the authors recognize that contaminated samples can also result from airborne sources.[4]

The pharmacy's sterile compounding process relies on human manipulations for preparing medications. However, relying on fallible and microbially contaminated humans to perform flawlessly and with perfection is a doomed strategy that will inevitably lead to aseptic failures and contaminated doses. While there are many sources of microbes that can lead to the nosocomial infections that plague our patients, it is the responsibility of pharmacists and all other compounding personnel to eliminate the sterile compounding process as a source of contamination that can potentially result in patient sepsis.

Sterile compounding personnel typically consider every unit that they prepare to be sterile. Too often, little consideration is given to the fact that inadvertent contamination of compounded units is actually occurring on a regular basis. Since sterile compounding was routinely conducted on actual drug products for human use by many of these individuals whose aseptic technique was evaluated during the time frame covered by this testing, the actual contamination rate for complex multicomponent medium-risk-level preparations administered to patients may have also been unacceptably high but not recognized. Indeed, contamination may actually be occurring more frequently in routine preparation than was found in the aseptic technique testing because the individuals may be on their aseptic technique "best behavior" during the observation and testing procedure and may be less so in day-to-day operations.

We believe the likeliest source of the contamination that we found in our aseptic technique evaluations is the individual compounding the preparations. The reality may simply be that there is an abundance of opportunities for fallible and microbially contaminated human beings to inadvertently contaminate the products, most probably by touch, during aseptic preparation manipulations. A pharmacy's actual contamination rate will be the result of all of the contamination risk factors, including the nature and complexity of the compounding operation, the quality of the preparation environment, and the skill of the preparer. Even with the best environmental controls and most highly skilled individuals, inadvertent contamination is a likely probability that should be considered and evaluated for its patient safety implications.

The essence of quality assurance in sterile compounding is proving that the pharmacy is, in fact, delivering what it purports to be delivering—a sterile preparation. The burden of responsibility is on all compounding personnel to reduce the contamination rate as much as possible. This is a level of care that patients have a right to expect and compounding personnel have an obligation to provide.

Conclusion

The use of protective chemotherapy gloves that were repeatedly disinfected with IPA decreased the contamination rate of pharmacy-compounded sterile preparations.

[a]Safeskin Purple Nitrile examination gloves, Kimberly-Clark, Roswell, GA.
[b]Biogel Skinsense N. Regent Medical, Norcross, GA.
[c]Allegiance, McGaw Park, IL.
[d]Chemo Safety, Ludlow Company, Chicopee, MA.
[e]NuAire, Inc., Plymouth, MN.
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Appendix—Medium-risk-level-aseptic technique assessment procedure

1. Using a 30-mL syringe and 18-gauge needle, reconstitute a vial of dry sterile trypticase-soy growth medium (vial 1) with 20 mL of sterile water for injection.
2. Using a 60-mL syringe and 18-gauge needle, transfer 50 mL of sterile water for injection from a 50-mL vial into a sterile empty 150-mL polyvinyl chloride (PVC) bag.
3. Insert a dispensing pin into a 30-mL vial (vial 2) of sterile liquid trypticase–soy growth medium. Using a 10-mL syringe, withdraw 5 mL of growth medium through the dispensing pin. Attach an18-gauge needle to the syringe, and transfer the growth medium into the PVC bag.
4. Using a 10-mL syringe and 18-gauge needle, withdraw 5 mL of sterile growth medium from the reconstituted vial 1 (from step 1), and transfer into the PVC bag.
5. Using a 20-mL syringe and 18-gauge needle, withdraw 10 mL of sterile growth medium from a 10-mL vial (vial 3), and transfer into the PVC bag.
6. Using a 10-mL syringe, make a second withdrawal of 5 mL of sterile trypticase–soy growth medium from vial 2 through the dispensing pin. Attach an 18-gauge needle to the syringe, and transfer the growth medium into the PVC bag.
7. Using a 10-mL syringe and 18-gauge needle, make a second withdrawal of 5 mL from the reconstituted vial 1, and transfer into the PVC bag.
8. Carefully open a 10-mL ampule of sterile trypticase–soy growth medium. Using a 20-mL syringe and 5-µm filter straw, withdraw 10 mL of the sterile trypticase–soy growth medium from the ampule. Remove the filter straw, and replace it with an 18-gauge needle. Transfer the growth medium into the PVC bag.
9. Using a 10-mL syringe, make a third withdrawal of 5 mL of sterile trypticase–soy growth medium from vial 2 through the dispensing pin. Attach an 18-gauge needle to the syringe, and transfer the growth medium into the PVC bag.
10. Using a 10-mL syringe and 18-gauge needle, make a third withdrawal of 5 mL from the reconstituted vial 1 and transfer into the PVC bag.
11. Label the bag, incubate at 25–35 °C over 14 days, and observe for cloudiness, turbidity, and discrete colonies that indicate microbial growth.