

Improve the ability to predict employee efficiency, cost of service and product wastage while simultaneously improving quality.

There are many areas within the health-care delivery system that are well managed or have externally defined practice standards providing a mandate for the delivery of consistent patient care; services; and, ultimately, customer satisfaction. One area that has been overlooked is sterile-product compounding. Compared to other aspects of the health-care system, there is a lack of uniform guidelines governing the practice of sterile-product preparation. Product quality may not be as high or as consistent as it is believed to be. Pharmacy managers can begin by looking at the current standard operating procedures (SOPs) that govern cleanroom practice at their organization. Questions that may need to be asked include:

- Are SOPs followed consistently?
- Do staff know and understand SOPs, do they embrace them, see them as helpful, see them as their own?
- Do SOPs incorporate checks and balances at likely points of failure?
- Is the compounding documentation complete?
- Does the documentation also serve as a data-collection tool relative to high-risk aspects of the operation?
- Are the policies and procedures well written, incorporating regular aspects of day-to-day business?

Completing this assessment allows the information to be systematically analyzed in the development and implementation of operational practices to achieve:

- Predictable cost of pharmacy production supplies and products,
- Optimal staffing levels,
- Expanded production capabilities,
- Enhanced clinical effectiveness,
- Efficient collection of quality management data,
- Predictable outcomes,
- Improved employee job satisfaction, and
- Additional recruitment and retention strategies.

The unknown variables in this analysis are the guidelines that will be used to develop SOPs and the manner in which sterile-product processes, once implemented, will be monitored to ensure compliance.

## Historical Context

Since the 1970s, several catastrophic patient-care events have occurred involving pharmacy-prepared sterile-product preparations.<sup>1-3</sup> One of the first groups to address this issue was the National Coordinating Committee on Large-Volume Parenterals (NCCLVP). This body developed and recommended standards of practice for the preparation, labeling and quality assurance ac-

# Improving the Management, Operations and Cost Effectiveness of Sterile-Product Compounding

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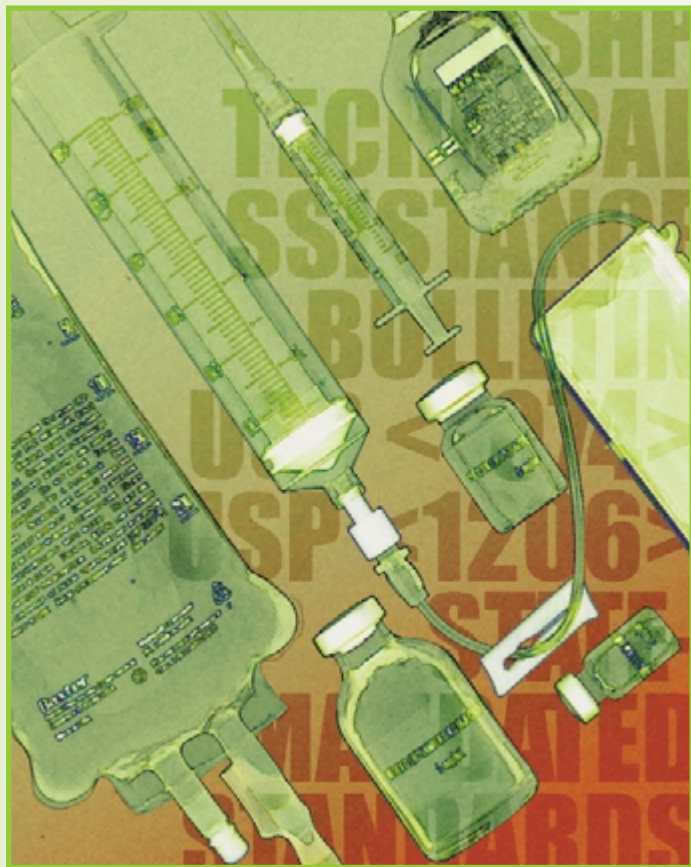
tivities of hospital pharmacy admixture services.<sup>4-10</sup>

Since the dissolution of the NCCLVP in the 1980s, the pharmacy profession and its professional organizations and associations continue to struggle to develop and adopt uniform standards of practice in this area. Many other health-care professions have adopted uniform standards of practice. The Oncology Nurse Society, Intravenous Nursing Society and American Medical Association are some organizations that have developed, adopted and implemented a number of guidelines that have become the “gold standard” within their respective practice areas.

In the early 1990s, many different pharmacy-related organizations (the American Society of Health-System Pharmacists [ASHP], the United States Pharmacopeial Convention [USP] and the National Association of Boards of Pharmacy) issued recommendations in an effort to provide a mandate and practice assistance to pharmacists and technicians responsible for preparing sterile products. A consistent theme running through these recommendations was that the pharmacist is responsible for ensuring that sterile-product preparations are prepared, labeled, controlled, stored, dispensed and delivered properly. The ultimate goal was to ensure the quality and integrity of pharmacy-prepared sterile products. None of these recommendations, however, has been uniformly adopted and accepted.

In 1992, the USP issued a draft recommendation, USP <1074>, “Dispensing Practices for Sterile Drug Products Intended for Home Use.” The intent of this general information chapter within the *USP/NF* was

... to detail the various procedures necessary to prepare and dispense sterile drug products intended for home use: the validation of sterilization and aseptic processes, the quality and control of environmental conditions for aseptic operations, personnel training, aseptic techniques, finished product release testing, storage and expiration dating, the con-



*trol of product quality beyond the pharmacy, patient or caregiver training, patient monitoring and complaints, and finally, a quality assurance program.<sup>11</sup>*

The United States Pharmacopeial Convention, Inc., which publishes the *USP/NF*, adopted USP <1206>, "Sterile Drug Products for Home Use," a variation of <1074>, which provides specific practice standards and operating guidelines.<sup>12</sup> The practice of pharmacy, however, does not have any accountability to the USP as a regulatory agency.

In 1993 the ASHP issued a Technical Assistance Bulletin entitled "Quality Assurance for Pharmacy-Prepared Sterile Products."<sup>13</sup> This defined the level and extent of recommended quality assurance measures to be used by pharmacy operations that prepare sterile products. These recommendations describe a variety of different operating parameters, such as physical plant, types of products used and length of product storage. This Technical Assistance Bulletin was developed to be applicable to a variety of practice settings, including hospitals, community retail pharmacies, long-term care facilities and home-care organizations. This document spawned the ASHP Risk Level categories (I-III) which, for some, have become the unofficial standard for the pharmacy profession. These recommendations stop short of

providing the degree of specificity that would make them useful to most pharmacy practitioners, which has impeded their integration and general acceptance. The rationale for not following any recommendations includes the perception that they are unnecessary, excessive, costly, and too time consuming. Others believe that they add no value to the process since there is insufficient evidence that their current practices need to be changed.

## Current Status

Few states have mandated detailed practice standards for pharmacies that compound sterile-product preparations. Most make statements that appropriate equipment, procedures and environments be used, without giving specifics. The lack of meaningful and detailed practice standards, along with the reasons mentioned above, has resulted in inconsistent practice conditions. Pharmacists and technicians have been permitted a significant degree of regulatory interpretation and professional discretion in this area.

There are many opportunities within the practice of pharmacy for pharmacists and technicians to vary the application of their knowledge to match the patient-care intervention required in a specific situation. Often, professional discretion in the area of sterile-product preparation means that "I can do it my way," as opposed to following systematic and validated operating policies, procedures and processes. This generous use of discretion has resulted in the creation of situations in which the basic aseptic guidelines recommended by all pharmacy-related organizations are basically nonexistent. Professional discretion relative to sterile-product compounding yields little or no product consistency. Out of consistency comes quality.

One element central to the total quality management approach is the focus upon quality and prevention of problems. Quality is the consistent production of products or services that the customer wants, with a simultaneous decreasing of errors. Though quality can be an outcome at a defined period of time, it is really a dynamic process leading to improvement of the output to customers. The practice of sterile-product preparation is no different. Many will say, "We have never had a reported problem with any of the products that we have prepared." This may be true only because no formal indicators or monitors were ever established to detect product quality deviation. Even if indicators could be established, there are too many variables outside the pharmacy's control that make detection difficult, if not impossible. This is all the more reason for building quality into the product. One cannot underestimate the importance of product sterility and accuracy, since the delivery of an improperly prepared or incorrectly formulated product can cause significant, if not life-threatening, situations.

In this day and age of cost containment and compressed operating margins, sterile-product compounding procedures continue to be thought of by some as significant costs that are of little value since no regulatory agency mandates their existence. It has been said that people respect what other people inspect. Since no "other

people” exist to monitor for sterile-product procedural compliance, negative consequences seldom ever occur.

The pharmaceutical industry, unlike the practice of pharmacy, is subject to extremely rigorous regulations that define all critical aspects employed in the manufacture of drugs. The Food and Drug Administration (FDA) publishes Current Good Manufacturing Practices (cGMPs) that apply only to sterile products manufactured by pharmaceutical companies. The purpose of cGMPs is to ensure that all pharmaceutical products are produced in such a manner as to ensure consistent quality and integrity. The FDA routinely inspects pharmaceutical operations to ensure regulatory compliance and holds companies accountable and liable for non-compliance. The penalties can be severe and lead to significant monetary fines and possible operational shutdowns.

On June 15, 1998, The New Jersey Board of Pharmacy made effective specific practice requirements that apply to all sterile admixture services in both retail and institutional pharmacy settings. These requirements combine many of the recommendations found in the ASHP Technical Assistance Bulletin and USP <1206>. They do not, however, provide detailed procedural specifics on how to meet the requirements. The new law mandates that pharmacies providing sterile admixture services in retail and institutional settings not already in compliance with the new requirements must significantly alter their standards of sterile-product preparation and physical operating conditions by December 15, 1999. The New Jersey Board of Pharmacy “...believes that the new, more stringent standards are a significant step toward further perfecting the sterile admixture preparation process for the protection of pharmacy personnel and the consumer.”<sup>14</sup> Many pharmacy administrators are in a quandary as to how to comply with the new law.

Today pharmacy has a renewed opportunity to refocus on developing a set of standards that all sterile-product operations can implement. It would detail activities specific to practice setting, patient volume and product type. It would facilitate acceptance and compliance. All this would occur in response to the profession’s recognition of the recent legislative changes and concerns over its own inconsistent practice standards. These standards could demonstrate the profession’s desire to take a proactive position in managing its own practice before others do.

## Interim Standards: USP Guidelines

Until more specific assistance from pharmacy-related agencies can be obtained, pharmacy managers can use the guidelines in USP <1206> as a template. Home Medical America, Inc., one of the largest home infusion providers, states in one of its policy statements that, “The Good Aseptic Procedures section of the Pharmacy Operations Manual is based on the USP standards for ‘Sterile Drug Products for Home Use,’” which is USP <1206>.<sup>15</sup>

In “Sterile Drug Products for Home Use,” <1206>, the USP defines some key factors for building quality into products, which include at least the following general principles:

1. Personnel are capable and qualified to perform their assigned duties.
2. Ingredients used in compounding have their expected identity, quality, and purity.
3. Critical processes are validated to ensure that procedures, when used, will consistently result in the expected qualities in the finished product.
4. The production environment is suitable for its intended purposes (addressing such matters as environmental cleanliness, control, monitoring and the setting of environmental microbial action limits as appropriate).
5. Appropriate release checks or testing procedures are performed to ensure that finished products have their expected potency, purity, quality and characteristics at the time of release.
6. Appropriate stability evaluation is performed for establishing reliable expiration dating to ensure that finished products have their expected potency, purity, quality and characteristics at least until the labeled expiration date.
7. There is assurance that processes are always carried out as intended or specified and are under control.
8. Preparation conditions and procedures are adequate to prevent mix-ups.
9. There are adequate procedures and records for investigating and correcting failures or problems in preparation, in testing, or in the product itself.
10. There is adequate separation of quality control functions and decisions from those of preparation.

These factors and their detail within <1206> can provide definitive guidance to pharmacists and technicians. With <1206> as a procedural backbone, a concept from the pharmaceutical manufacturing industry known as *systematic process control* can be employed. *Systematic process control* is defined as policies, procedures and processes that are validated and used to consistently produce products of the highest quality. Systematic process control strives to eliminate employee variability and “professional discretion” by breaking down processes and identifying each of the critical tasks necessary to achieve a product of consistent yield and quality. It also allows critical indicators to be built into the process, thereby generating crucial data that ensure optimal product quality. One of the cornerstones of systematic process control is demonstrating process, personnel, and product control over time through complete and consistent data collection.

## Components of Systematic Process Controls for Sterile-Product Operations

### Data

There are several activities that yield crucial data, which can provide a complete picture of product quality and physical plant fitness. If any of these activities are out of normal operating limits,



product quality and operational fitness can be impacted. These activities include but are not limited to:

- Compliance with operating policies, procedures and processes and the documentation generated from their execution;
- Initial and ongoing employee education using didactic, practicum and on-the-job training strategies;
- Personnel controls such as proper handwashing, gowning and gloving procedures and successful aseptic technique validation; and
- Air and surface sampling tests of critical work areas.

Systematic process control relies on prospective data monitoring and collection versus retrospective analysis such as end-product testing. The results of end-product testing (sterility or quantitative analysis) are generally not known prior to product release for patient use. Routine and systematic data collection occurs in combination with direct observation of employee job performance and

against written policy and procedure compliance. Data collection points are designed to monitor high-risk and high-volume activities that involve some level of human intervention. These processes do not need to be cumbersome. They can be integrated seamlessly into production (compounding) documentation.

There are four significant advantages to an integrated data-collection approach.

1. Data are observed and collected at the point of production so that immediate decisions can be made regarding the fitness of the product as it moves through the production cycle. Should a deviation occur, it can be dealt with immediately with little risk to the patient.
2. Data can be considered more reliable because they are collected every day instead of sporadically. Consistent data collected daily eliminate test phenomena since multiple points of information enhance reliability and confidence.
3. Multiple data can be trended and used to identify problems or process variations before they become critical and adversely impact products, processes or personnel. Systematic process control helps identify potential points of failure and allows for timely modification and prevention.
4. The process is transparent and eliminates the end-of-the-month, quarterly or yearly scramble of data collection, which causes many to consider sterile-product-compounding processes to be too time consuming and costly and somewhat useless since the data are too old and cannot be used constructively in the management of the process.

### Proactive Employee Management

Systematic process control also involves proactive employee management. The market is changing around us, and the health-care sector is being challenged to do more with less. Approaches to employee education and training need to be relevant to the activities and tasks that occur in the workplace on a daily basis. These approaches can be integrated easily into daily workflow and can be meaningful to the employee. This will help to maintain job satisfaction and increase the ability of individuals and the team to produce greater output. The development of structured job descriptions and breakdown of critical operational tasks, along with training and ongoing educational strategies, can be used effectively to validate employee performance easily and objectively. An objective performance evaluation allows the employee to receive necessary support in order to perform at an optimal level. Employees should know how to perform their job responsibilities properly and training facilitates that ability, along with fostering the understanding that they are part of a team. Variation in job performance impacts product quality.

Compounding personnel are the most significant source of particulate matter, which can contaminate sterile products. A variety of activities that can impact product quality can be controlled by personnel, including:

- Proper handwashing, gowning and gloving procedures,

- Efficiently organized and planned compounding tasks, and
- Minimized movement in and out of compounding hood or cleanroom.

These critically controlled activities, along with validated, proper, aseptic technique, can ensure that quality products can be produced.

### Process Simulation Testing

The art and science of sterile-product-preparation technology has not advanced as quickly as other areas of health care. Fluid-delivery technologies (internal and external infusion devices) used in patient care have undergone phenomenal development. Advances have produced devices capable of delivering medications and fluids in an almost infinite number of ways and under a variety of operating conditions. The operating tolerances of these devices are very tight and produce consistent results with minimal intervention. The technology employed in the preparation of sterile products has not advanced as far. Compounding personnel must still perform many critical manual manipulations. It is generally and somewhat erroneously assumed that all pharmacy pro-

fessionals (pharmacists and technicians) can successfully perform critical aseptic manipulations, activities and tasks required to produce sterile parenteral solutions. It is important that process simulation testing be employed to test and validate the aseptic technique of all personnel directly involved in the aseptic manipulation of pharmaceutical components used in the preparation of patient-specific sterile products. Process simulation testing validates the ability of all aspects of process and operation to produce aseptic product while simultaneously validating:

- Aseptic technique of individual compounders,
- Cleaning and maintenance of controlled environments,
- Handwashing, gowning and gloving procedures,
- Compounding equipment used to produce aseptic patient product, and
- Operational fitness of the physical plant (cleanroom/ anteroom/ prep area).

Process simulation testing can validate that compounding personnel can successfully prevent contaminants, such as particulate matter and microorganisms, from inadvertently being introduced by technique and process-related activities performed on a



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routine or daily basis. Process simulation testing is also designed to be rigorous enough to mimic worst-case operating conditions so that any testing phenomenon seen in small-size test samples can be eliminated. A microbiological growth medium, such as trypticase soy broth, is commonly used, which will support the growth of a wide spectrum of microorganisms. In addition to individual personnel testing, compounding equipment should also undergo process simulation testing in order to validate its operational capability under worst-case operating conditions. Manufacturers validate their equipment's ability to accurately measure components from source containers. They do not test the equipment's ability to produce accurate products that are sterile.

### Monitoring the Cleanroom

How do we know if compounding personnel are performing proper handwashing, gowning and gloving procedures correctly? How do we know if our daily cleaning of the cleanroom is being done consistently and properly? How do we know if our processes are causing unnecessary movement and the generation of particles?

Monitoring environmental cleanliness and microbial bioburden allows data to be collected about whether the physical plant is operating as anticipated, along with the degree to which operating procedures and processes are effective. This is accomplished by collecting air and surface samples using a microbial growth medium. Air settling or surface Rodac™ plates capture actual air and surface conditions. The presence of microorganisms is manifested by the formation of colony-forming units. The colony-forming-unit count is used as a macro index of microbial bioburden. These data allow trending of bioburden and provide the ability to monitor shifts that would permit early detection, intervention and remediation. The USP <1206> provides practical information about how to set up an environmental monitoring program. It also describes how to determine acceptable and out-of-limit conditions in a given controlled environment.

### Putting It All Together

By initiating the strategies detailed in this article, pharmacy managers can start to develop a sterile-product compounding service that will create an environment of employee pride and ownership; product consistency and quality; predictable product, supply and operating costs; and organizational efficiencies that can be applied to the management of direct patient care.

Service organizations that are structured in a systematic manner greatly reduce management by opinion and allow for management by fact. Systematic process control generates the necessary data to provide consistent patient care; services; and, ultimately, customer satisfaction. This approach has other benefits. By integrating systematic process controls, the burden of end-product testing costs can be eliminated or lessened substantially. Routine testing of outputs substantially similar to the end-products themselves continuously validates product quality. It also provides mean-

ingful information by which to judge the status of the operation. Another important result of adopting this philosophy is that it puts the pharmacy department in a position that is consistent with other organizational departments. Many have begun cost-reduction/containment initiatives. This approach to pharmacy cleanroom activities improves the pharmacy manager's ability to predict employee efficiency, cost of service and product wastage while simultaneously improving quality. It also brings the mystical pharmacy cleanroom environment into the mainstream of a health-care system focused on achieving higher-quality outcomes for patients while effecting more efficient resource utilization strategies; in other words, doing more with less and proving it. Pharmacy cleanroom operations can do it, too.

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