Profiles in CSP Insourcing: Scripps Health

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Hospital Profile

Scripps Health is a private, nonprofit integrated health system in San Diego, California. The system comprises hospitals on five campuses. A network of Scripps Clinics and Scripps Coastal outpatient locations across San Diego county also are part of the system.

Scripps Memorial Hospital Encinitas is a 158-bed community hospital that provides 24-hour emergency care and includes the North County's first primary stroke center. Located in La Jolla, Scripps Green Hospital is a 173-bed teaching hospital whose services include organ transplantation, oncology care, and blood and bone marrow transplantation. Scripps Memorial Hospital La Jolla has 444 licensed beds and is home to the Prebys Cardiovascular Institute, a center for cardiovascular medicine, research, and training. Scripps Mercy Hospital is a single hospital with campuses in San Diego and Chula Vista. Together, they comprise the largest teaching hospital in the county with more than 700 licensed beds and provide services as a level 1 trauma center.

Scripps Central Pharmacy Production Center (CPPC) was licensed as a centralized hospital packaging pharmacy in February 2014. In addition, it is licensed as a hospital pharmacy—although it is not physically located in a hospital—and maintains a sterile compounding license issued by the California State Board of Pharmacy. As a centralized hospital packaging pharmacy, Scripps CPPC may prepare unit dose packages, compounded sterile preparations (CSPs), and compounded unit dose medications for administration only to inpatients within the general acute care hospitals under common ownership of Scripps Health as long as those hospitals are within 75 miles of Scripps CPPC.

Scripps CPPC is located centrally to serve the Scripps hospitals. It is a 3600-square foot facility designed for sterile and non-sterile compounding and packaging. The ISO class 7 buffer room has 650 square feet and contains five laminar airflow work benches and one automated compounding device for CSP production. The Scripps CPPC operates Monday through Friday from 0600 to 1630. The formulary of CSPs includes those that are prepared in batches and assigned beyond-use dates (BUDs) consistent with USP chapter <797> and batches of CSPs to which an extended BUD is assigned. For the extended-BUD products, initial testing includes potency,

sterility, pH, particulate matter, endotoxin, and container closure integrity. All CSP product lines are subjected to potency testing annually.

The Scripps CPPC conducts no high-risk (non-sterile to sterile) compounding.

Non-sterile compounding is currently limited to repackaging and barcoding oral drugs in solid form from bulk bottles. Pharmacy automation technology is used for these processes. In 2015, the decision was made to stop unit dose packaging of bulk liquids. We elected to discontinue this service due to an abundance of low-cost outsourced options available to meet our health-system needs.

Compounded Sterile Preparations Timeline

Prior to Fall 2012

- All Scripps hospitals operated semi-independently in the administration of the sterile compounding programs.
- Outsourcing of CSPs varied from one Scripps hospital to another. Some sites requested quality assurance (QA) reporting from vendors, and others did not. Outsourced CSPs included:
    - Parenteral nutrition solutions
    - Antibiotic syringes (cefazolin)
    - Vasopressors
    - Controlled substances (i.e., patient-controlled analgesia)

January 2014

Scripps Health implemented a system-wide environmental sampling program. Initially, all sampling at the hospitals was conducted by pharmacy technicians from the CPPC.

February 2014

Scripps CPPC was licensed as a centralized hospital packaging pharmacy.

February 2014

CPPC began production of antibiotic syringes.

March 2014

Pharmacy leadership (directors, operations managers, medication safety officers) received formal sterile compounding training.

March 2014

CPPC began production of vasopressors and other selected intravenous piggyback (IVPB) CSPs.

May 2014

Scripps Health approved a system-wide sterile compounding policy that included:

- Education and competency requirements for all personnel who perform or oversee sterile compounding
- Standardization of training for environmental services technicians who clean pharmacy areas, including buffer rooms and ante-areas where CSPs are produced
- A comprehensive quality management plan that governs the environmental sampling of all hospital pharmacy sterile compounding areas

June 2014

Safety technicians from the environmental health department assumed sampling responsibilities while responsibility for media incubation and the reading of media plates was retained by the CPPC.

March 2016

Pharmacy leadership produced a white paper to define and describe necessary steps for Scripps Health hospitals and clinics to take to comply with USP chapter <800> requirements for hazardous drug handling in healthcare settings.

April 2016

Beyond-use date (BUD) committee described rationale and action for BUDs assigned to medications dispensed for administration in a syringe, including stability and sterility testing requirements and maximum BUD in the absence of specific stability information

December 2016

Facility construction waivers submitted to California State Board of Pharmacy for four Scripps Health hospitals that will be unable to meet facility requirements related to hazardous drug compounding as outlined in the California State Board of Pharmacy regulations effective January 1, 2017.

December 2016

Scripps CPPC Initiated container closure integrity tests for all extended-BUD CSPs on formulary to meet new California State Board of Pharmacy requirements for sterile compounding.

Product Line Changes – *How has the balance of outsourcing to insourcing changed over the past 5 years?*

Prior to the licensing and opening of the Scripps CPPC, the hospitals obtained CSPs from a number of outsourcing compounding pharmacies.

When the CPPC first started CSP production in February 2014, it started with antibiotic syringes. Cefazolin 1 g, ceftazidime 1 g and 2 g, and ceftriaxone 1 g and 2 g syringes were produced. The decision to produce these particular CSPs was driven in part by challenges encountered with the items obtained from the outsourcing compounding pharmacies. The problems did not lie with stability or sterility, but with the process used in applying and documenting the BUD for these products. The antibiotic syringes were received from the outsourcing compounding pharmacy in a frozen state with a 42-day BUD. It was the responsibility of Scripps

pharmacy personnel to thaw the frozen product and apply a sticker with a BUD of 9 days under refrigeration, as long as the 9 days did not extend beyond the original 42-day BUD for the frozen product. The assignment of an incorrect BUD was a risk inherent in this process. Our solution was to produce these antibiotic syringes at the CPPC and dispense them refrigerated with a 9-day BUD on the label to the sites. In this manner, it was the duty of the CPPC staff to choose the correct BUD for the label, and the risk for error was shared by many fewer individuals.

One of the next line items added to the formulary was promethazine 12.5 mg in 50 mL of normal saline (NS). The decision to include this line item was driven by a system-wide decision to adopt the safe practice recommendation of diluting promethazine prior to administration to reduce the risk of tissue damage from intravenous (i.v.) administration of undiluted or insufficiently diluted medication. The standard dose and concentration for promethazine administration at Scripps Health became 12.5 mg/50 mL NS. To promote the use of this concentration, vials were removed from automated dispensing cabinets, and IVPBs of this concentration were stocked. The CPPC produced the product and conducted the appropriate potency testing to allow for storage at 9 days under refrigeration, consistent with USP chapter <797> requirements for medium-risk compounding. System-wide standardization of the concentration is expected to improve patient safety by reducing the risk of infusion-related adverse events and administration of the wrong dose.

Later in 2014, the next series of CSPs identified for production by the CPPC included medications that were often ordered STAT or needed to be available in automated dispensing cabinets in critical care areas. Amiodarone 900 mg/500 mL dextrose 5% in water (D5W), diltiazem 125 mg/125 mL D5W, norepinephrine 4 mg/250 mL D5W, and phenylephrine 50 mg/250 mL D5W were identified by pharmacy operations and clinical managers as CSPs that should be produced in the CPPC and made available in critical care areas. Because of the desire to stock these items in automated dispensing cabinets, testing was conducted by a third-party laboratory service to provide the evidence needed to extend the BUD for these items. Once the master formula record was produced and process validation was completed, three batches of each medication were produced and tested for sterility, stability, pH, endotoxin, and particulate matter (we now also conduct a closed container integrity test) to support a BUD of up to 75 days stored at room temperature or refrigerated, depending on required storage conditions. To help meet the needs of the labor and delivery department, the CPPC began producing CSPs containing magnesium 25 g/250 mL NS, oxytocin 15 units/250 mL NS, or oxytocin 20 units/1000 mL NS. The same testing standards used for amiodarone, diltiazem, norepinephrine, and epinephrine were applied to these CSPs.

Towards the end of 2014, as the capacity for the CPPC to expand its formulary increased, the pharmacy leadership explored medications that were prepared in batches at the hospitals in varying amounts. A decision was made to compound vancomycin 750 mg/250 mL NS, vancomycin 1250 mg/250 mL NS, and vancomycin 1500 mg/500 mL NS in batches. These were the doses and concentrations that were compounded at the sites, and they were often prepared in batches at the larger hospitals. The BUD for these products was 9 days under refrigerated storage, consistent with USP chapter <797> requirements for medium-risk compounding. At about this same time, there was a request from the sites for the CPPC to prepare batches of CSPs used in the cardiac

catheterization lab. Intracoronary nitroglycerin 1 mg/10 mL D5W and verapamil 1 mg/10 mL NS were identified as appropriate CSPs for batch preparation by the CPPC based on use throughout the Scripps system. Potency and sterility testing were conducted on both of these CSPs.

Throughout 2015 and 2016, the CPPC formulary of CSPs remained relatively stable. Only a few items were added or removed, based on system-wide utilization. One need that continues to go unmet by the CPPC are the CSPs required for the Scripps Health outpatient clinics. Due to the licensure as a centralized hospital packaging pharmacy, the CSPs prepared may only be administered to inpatients of acute care hospitals under common ownership. This means that the Scripps outpatient clinics may not utilize our CSPs. This is one area that continues to resurface because the clinics would like to utilize our services but they are not able to.

Personnel – ***Who was involved in the strategic planning of CSP-related projects or changes?***

A desire to ensure the production of accurate and safe sterile compounded medications for patients of Scripps Health was part of the initial motivation for creating a centralized compounding pharmacy. The complementary goals of improving quality and embracing cutting edge sterile compounding technology helped drive the establishment of a centralized production facility for our health system. Key members of the leadership who shepherded the project to completion included the executive director of pharmacy for the health system and individuals who eventually became the director of pharmacy and quality manager of the not-yet-built CPPC.

The original goal was to create a single facility to centrally produce sterile products for all of the hospitals in Scripps Health in an efficient and cost-effective manner. Secondarily, there was a belief that by establishing a sterile compounding model centrally for the system, we would also be able to drive quality at the various individual hospital locations. Standard work procedures, best practices, and environmental monitoring would be developed at the CPPC first and later implemented at the hospital sites.

At the time the Scripps Health pharmacy leadership considered the creation of the CPPC, state regulations in California did not permit batch compounding from a central location even within facilities under the same ownership. The Scripps pharmacy leadership approached the California State Board of Pharmacy to develop the necessary state legislation that ultimately became Assembly Bill 377. Emphasizing the improved safety and quality that we could provide to our patients by utilizing technology with costs spread across a health system rather than burdening a single hospital was a key to the success of the legislation. When developing the standard operating procedures for the CPPC, the pharmacy leadership used the Food and Drug Administration (FDA) current good manufacturing practices as a model. The intent was not to register with the FDA as a human drug compounding outsourcing facility under section 503B of the Federal Food, Drug, and Cosmetic Act, but to set the bar high with respect to the standards that we would maintain.

Since the opening of the CPPC, the Scripps pharmacy leadership structure has changed. The executive director of pharmacy and director of the CPPC continue to play significant roles in the direction taken by the CPPC, but there is no longer a quality manager. A pharmacy supervisor, who reports to the CPPC director, and the pharmacy buyer play critical roles in decision-making processes for the CPPC. The most common changes that we have made are related to formulary expansion based on needs. These needs are typically identified by the clinical managers, buyers, and pharmacy leaders at the various hospital sites. Often a CSP that has been outsourced is identified as something that is better insourced, either due to the high cost or lack of timeliness of

availability from an outsourcing compounding pharmacy. Other times there is a desire to standardize the dose, concentration, and delivery of a medication, often driven by patient safety considerations, and this desire will spur consideration for formulary addition. Ultimately, a recommendation is made by the supervisor and buyer to the CPPC director about the feasibility of a proposed formulary change. Factors that enter into this recommendation include but are not limited to the number of units to be produced, potential cost savings from insourcing, and operational impact on current services provided.

CSP Related Challenges

Before the CPPC produced its first CSP, the staff assumed responsibility for administering the environmental monitoring program for the entire health system. Substantial variation was identified in the initial assessment of the five hospitals and their environmental monitoring programs. Designing an environmental monitoring program that could be applied to all of the hospitals and ultimately the CPPC was the challenge.

Using USP chapter <797> as a guide, the CPPC supervisor created maps of the sterile compounding areas, including all primary and secondary engineering controls, at all five hospitals. The precise locations of where surface, viable air, and non-viable air samples would be taken were overlaid on these maps. A sampling log specific to each location was also created. A template for media labels was developed for use when the samples were taken. A decision to conduct environmental sampling monthly was made, although this is far more often than required by either USP chapter <797> or California State Board of Pharmacy regulations. The pharmacy technicians were trained to use the sampling equipment based on instructions from the users manuals. A calendar was created to coordinate the monthly sampling visits at the hospitals. Once the CPPC began operation, similar sampling maps and logs were developed, and the CPPC was placed in the monthly rotation with the hospitals. Nowadays, pharmacists and pharmacy technicians at the various sites have been trained in using the sampling equipment at their locations. The equipment and media are still maintained at the CPPC, and the media plates are incubated and read at the CPPC by pharmacy technicians and reviewed by the pharmacy director, with results reported immediately to the site.

End-product testing for our extended-BUD CSPs has posed several challenges for our operations and processes. All extended-BUD preparations are quarantined after compounding and kept for 14 days until negative sterility test results are received. At the current time, all laboratory testing is outsourced, so controlling these costs is a concern. There has always been a desire to maximize batch sizes and achieve a balance between workload and number of batches requiring testing. Initially, we used a strategy with batches split between one, two, or three compounders (i.e., pharmacy technicians) so that no one person was overburdened with a large batch, and we could minimize costs by sending one batch for testing instead of two or three batches. This process appeared to work fine until we thought about how we would address a failed sterility test. If a batch that had been split between multiple compounders working in different hoods failed a sterility test, the cause—human error, equipment problem, or environmental concerns—would be difficult to identify because of the many variables. Ultimately, we have adopted a “one batch, one compounder, one hood” rule, and each batch is sent for sterility testing. We continue to have the compounder work on the largest batch size that is reasonable to keep testing costs down, and we strive to ensure that the compounding area is ergonomically sound to allow the compounder to work efficiently in the best possible environment.

Increased automation continues to be a goal, and automation has been the source of several challenges. The most recent challenge is the discontinuation of manufacturer support for the robot used CPPC use to produce

CSPs in 10-mL syringes. This robot has been a great piece of automation equipment that we have used enthusiastically for the production of 10-mL syringes of cefazolin, ceftriaxone, succinylcholine, and phenylephrine. We will now be forced to look for alternative equipment. At this time, we intend to utilize repeater pumps for the manual production of CSPs in syringes, and we hope to identify automation equipment for syringe labelling to support our continued production of syringes.

Future CSP-related Projects

As our CPPC continues to grow and evolve, some changes are pursued and some are forced on us. And typically, when changes are forced on us by external circumstances, there is a condensed timeline and sense of urgency to implement the changes as quickly as possible. The 2016 publication of a draft FDA guidance on 503A compounding pharmacies that serve health systems requiring a patient-specific prescription and location within a 1-mile radius of the pharmacy prompted us to explore what efforts would be required to register as a 503B compounding pharmacy instead. We are still early in the exploration process, and we have not made a final decision because the FDA guidance is not yet final. In our efforts to fully examine this option, we have visited local 503B outsourcing compounding pharmacies to observe their operations. We also have spoken with out-of-area personnel to gain a more full understanding of the requirements associated with registering with the FDA. And finally, we will consider hiring a consulting group to provide a gap analysis of our current CPPC operations and the requirements for registration as a 503B compounding outsourcer.

Although our initial analysis indicates that our physical plant and daily operations closely mimic those of a 503B compounding outsourcing compounding pharmacy, it does identify obstacles to registration. The biggest gap is related to quality assurance and testing requirements. We do not have a separate quality manager or associated staff who do not report to the director of pharmacy and who would have the authority to stop operations if conditions suggested the need to do so. This quality assurance arm of the pharmacy would need to be established prior to registration with the FDA. Another consideration relates to testing requirements. We currently outsource all of our laboratory testing. We would not be able to support the higher costs associated with testing requirements for a 503B facility. So another big step would be for us to insource laboratory testing services to minimize costs.

USP chapter <800> and its standards for hazardous drug compounding have driven us to consider the possibility of centralizing this type of compounding for the infusion centers and outpatient clinics of Scripps Health. Because our central pharmacy licensure in California allows us to provide medications only for inpatient administration, this idea necessitates the building of a second compounding pharmacy, with different licensure that allows for the compounding, pursuant to a prescription, for our outpatient clinic locations. The rationale is that it makes more sense to build a single facility for centralized compounding that meets the requirements of USP chapter <800> and California State Board of Pharmacy regulations than building out multiple i.v. clean rooms designed for hazardous drug compounding in several outpatient clinic settings. This proposed plan also is in the early stages of discussion. Infusion center operations would be substantially affected because hazardous drugs would need to be compounded for the day's appointments early in the day and transported to the various clinic locations. This approach would entail significant scheduling and logistical challenges.

Reference

Anon. Regulatory alert: FDA issues three guidances on pharmacy compounding. *Am J Health-Syst Pharm.* April 18, 2016. Available at: http://www.ashp.org/menu/Advocacy/FederalIssues/Compounding/FDA-Issues-Three-Guidances-on-Pharmacy-Compounding.aspx (accessed 2017 Feb 10).