



IMPLEMENTING A SUCCESSFUL REGIONAL COMPOUNDING PLAN: ISSUES AND REQUIREMENTS

Lou Diorio, RPh
Dave Thomas, RPH, MBA
Principals
LDT HEALTH SOLUTIONS, INC.



EXECUTIVE SUMMARY

The hospital segment of the health care industry is facing extraordinary pressure to provide better patient care and demonstrate improved patient outcomes, while continuing to achieve measurable cost reductions. As one tactic in attaining these goals, health-system pharmacy departments are re-engineering their workflows through the implementation of process shifts that facilitate new pharmaceutical care models. Consequently, they have employed technology to automate the distribution of drug product throughout the organization. These automation advances include barcode tracing of doses from the pharmacy to the patient bedside.

In addition, health-system pharmacies are increasing their focus on outsourcing certain compounded sterile preparations (CSPs) to contract compounders, thus enabling their own professional staff to be redeployed to other essential clinical and direct patient care activities. Due to the unique makeup of each health-system, this shift in the pharmacy service model has both positive and negative impacts. The central focus of any organization contemplating an operational shift is to formulate a plan that is consistent with the core organizational goals. The health-system must recognize and understand the economic impact that may occur during the implementation of an outsourcing program, while at the same time retaining the central focus of any care model – serving patient needs.

This paper discusses some of the pros and cons of outsourcing CSP production and provides a model for developing a successful regional compounding plan that offers many of the benefits of outsourcing while providing significant operational efficiencies to the organization.

OPPORTUNITIES

In a recent *Pharmacy Purchasing & Products* magazine survey of hospitals, a majority (64%) of respondents indicated they outsource some part of their compounding activities to third parties. Furthermore, the results of the study revealed 26% of respondents would increase their use of contract compounders in the future.¹ This movement to the increased outsourcing of more pharmacies' compounded sterile preparation (CSP) workload has created some interesting shifts in the average pharmacy's budget.

Since the introduction of USP General Chapter <797>, pharmacies have encountered economic burdens that accompanied compliance efforts, as well as operational and implementation challenges. In an ASHP national survey, Candy, Schneider and Pendersen, described the effects on resource allocation in two key areas when speaking about USP General Chapter <797> compliance: budgetary spending and labor spending.² Similarly, in an article that appeared in the *American Journal of Health-System Pharmacy (AJHP)*, Eric Kastango predicted that measurable increases in addressing the quality domains of USP General Chapter <797> would occur in eight key areas, requiring additional spending for the average hospital pharmacy.³

¹ State of Pharmacy Compounding (2010) Pharmacy Purchasing and Products Magazine (www.pppmag.com)

² Candy, Schneider, Pendersen- Impact of USP Chapter <797>; Results of a National Survey, JASHP 2006

³ E Kastango – Blueprint for Implementing USP <797> for compounding sterile preparations in pharmacy JASHP 2005

With the re-engineering of the modern pharmacy department toward a more efficient model of service, the application of modern business principles and strategies long accepted in other business sectors must be considered. The decision process must begin with an examination of the organization's practice philosophy. The fundamental question health-systems need answered is; "What do you intend to do once this re-engineering is complete?" More often than not, the impetus for questioning current practice in any organization is either a budgetary review or some negative quality indicators relating to service.

If budgetary review is the case, a careful review of the figures is in order. It is not satisfactory, nor prudent, to re-engineer a process as complex as the compounding of sterile drugs for human use by simply comparing the drug and the diluent price tag against the pricing of the outsourcing vendor or contract compounder. A clear understanding of all of the costs impacting the provision of each CSP to the organization is key to determining the true "return-on-investment" (ROI) that changing the CSP procurement process will have on an organization. Calculation of these "realistic-ROIs" (r-ROIs) can be done only with a clear understanding of all of the costs involved in the provision of a finished CSP dose to a patient.

Beyond the simple drug and diluent costs, health-systems need to factor in the labor cost (both pharmacist and technician) to compound, check, label, package, store and deliver the CSPs. Health-systems must also examine their current ability to assign meaningful Beyond-Use Dates (BUD) to the preparations they are compounding, as opposed to the extended BUDs they may have from an outsourcing vendor; the testing costs when and if extended BUDs are necessary; the CSP expiry waste; the batch quantity needed of the CSP; the overhead costs including compounding supplies and materials; and the efficient utilization of the pharmacy's scarce resources to provide clinical and cognitive services for direct patient care.

COMPLIANCE AND REGULATORY HURDLES

Historically, pharmacies were only permitted to prepare and dispense CSPs to patients pursuant to a valid prescription written by an authorized prescriber. The Food and Drug Administration (FDA) and State Boards of Pharmacies have taken a keen interest in pharmacy operations that compound inordinate amounts of non-patient specific CSPs and/or operate outside of the classic physician-patient-pharmacist ("triad") relationship. These pharmacies prepared CSPs under the guise of pharmacy practice but may not be able to demonstrate evidentially that a recognized relationship (physician-patient-pharmacist or physician-patient-pharmacist-pharmacist) exists.

The practice of pharmacy has evolved, as has the need to improve patient safety through the development and implementation of new and innovative pharmaceutical care models; however, state pharmacy practice acts have not always kept pace with these changes. This issue is most readily apparent in the desire of hospitals to outsource compounding of complex and/or large volume CSPs to specialty providers; allowing the hospital to focus on provision of clinical management of patients and other cognitive services. Though this trend appears to be growing, most states do not recognize this service model in their pharmacy practice regulations.

In the 1980's, in order to support their hospital clients with compounded preparations, Travenol® Regional Compounding Centers (TRC)/ Baxter® Healthcare operated Regional Compounding Centers (BRC) offered "compounded drugs" to hospitals, doctors' offices and home infusion companies. These products included chemotherapy preparations, TPNs, antibiotics and specialty renal products. The FDA determined that Baxter violated NDA and cGMP regulations under this model due to the manner in which the products were being offered to the hospital and home infusion market. Baxter was forced to exit the hospital and home infusion business, was fined by the FDA and required to sign a Consent Decree, prohibiting them from offering this service from a cGMP operation in the future. Baxter pharmacies were not affected by the consent decree and could provide CSPs directly to the doctors' offices.

In 1991, BBraun Central Admixture Pharmacy Services (CAPS) started to provide outsourced compounding services to hospitals under pharmacy licenses, which were technically in violation of prevailing pharmacy law. In response to CAPS, which was capturing a large share of the nutritional solution components from the Baxter marketplace, the Baxter Clintec® Nutrition Division entered the market by creating the COMPASS® group to provide similar services to prevent the market-share erosion CAPS was creating. The Baxter Clintec® Nutrition Division petitioned the FDA for permission to compound for hospitals in a manner that did not violate the Consent Decree still in place. The FDA stipulated that the Clintec® Nutrition Division could enter the market, but only if it complied with CFR 21 Part 211 – *General and Current Good Manufacturing Practice For Finished Pharmaceuticals*, and the compounded medications were provided with patient-specific labeling and on the order of a physician. Simultaneously, the Clintec® Nutrition Division filed a complaint to the FDA that CAPS was not subject to the same requirements as Baxter/COMPASS. In response, the FDA forced CAPS to register their operations as manufacturers.

FDA oversight of outsourced compounding has created a quandary for the FDA, since none of the national providers fully and completely comply with all of the requirements of CFR 21 Part 211. In pursuing this course, the FDA inadvertently created a hybrid compounding model that does not neatly fit into FDA regulation, nor into any State Board of Pharmacy practice regulations.

Individual state boards of pharmacy were not responsible for the oversight of this new pharmacy service model since they did not have adequate regulation to address or control the practice, especially in cases where the pharmacy was providing CSPs from out-of-state. The FDA has quietly accepted or tolerated the activities of all the large national providers as long as they show significant compliance to the provisions of the CFR 21 Part 211. Those provisions include proper employee training, proper engineering controls, environmental control and monitoring, process validation, label control and robust documentation of operations.

The initial requirement to provide patient-specific compounded preparations to clients has slowly evolved to include limited numbers of non-specific compounded preparations to clients. This service creep has been accepted by the FDA for these FDA-registered operations. It is important to note that it is understood that these operations provide institutionally specific fixed formulas (hospital-specific formulas), which they prepare on the hospitals' behalf.

In May 2002, the FDA issued a guidance document for FDA staff and the industry- SEC. 460.200-*Pharmacy Compounding*. In this document the FDA recognizes that, “pharmacists traditionally have extemporaneously compounded and manipulated reasonable quantities of human drugs upon the receipt of a valid prescription for an individually identified patient from a licensed practitioner. This traditional activity is not subject to this guidance.” The FDA goes on to state that it would defer to state authorities regarding “less significant violations of the [Food, Drug, and Cosmetics] Act...”

The guidance stipulates the nine (9) acts that a pharmacy could not engage in and which would trigger “enforcement action” by FDA:

1. Compounding of drugs in anticipation of receiving prescriptions, except in limited quantities.
2. Compounding of drugs or combinations that were withdrawn from the market for safety reasons.
3. Compounding of drugs from bulk active ingredients that are not components of FDA-approved drugs in the absence of a valid Investigational New Drug (IND) application.
4. Receiving, sorting or using drug substances that were not made in an FDA-registered facility.
5. Receiving, storing or using drug components not guaranteed or otherwise determined to meet official compendia requirements.
6. Using commercial-scale manufacturing or testing equipment for compounding drug products.
7. Compounding drugs for third parties who resell to individuals or patients or offering compounded drug products wholesale to other state-licensed persons or commercial entities for resale.
8. Compounding products that are already commercially available in the marketplace or producing copies of commercially available FDA approved drugs.
9. Failing to operate in conformance with applicable state laws regulating the practice of pharmacy.

This FDA guidance was issued in part as a response to failed attempts in the early 1990s by the American Society of Health-System Pharmacists (ASHP), the United States Pharmacopeial Convention (USP) and the National Association of Boards of Pharmacy (NABP) to issue recommended practice guidelines of their own for Compounded Sterile Preparations. Eventually, this failure led to the genesis of USP General Chapter <797> guiding practice for compounding sterile products.

A key issue in this service model is accountability and the facility to recall compounded CSPs, where necessary. The regional compounding of CSPs depends in part on the production of doses that are properly labeled, but are not labeled as patient-specific preparations. This causes some Boards of Pharmacy to question their definitions of “*compounding*” versus “*manufacturing*.” Working with both Federal and State authorities is critical when designing a health-system pharmacy service model that is both functional and compliant to prevailing regulations.

CHANGING SERVICE MODELS

“Contract Compounders” operate under the premise that through a formal and legally binding agreement between themselves and a health-system pharmacy, the contractors are the designated compounding arm of the pharmacy; preparing solutions that the health-system is permitted to compound in anticipation of its need. As part of this agreement, the health-system Director of Pharmacy (DOP) who contracts the services of a Contract Compounder is responsible for the preparation, quality, sterility and potency of all of the CSPs provided by the Contract Compounder. S/he also is directly responsible for retrieving and segregating any provided CSP product that is recalled.

In the 2010 Outsourced Pharmacy survey conducted by *Pharmacy Purchasing & Products* (PP&P) magazine⁴ it was identified that no fewer than 11 national contract compounding vendors were in use. State Boards of Pharmacy have accepted this service model as a logical extension of the anticipatory compounding codicils within their practice acts. While state and local officials are becoming more and more comfortable with these new service models, the satisfaction with national outsourcing providers is actually trending downward. The same PPP survey had Directors of Pharmacy rating 87% of their outsourcing providers as “good” or “excellent” – a decrease from the 2009 survey, which indicated a 91% rating of “good” or “excellent.” This trend is also supported by the fact that a majority of Directors of Pharmacy use multiple outsourcing vendors to provide a wide range of preparations (oxytocin, epidurals and pain management therapies being the most common).

Further, it is not uncommon for health-system pharmacies to have a service model that contains a combination of the following components in order to service their patient populations:

1. A fully functional cleanroom.
2. A national outsourcing provider/vendor.
3. A local contract compounder.
4. Proprietary vial and bag systems in ready-to-use (RTU) commercially available dosage forms.

DEVELOP THE IMPLEMENTATION PLAN

Once a health-system determines a need to re-engineer their pharmacy workflow for CSP production, whether to update processes for regulatory compliance, to allow redeployment of clinical resources, or to improve waste management and reduce drug preparation costs, the first step is to develop and implement a plan. Before completing a needs assessment for the project, it is important to establish a baseline inventory of the human, capital and other resources within the health-system. This step is essential to determine the amount of CSP compounding that can take place with the number of people, compounding space, physical IV room size, compounding equipment capacity and physical limitations of moving materials in and out of the IV room. This assessment must also consider the organization’s current USP <797> compliance readiness.

⁴ State of Pharmacy Compounding (2010) Pharmacy Purchasing and Products Magazine (www.pppmag.com)

To assess the “current state” for CSPs within the organization, each pharmacy must review their compounding needs:

- What CSPs can realistically be batched?
- What is each CSP’s chemical stability?
- What specific BUD for these CSPs can be documented?
- What is the USP <797> Risk Level for each CSP?
- How much time is required to compound each unique CSP?
- What specialized equipment or automation is required?
- Are there any special shipping requirements for each CSP?
- If so, what is the appropriate shipping container for each CSP?
- How must these CSPs be stored (and transported)?
- Do you have sufficient warehouse (storeroom) space for storage of CSPs?
- What is the impact of CSP compounding on the overall pharmacy resources; that is, what clinical and cognitive services are needed from the pharmacy operation to support direct patient care?

Once the baseline resources inventory and CSP needs assessment have been documented, each pharmacy within the health-system must establish requirements for each CSP required:

- Compounding time
- Compounding methodology
- Documented BUD
- Batch quantity
- Dose stability
- Risk level
- Testing requirements
- Physical size
- Storage requirements

Production of CSPs requires a variety of compounding methodologies. CSP compounding methodology should be matched to each unique CSP to ensure the simplest and most accurate method. Written compounding documents are required to verify the CSP preparation process, as well as documenting the ingredients used to prepare the final CSP. In some cases, pharmacy automation will provide the best compounding methodology for the health-system needs. Automation technology should be evaluated based on the benefits it offers to the health-system pharmacy in terms of process control and dose safety to determine if it represents the best approach to meeting CSP production requirements.

A formal analysis of computer hardware and software needs should be completed. This includes a determination of the number of labels needed, label stock, computer equipment to produce and control labels, backup equipment, maintenance of hardware, software

requirements, testing protocols, and documentation. Policies must be in place for the strict control of labels including printing, counting, sample, and documentation.

A comprehensive quality indicator and monitoring system must be designed to properly test environment, operations and equipment on an initial and ongoing basis. This system is paramount to confirming sterility controls are operational and not compromised. USP <797> also stipulates that beyond the simple identification of problems this system must also be able to assist in the timely correction of problems.

A policy and procedure system must be established. This process ensures all operations are completed in the same manner, changes are addressed timely, CSPs are properly documented, BUDs are standardized and systemic gaps are addressed. This P&P system is not static and needs to be reviewed and updated on an ongoing basis to serve the pharmacy's needs. USP <797> outlines the minimum requirements for such policies, but the list included in the chapter is not comprehensive enough to be complete.

Production plans should be developed for the evaluation of any pharmacy automation or dose management software intended for use in compounding sterile products. This evaluation ensures a consistently safe CSP and provides the organization with the assurance that they have chosen their compounding methodology to meet its individual needs in terms of the resource inventory and needs assessment completed earlier in the process.

Among the considerations for determining the value of pharmacy automation and software to support CSP production are:

1. Experience and reputation of the vendor
2. Lease/purchase cost of any management software
3. Lease/purchase cost for any pharmacy automation devices
4. Ongoing cost for device disposables
5. Service and maintenance costs
6. Software/device setup time, and time for setup verification if required, and its associated cost(s)
7. Device delivery accuracy and speed
8. Ability of software/device to promote and support best practice for compounding methodology
9. Software/device complexity (ease of use)
10. Device/software integration with other pharmacy systems and technologies (Pharmacy Information Systems, bar codes, etc.)

IMPLEMENT THE PLAN

The real work begins once the organization has assembled the necessary resources, developed and reviewed its plan, and assembled the team that it will depend upon to provide CSPs to its network. Implementation of a successful regionalization plan requires the commitment of many healthcare professionals within an organization – both within and outside of the pharmacy.

Health-systems should consider the following before committing to firm implementation dates for its plan:

- Completion of the regulatory compliance checklist for the pharmacy compounding area(s) uncovered by the situational “gap” analysis
- Completion of the P&P review for pharmacy operations
- Completion of competency-based learning tools (and documentation) for all compounding personnel
- Completion of all media qualification testing (including fingertip and thumb plating) for all compounding personnel
- Final development of the CSP formulary to be offered
- Final development and approval of all BUD determinations for that formulary
- Determination of the formulary review interval (quarterly, semi-annually etc.)
- Development and approval of all compounding documentation (including all package and container labeling)
- Verification of all processes (and documentation) to support pharmacy automation
- Choice of an implementation “ramp-up” period (offering limited CSPs from the formulary)
- Scheduling of regular assessment meetings between the production component and the end-user of the CSPs

Assembly of the key elements listed above will assist your organization in formulating a comprehensive action plan for the implementation of a regional compounding program. Whether the coverage area of your organization is several buildings or service areas on one campus or several campuses in a geographic region, the principles are the same. The proper utilization of available resources both inside and outside your organization will empower your staff to provide the safe high quality your patients deserve.

SUMMARY

Regardless of the service model chosen by the health-system, there are key issues to recognize and address in ensuring a safe program for compounding sterile products. Challenges occur with all models, and surveys indicate that many health-systems use a “hybrid” program of insourcing and outsourcing sterile compounding activities to meet their individual needs. Regionalization of CSP activities provides an economical and effective alternative to outsourcing that can be implemented successfully when well planned and executed. In addition, outside resources (consultants, pharmacy automation and software tools) are available to assist program directors and others in assessing and addressing their specific organizational needs to ensure their regional compounding programs meet organizational goals and patient needs.