Compounding sterile products during a personal protective equipment shortage

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Purpose. To describe our pharmacy department’s plan for conservation of personal protective equipment (PPE) during the coronavirus disease 2019 (COVID-19) pandemic to ensure continued availability of sterile compounded products.

Summary. PPE shortages impacted hospitals throughout the nation in the early months of the COVID-19 pandemic response. The PPE requirement for sterile compounding and need to maintain supplies within the pharmacy cleanroom are often overlooked. A sustained supply of PPE is critical to ensure an uninterrupted supply of compounded medications to our patient population. Multiple conservation strategies, including staffing changes, communication, adjustments to training, and even reuse of select PPE, can assist with conservation.

Conclusion. PPE in pharmacy cleanrooms is critical for the continued provision of sterile compounds with appropriate beyond-use dates and effective patient care. Pharmacy departments must employ multiple conservation strategies to ensure PPE is available for continued compounding of sterile products, and early planning and implementation of conservation strategies are key.

Keywords: COVID-19, disinfection, pandemic, patient safety, personal protective equipment, pharmacies

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The coronavirus disease 2019 (COVID-19) pandemic has required health systems to quickly plan for and react to interruptions in the supply of critical personal protective equipment (PPE). The impact of the pandemic has been seen within multiple service lines throughout our health system, including but not limited to nursing, laboratory, surgical, and pharmacy services, with each of these service lines facing unique challenges. The detrimental effect of not being able to acquire and supply personnel with the protective equipment needed could be universally severe, with the resultant inability to complete crucial patient care activities. The specialized and unique PPE and compounding supplies required by pharmacies, particularly for the sterile compounding environments and hazardous drug manipulation, has made the need for strategic planning and conservation critical for our health system.

Pharmacy departments have become expert in managing shortages of medications and have perfected these methods over time. Through the development of a task force for pharmacy PPE conservation, our pharmacy department identified that similar strategies could be applied to PPE. Concepts that were universally applied included identifying alternative manufacturers, utilizing alternative but equally effective equipment (eg, respirators in place of masks), and implementing criteria for use of PPE throughout our compounding locations. While shortage management was not a new scenario for our department, the scale of this shortage was uniquely compounded by demand from the general public in addition to the high demand from healthcare organizations that is typically seen with drug shortages. Additionally, the United States had
relied on importing much of our PPE from other countries, including China, where the outbreak occurred and where approximately “50% of the masks and respirators around the world” were manufactured.1 The subsequent border closures in this area and inability of workers to continue manufacturing placed additional strains on the PPE supply chain. In this publication we outline our successful strategic conservation of PPE and sterile compounding supplies during the COVID-19 pandemic response.

Risks of limited PPE

Personnel who compound sterile drugs use PPE to reduce the risk of microbes and other particles present on human skin, hair, and clothing contaminating a drug product they are preparing.2 The inability to maintain even one of the critical components required for appropriate garbing practices would have potential impacts on workflow within the pharmacy department and beyond. Without the appropriate garb the pharmacy could not meet the garbing requirements for low- or medium-risk compounding in an ISO-5 environment, as outlined in United States Pharmacopeia general chapter 797 (USP <797>) and would require an adjustment of the compounding risk category to high risk or an adjustment to the beyond-use date (BUD).3,4 Our pharmacies do not compound high-risk products, and the testing required to set this up would have increased the use of PPE during a time when none could be spared. In lieu of converting to high-risk compounding, our alternate option would have been a default to immediate-use dating, defined as 1 hour in USP <797> at the time of writing. If the pharmacy department continued to compound with the determined 1-hour BUD, this would impact turnaround times for critical drips and cause potentially fatal delays in patient care. Alternatively, compounding could be transitioned to nurses, with the same 1-hour dating used, but this would have significantly increased the workload on our nursing teams. Significant workload is identified by the Institute for Safe Medication Practices as an environmental factor or key element that can contribute to medication errors.5 If compounding were transitioned to nurses on the units, the risk of compounding errors may be increased as a result of placing responsibility for the task of compounding medications on a nursing staff already dealing with unprecedented patient loads. Neither of these situations is ideal, and while compounding in an ISO-5 environment within the pharmacy offers assurance of air quality, the operational impact of a 1-hour turnaround time had multiple safety implications, as described above.

While the inability to obtain PPE was the initial challenge, an unexpected complication was identified from the process of alternate sourcing. With limited resources, the pharmacy department was asked to use alternative garb such as exam gowns, which are not tested for their level of particulate shedding. These alternative products introduce the risk of additional particles into our cleanrooms and impact our state of control in the sterile compounding areas. This risk is hard to quantify, as air testing is performed under dynamic conditions during which staff are garbed in their normal compliant garbing. If use of these alternate products were deemed necessary, it would require risk assessment completion, adjustments of BUDs, or increased air testing and environmental monitoring.

Pharmacy PPE conservation task force and early planning

Early in the pandemic, the pharmacy department realized the impact limited PPE and sterile compounding supplies would have on the sterile compounding program throughout our health system. As one group of clinicians involved in the COVID-19 pandemic response wrote, “Medication management services are still needed to promote safe and cost-effective drug utilization during the public health crisis.”6 As the pandemic progressed, the need for compounded medications, such as vasopressors and sedatives, significantly increased. Outsourcing facilities struggled to maintain supply, and most of these medications had to be compounded internally, which further exacerbated the challenge of PPE conservation.

In addition to PPE, the challenges of keeping a reliable stock of sterile cleaning and disinfection products compatible for use with cleanroom environments began to surface. Many of our contractors of garbing supplies were also those that provided “cleanroom compatible” cleaning and disinfecting solutions, and alcohol-based hand rubs. Supplies of sterile alcohol and sporicidal agents became scarce, and strategies for conservation and alternative procurement were needed.

A pharmacy task force was created and worked to understand each facility’s needs, current supply, and usage rate for the current stock. Our health system includes 16 separate compounding locations (8 hospitals, 5 infusion centers, 2 investigational drug service pharmacies, and 1 central fill distribution center), each with differing sterile compounding structures, ranging from complete cleanroom suites
to segregated compounding areas. The task force was led by the health system’s director of policy and quality and the quality manager for the central fill distribution pharmacy and was supported by a centralized buyer and operations managers from each location. The task force met 3 times per week virtually early in the pandemic. In March 2020, the task force requested that each facility begin tracking critical supplies such as sterile masks, frocks, chemotherapy preparation gowns, sterile gloves, hair covers, shoe covers, beard covers, sterile alcohol, and sporicidal agents. The task force determined conservation strategies would be implemented when supply levels reached a days’ supply of less than 60 days or if backorders indicated an interruption in the supply chain. Supply levels were regularly monitored, and consideration for continued conservation was reevaluated when the days’ supply of a given item was greater than 60.

When discussions around the reuse of garbing began at the organization level, the task force took action to ensure any required reuse of garb did not adversely impact our sterile compounded products and worked directly with our clinical leadership team and infection prevention experts to understand the state of our supply and a timeline for discontinuation of the reuse process. The leaders of the task force ensured frequent written communication and phone calls were made to the infection prevention and clinical teams to obtain updates on supply levels and to ensure the leadership team understood the impact that lack of PPE would have on the pharmacy’s ability to deliver sterile compounded products.

**Strategies implemented to maintain sterile compounding**

Several strategies to preserve the state of microbial control of the compounding environments during times of supply shortage were evaluated. We implemented the following conservation methods in a phased approach, as described below.

**Communication and redistribution**. Our organization has 16 compounding locations, and though we share a common materials management center and ordering system, each location has access to different direct distributors. Through weekly communication of PPE quantities, we were able to redistribute as needed from locations with extra supply to those in dire need. Each week, pharmacy managers at direct care sites were asked to enter their supply numbers into a shared and secured spreadsheet, and the items of concern were discussed on a weekly pharmacy department call. Through these collaborations, we have been able to maintain adequate supply of PPE at each of our care sites throughout the pandemic. Without implementing this type of communication method and tracking methodology some locations may have been at risk of running out of PPE entirely. Through tracking and redistribution, we have been able to keep all open compounding sites up and running throughout the pandemic.

**Strategic staffing and cleanroom practices**. To ensure conservative use of the stock of PPE, managers were asked to staff the cleanrooms with the minimum personnel required for essential compounding, to prepare sterile compounds in anticipation when possible, and limit entries to the cleanroom. To balance these practices, they were also asked to give meticulous attention to cleaning of the commonly touched areas and review hand hygiene techniques with staff. Strategic staffing posed little additional risk to the compounding environmental, and while anticipatory compounding is thought to be deemed riskier than patient-specific compounding, it can be restricted to small numbers to decrease any theoretical risk. Without these strategies, each location ran the risk of using PPE unnecessarily and further decreasing our current supply. For sterile compounding alone, our 2,966-bed system needed 489 masks per day and over 14,000 masks per month to continue sterile compounding, even with no operational or PPE changes at our patient care sites. Through the strategic staffing conservation methods, we were able to decrease our utilization to fewer than 300 masks per day. The decreased demand allowed us to extend our available resources and provided enough inventory for the department to continue compounding services. Figure 1 shows the initial decreased utilization of masks.

**Figure 1.** Utilization and supply of masks at compounding sites during early weeks of pandemic.
Use of reusable respirators in place of surgical masks. In a sample assessment form for garbing found in USP <797>, it is recommended that a face mask cover the “bridge of the nose down to include [the] chin.” While surgical masks are the accepted standard, the specification for face masks are not detailed in the personnel cleansing and garbing section of USP <797>. The intent of a face mask while compounding is to provide a barrier between the person compounding and the product. Based on an assessment of the language in USP <797>, the task force determined reusable respirators met this intent. The Honeywell North Half Mask respirator (Honeywell International, Charlotte, NC), available through our employee clinic, was evaluated and selected as an approved alternative for surgical face masks. As an early conservation method, we developed a list of essential compounding personnel and ensured they were appropriately fitted and provided with an approved dual-chamber respirator or face covering to use when surgical masks became unavailable. Cross contamination was a possible risk with the introduction of respirators to sterile compounding areas; therefore, detailed cleaning instructions were provided. The task force did consider the respirator outlet as part of the assessment and determined there was minimal risk to the sterile compounded product but, when universal employee masking was implemented, ensured that employees covered this outlet with a surgical face mask to follow company policy.

Temporary postponement of training of new compounding staff. Training of compounding staff uses a minimum of 2 additional full sets of PPE each day if the room entries are limited to morning and afternoon only. Training was restricted to renewals for already qualified compounding staff to reserve the remaining PPE for essential compounding only. The task force instructed campuses to weigh the risk of utilizing PPE to train new personnel against the benefit of having additional personnel trained if compounding staff availability was limited.

Decreased testing frequency of personnel. In preparation for the release of the proposed USP <797>, our organization adopted the recommendations for media fill and gloved fingertip testing of personnel every 6 months. To conserve PPE for sterile compounding, during the early COVID-19 pandemic response we transitioned all employees back to the required annual frequency detailed in the currently published chapter. While increased testing allows documentation of appropriate compounding practices, it is only a snapshot in time, and detailed supervision of compounding, which is a standard expectation at all compounding sites, should identify any poor compounding practices and offset any risk associated with the decreased testing frequency.

Decreased environmental testing frequency. USP <797> requires that environmental air sampling occur at a minimum, every 6 months, and surface sampling periodically. Our organization has insourced our environmental monitoring program, and we test above the minimum frequency requirements. The task force evaluated the current testing practices and the amount of PPE required for sample collection, and consideration was given to any locations with trending samples. To eliminate all unnecessary use of PPE, we scaled back testing in all locations to meet the minimum frequency requirements. To counterbalance any risk related to the reduction in these best practices, we increased the frequency of sampling of our primary engineering controls (PECs), without increasing the use of PPE, by training our compounding staff to collect a sample from their PECs at the end of their compounding sessions. We provided detailed instructions for collecting and submitting samples for analysis. Over the course of 4 months, there were 3 actionable recoveries made from 69 sampling sessions of the PECs (aligning with historical environmental monitoring data), indicating that, in large part, our cleanrooms were able to handle the additional bioburden from our PPE reuse and validating that our mitigation techniques and attention to cleaning and aseptic practices were effective to prevent reuse from impacting the direct compounding areas. Actionable recoveries were remediated through investigation and action plans, including an evaluation of where garb (including any reused masks) was stored and if that storage was compliant with instructions provided.

Developing list of alternatives. There were instances in which standard contracted items could not be obtained. It was important to ensure that any alternative supplies met our currently required standards or provide alternative evidence that the product met our criteria. We worked directly with the garbing manufacturers to obtain documentation of their testing methods, prior to using alternative garb. For disinfecting agents, in the event sterile isopropyl alcohol became unavailable, we provided guidance on other approved one-step agents for cleaning and disinfecting agents for material transfer and cleaning of secondary engineering controls. The task force instructed that sterile isopropyl alcohol be reserved for disinfecting PECs. For other surfaces such as cleanroom worktables, walls, floors, etc, we evaluated efficacy data for available agents against organisms recovered from years of environmental monitoring (air and surface sampling) data; this ranged from sporicidal agents such as Peridox (Contec, Inc., Spartanburg, SC), SporKlenz (Steris, Mentor, OH), and DeconSpore (Veltis Associates, Malvern, PA) to germicidal agents such as PREempt (Virox Technologies, Inc.). These agents were reserved for use in the cleanroom and CaviWipes (Metrex Research, Orange, CA) and Sani-Cloth (PDI, inc., Woodcliff Lake, NJ) were reserved for the sanitization of noncleanroom supplies and equipment. Specialized agents were held in reserve for more critical sanitization requirements, while noncompounding areas such as
breakroom tables and time clocks were disinfected by our housekeeping teams.

**Outsourcing.** While USP does not specify a percentage of alcohol required in hand rub for sterile compounding areas, it requires that the product’s labeling include a claim of “persistent activity.” As supplies and distributors of alcohol-based hand rubs became scarce, the task force evaluated the Food and Drug Administration document “Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency Immediately in Effect: Guidance for Industry,” which detailed recommended recipes and processes. The Centers for Disease Control and Prevention and USP supported these references, and risk was determined to be minimal. We were able to outsource hand sanitizer to supply our nonsterile pharmacy areas and reserve the remaining supply of alcohol-based hand rub with a documented claim of persistent activity for our sterile compounding areas.

**Discontinuation of select PPE in locations with restricted access barrier systems where USP <797> allows.** When restricted access barrier systems (RABS) are the source of the ISO-5 compounding environment, USP <797> instructs that normal garbing and gloving requirements for compounding personnel apply unless “the isolator manufacturer can provide written documentation based on validated environmental testing that any component(s) of PPE or personnel cleansing are not required.” A thorough assessment was performed by designated persons from each pharmacy department where RABS are in use as the PEC. This involved evaluation of 3 different models from 2 different manufacturers. Based on official statements, user manuals, and/or study data provided by the PEC manufacturer, it was determined that some PPE may be omitted with these isolators in use. These claims were substantiated with environmental testing data obtained in dynamic conditions in which users did not don any PPE, and the device was able to maintain ISO-5 quality air. Conservatively, manufacturers still recommended certain components of garbing depending on the compounding performed (ie, hazardous vs nonhazardous). These recommendations were considered, and select PPE remained a requirement. While our organization experienced

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**Figure 2.** Garbing assessment for risk assessment inclusion. PPE indicates personal protective equipment.

| PPE Recommendations by Manufacturer/Model | Non-Hazardous Compounding | Hazardous Compounding |
|-------------------------------------------|---------------------------|-----------------------|
| **PPE Action**                             | Baker (SteriShield®)      | Baker (ChemoShield®)  |
| **Non-Hazardous Compounding**              | Germ Free (LGFI® Series)  | Germ Free (LGFI® Series)  |
| Face Mask                                 | Face Mask                 | Face Mask             |
| Hair Cover and/or Beard Cover             | Hair Cover and/or Beard Cover | Hair Cover and/or Beard Cover |
| Shoe Covers                               | Shoe Covers               | Shoe Covers           |
| Gown                                      | Gown                      |                       |
| **Required — Continue Use**               | Sterile Gloves            | Sterile Gloves        |
|                                           | Sterile Gloves            | Sterile Gloves        |
|                                           | Sterile Chemo Gloves      | Sterile Chemo Gloves  |
|                                           | Chemo Gown                | Chemo Gown            |

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more significant disruption in supplies of masks and gowns, the supply chain for booties, beard covers, and hair covers was also impacted. To conserve all PPE possible, the decision was made to utilize only that PPE that was required by the manufacturer of the RABS, and we ultimately implemented criteria for use based on the manufacturer’s recommendations. The permitted omissions and PPE recommendations specific to each of the RABS were summarized in a risk assessment, and related supporting documentation was cataloged in the compounding compliance software at each impacted location. The details of the risk assessment and required garb for each restricted access barrier system can be seen in Figure 2.

Reuse of masks. Many facilities throughout the nation were forced to reuse masks early in the pandemic, and compounding organizations and boards of pharmacy were forced to speak out and provide guidance in these situations.8 The task force evaluated the risk of potential microbial contamination in our compounding areas if mask reuse were to be implemented. Consideration was given to the use of cloth sterilizable masks to avoid reuse, but availability was limited. While we were able to delay the reuse of masks for a time, the day came when reuse was mandated from an organizational level. When looking for guidance from boards of pharmacy, we found that the Iowa Board of Pharmacy provided reuse recommendations including storing reused masks in a paper bag, retaining masks where they are donned, and replacing masks if visibly soiled.7 Ultimately, we provided guidance to our teams to reuse masks and provided instructions for donning, doffing, storage, retrieval, and disposal. We followed the available guidance, and to ensure a state of control in our cleanrooms, we suggested weekly surface sampling of PECs where reuse of masks was occurring.

The strategies above were implemented in a phased approach to avoid reuse of PPE, starting first with only operational changes to staffing and anticipatory compounding sterile products when possible. While operational changes were enough for a short period, our organization eventually reached a point where reuse of masks was necessary for conservation of the remaining supply, and the pharmacy department strategically implemented risk mitigation strategies around that directive. As of August 2020, the pharmacy department was exempted from the mask reuse policy and has returned to using 1 mask per entry into the cleanroom space, and supplies have stabilized. Without the above conservation efforts, the pharmacy department would have experienced an extended period wherein reuse of garb was required, and additional environmental monitoring would have been needed. These efforts extended our supply of PPE and allowed us to continue compounding and providing quality sterile products to our patients.

Summary

The pandemic resulted in PPE shortages throughout the nation, and our organization began consolidation and central distribution of masks and other PPE critical to the sterile compounding process. The pharmacy department is in a unique position because the continuation of compounding services is dependent on maintaining adequate and appropriate supplies of PPE and sterile compounding disinfecting supplies. This will not be the last PPE shortage we face in healthcare, and organizations should be prepared with preventive steps for conservation if a future pandemic arises. Pharmacy staff use PPE and disinfecting agents to protect sterile compounded products from contamination, and a shortage of these items has a direct impact on patient safety. Pharmacies must have an arsenal of alternative PPE strategies that both protect the sterile compound and help in the organization’s conservation efforts to allow for provision of patient care and continued provision of sterile compounded products with reasonable beyond-use dating. Implementing one or all of the above conservation methods for PPE can be a key to both the pharmacy department’s and the organization’s continued provision of safe patient care.

Disclosures

The authors have declared no potential conflicts of interest.

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