Implementation of Drug Vial Optimization to Reduce Drug Waste

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In 2009 the University of North Carolina (UNC) Medical Center opened the North Carolina Cancer Hospital to serve as the premier location for oncology patients in the state. For the Department of Pharmacy, this required combining three existing pharmacy locations that prepare hazardous drugs for oncology patients into one location. Located on the third floor of the North Carolina Cancer Hospital, the Cancer Hospital Infusion and Inpatient Pharmacy prepares hazardous drugs for all outpatient and inpatient units at UNC Medical Center and non-hazardous drugs for outpatients within the North Carolina Cancer Hospital. This includes preparations for adult and pediatric patients.

Rationale for Drug Vial Optimization Need

All health systems across the country are looking for ways to reduce the cost of patient care. Unlike other health system departments where salary dollars are the largest expense, the largest expense at departments of pharmacy are medications; therefore, the focus in pharmacy is to reduce drug expense.

As a department, focused efforts had already been made to optimize contracts and move therapies to lower cost alternatives when appropriate. Pharmacists were embedded into medical teams and ensured that the most appropriate and cost-effective regimen was selected for each patient. In addition, efforts were underway to improve operational efficiency and decrease waste within the pharmacy.

It was recognized that the Department of Pharmacy was discarding partial vials of medications per United States Pharmacopeia (USP) <797> recommendations. Pharmacy sought to quantify the amount wasted and determine whether there was a method to safely use the remaining amount.

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To prepare a chemotherapy or hazardous sterile preparation, the pharmacy uses mostly single-dose vials from manufacturers. Vials often contain more drug than the patient needs; on other occasions, several vials are needed to generate a patient's full dose. Because of this, the pharmacy ends up with a remaining partial drug vial. Based on pharmacy compounding guidelines within the *United States Pharmacopeia Chapter* <797>, this partial amount can be used for another patient up to six hours after it has been opened.[1] After this beyond-use date, the vial must be discarded even if drug is remaining. This guideline is based on the theory that after six hours, growth of microbial contamination could occur in the vial.[2] However, this theory is based on using solely a syringe and needle to withdraw drug from the vial.

North Carolina Cancer Hospital, Chapel Hill, N.C.

Our pharmacy uses a closed-system transfer device, BD PhaSeal™, to prepare chemotherapy and hazardous drugs. UNC had used PhaSeal for several years prior to the opening of the North Carolina Cancer Hospital. The concept for a closed-system transfer device is to protect employees by not allowing hazardous drug or vapor contamination to escape the vial.[3] Because PhaSeal utilizes an airtight seal to prevent vapors from coming out of the vial, no transfer of environmental contaminants should enter the vial. The ability of PhaSeal to prevent microbial ingress has been studied and well documented; studies show that the device extends a vial's sterility from 6 hours to 168 hours (seven days).[4-6] The phrase "drug vial optimization" is used to describe the extension of a single-use vial's sterility up to seven days or the drug's chemical stability, whichever is shorter, when using the PhaSeal closed-system transfer device. This maximizes the useful life span of a drug within a single-dose vial and presents a significant opportunity for cost savings.

Drug Vial Optimization Implementation

UNC Medical Center's Department of Pharmacy implemented a comprehensive drug vial optimization program in October 2011. The comprehensive program includes:

- Use of the PhaSeal closed-system transfer device.
- A compendium resource to determine the beyond-use date of each single-dose vial.
- Maintenance of institutional practices and procedures in accordance with USP <797> (i.e., hand hygiene and garbing, aseptic technique, cleaning and disinfecting, and International Organization for Standardization standards for air and environmental quality).
- Monthly quality assurance testing.

Drug vial optimization was implemented in three phases: pre-implementation, implementation process, and post-implementation.

Drug Vial Optimization: Pre-Implementation

Three key structural elements were needed prior to the implementation of drug vial optimization to ensure risk mitigation with the program:

1. Site-specific sterility testing
2. Development of a process to identify beyond-use dates for each single-dose vial
3. Staff competency and training.

The site-specific sterility testing was done in accordance with the internally validated study that determined the ability to extend beyond-use dates of single-dose vials to the drug's chemical stability or a maximum of seven days.[4] Having internal sterility data is fundamental to the risk mitigation of the program, because it ensures the air quality environment, allows for the extension of sterility, and follows the previously mentioned allowance within USP <797>. Because each oncology disease state clinic at North Carolina Cancer Hospital is scheduled to occur at least every seven days, the drugs would likely be used in a seven-day time frame.

The development of a process to identify beyond-use dates for single-dose vials is critical to ensure that a vial is not used past the drug's chemical stability or seven-day maximum. Staff used a hazardous drug compendium that detailed the specifics for each product (see Table 1, right). The column "Vial Beyond-Use Date" previously listed six hours for all single-dose vials based on the ability to be stored at room temperature or under refrigeration. This column of the compendium was updated with the drug's chemical stability (or a maximum of seven days) using the package insert, documents from the company's medical affairs division on extended chemical stability, and primary literature. References for where the information was obtained are listed next to each drug on the main document (not listed in the example shown) for quick reference and transparency. Because this compendium is used by all technicians and pharmacists preparing and checking chemotherapy and hazardous drugs, drug vial optimization was able to be incorporated into the normal workflow comfortably. In addition, a calendar was placed underneath the clock in the cleanroom for staff to identify the current date and determine the date and time of a vial's beyond-use date. A sticker purchased from a commercial healthcare retailer had previously been used to keep track of the reconstitution diluent (if applicable), concentration, and beyond-use date of the vial. This same sticker was used to write the date and time for the new beyond-use date of the vial. Pharmacists verified the accuracy of the beyond-use date as part of their final product-checking process.

Staff training occurred in the weeks leading up to drug vial optimization implementation. Though most of the staff had participated in the internal sterility testing, it was still important to ensure that everyone understood and complied with drug vial optimization to maintain patient safety. Training modules were built for all pharmacists and technicians. Each individual then took a written exam to ensure their understanding of drug vial optimization. A passing score of 100 percent was required because

Table 1. Example from the Cancer Hospital Compounded Sterile Products Stability Compendium

	Vial Beyond-Use Date	
Drug	**Refrigerate**	**Room temperature**
Abatacept (Orencia) (H)	24 hours	24 hours
Bortezomib (C)—subcutaneous administration	7 days	n/a

(C) = chemotherapy, (H) = hazardous.

Our multidisciplinary Pharmacy and Therapeutics Committee required monthly quality assurance testing as part of the risk mitigation program to ensure that sterility of the single-dose vials was in accordance with the initial sterility testing.

the safety components were too critical to have any lingering questions. Individuals who did not pass were required to repeat the training modules and retake the exam to achieve a perfect score. Twenty-three of the 24 staff (96 percent) passed on the first attempt; the one individual who did not pass on the first attempt passed on the second following retraining.

Drug Vial Optimization: Implementation

Integration of drug vial optimization into the existing workflow was critical to ensuring that partial vials were used first and for the appropriate duration prior to opening a new vial. The process is described in Figure 1, page 48. Key elements in the workflow included having a sticker on the vials to keep track of the appropriate beyond-use date and using a partial bin container. A bin was placed in the middle of the cleanroom checking table for the pharmacist to place the partial vial in after checking the product. Drugs that required refrigeration were placed in the refrigerator in the front of the drug-specific storage location. Staff was trained to look in the partial vial bin first and then look in the front of the drug-specific storage location within the cleanroom prior to opening a new, unused vial.

This process was implemented manually as described and has since transitioned to an automated process. With the implementation of BD Pyxis™ IV Prep—a medication workflow software—a label prints out for each partial vial and assigns a unique number to that vial. When that drug is to be prepared again, the system directs the technician to use that specific vial to ensure that partial vials within the beyond-use date are used first. The process can be done using either manual or automated tracking.

Drug Vial Optimization: Post-Implementation

Our multidisciplinary Pharmacy and Therapeutics Committee required monthly quality assurance testing as part of the risk mitigation program to ensure that sterility of the single-dose vials was in accordance with the initial sterility testing. Each month, 10 partial single-dose vials are randomly selected for quality assurance sterility testing. Each vial must contain 1 mL of drug, because 0.5 mL is plated on a trypticase soy agar plate and 0.5 mL is plated on a sheep blood agar plate. This process is repeated for all 10 vials. Plates are incubated at 37°C and evaluated for microbial growth at 24 hours, 48 hours, and seven days. Any positive results are speciated by the Epidemiology Department. In addition, a hazardous waste log is kept to track any changes in waste.

Our Results

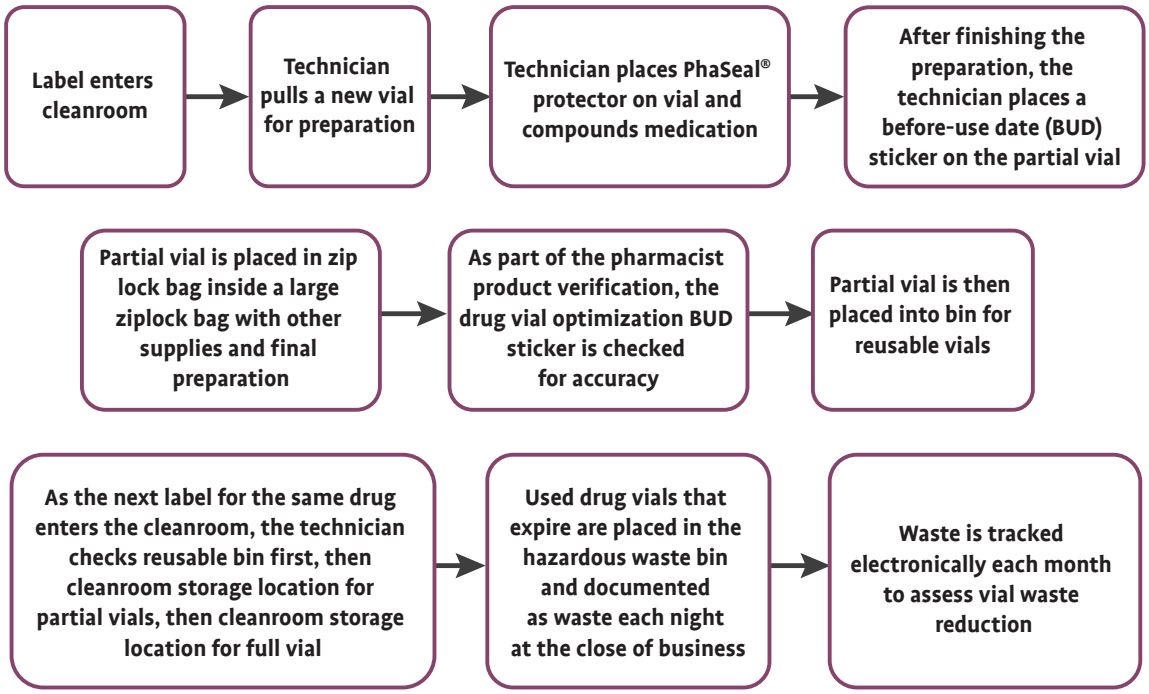
Prior to implementation in 2011, drug waste was calculated for 19 drugs, which had a range of drug chemical stability from 30 minutes to more than seven days. This meant that drug vial optimization would impact several drugs on the list but not all would have a beyond-use date of the seven-day maximum. This represents a realistic sample of the overall compendium.

As of June 2018, drug waste through the use of drug vial optimization for the original 19 drugs measured has decreased 94 percent when compared to 2011 (see Figure 2, page 49). This continued decrease results from sound implementation infrastructure with an embedded and fully optimized process, as well as primary literature demonstrating drugs' chemical stability to be longer than stated in the package insert.

Extrapolated to the full chemotherapy drug budget (all hazardous and chemotherapy agents including, but not limited to, the 19 drugs), drug vial optimization has saved $43.8 million in drug expense (see Figure 3, page 49). The institution's average acquisition price for each drug was calculated and then used to determine the average cost per milligram (cost of drug divided by milligram per vial). The total waste per drug was recorded monthly and then summed for each fiscal year; the total annual waste per drug was then multiplied by the cost per milligram,

(continued on page 50)

Figure 1. Standardized Workflow Process for Drug Vial Optimization Implementation



2018 ACCC Innovator Award-Winning Team. Left to right: Scott Savage, PharmD, MS; John Valgus PharmD, MHA, BCOP; Lindsey Amerine, PharmD, MS, BCPS; Erinn Rowe, PharmD, MS; Stephen Eckel, PharmD, MHA, BCPS; Richard Redding, BA, CPhT. Not pictured: Rowell Daniels, PharmD, MS, FASHP.

Figure 2. Annual Cost of Drug Waste with 19 Drugs Measured Each Year

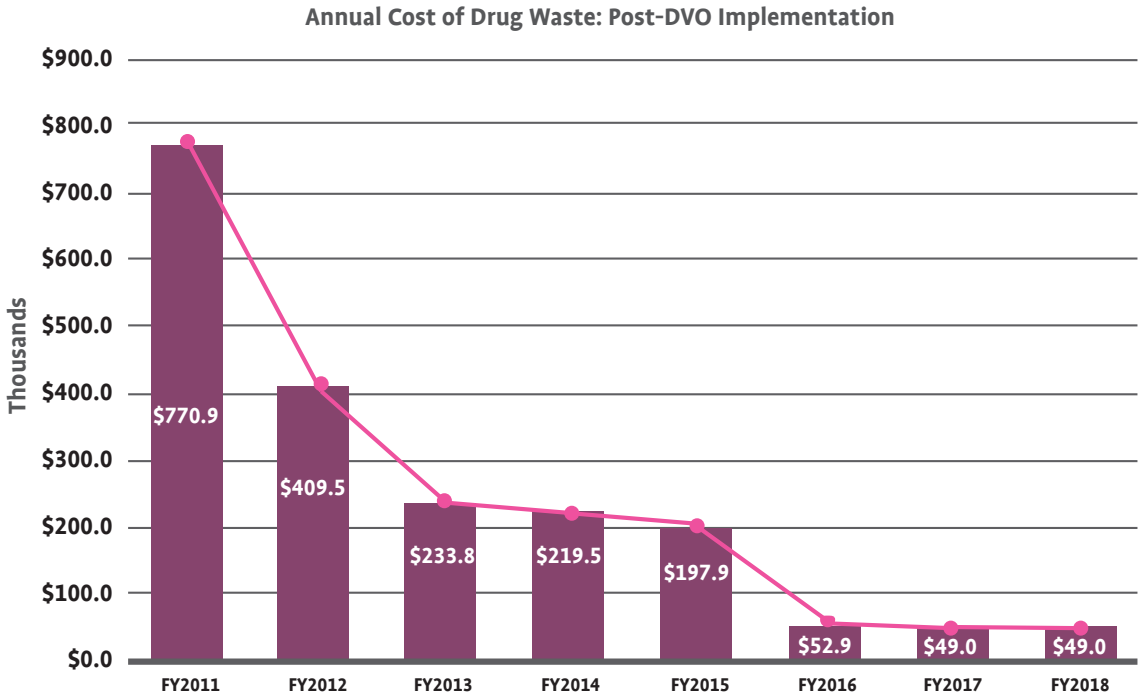
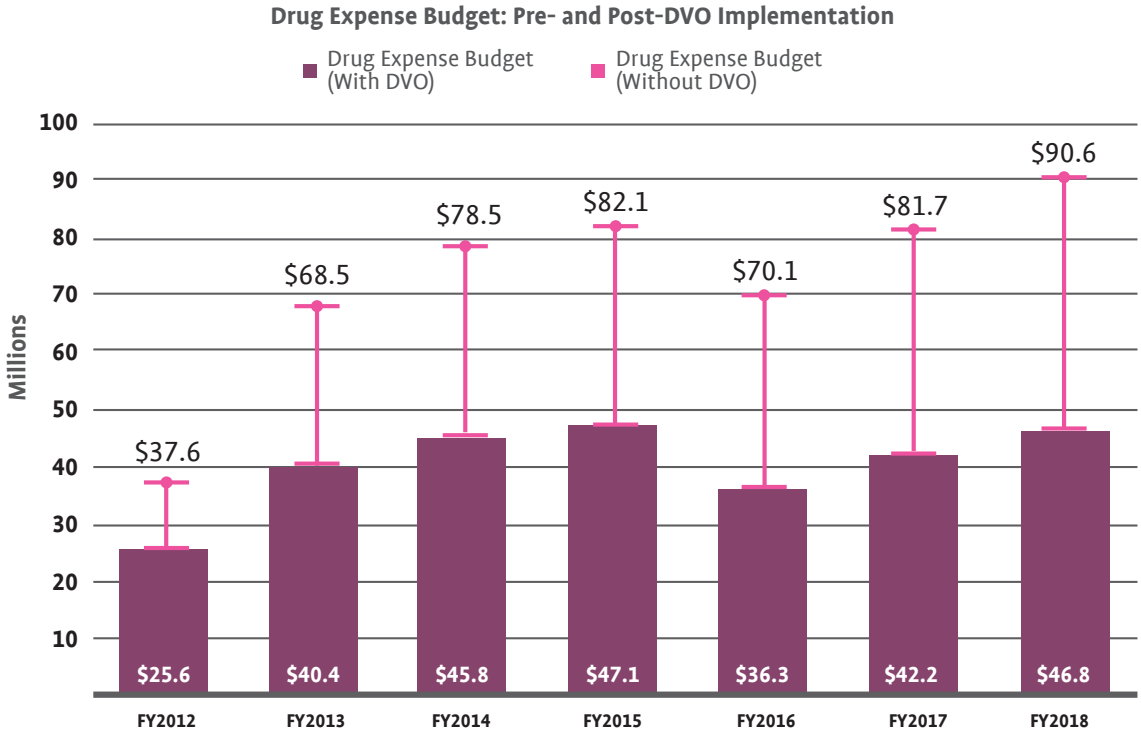


Figure 3. Financial Impact of Drug Vial Optimization (DVO) on Drug Expense Budget



Cancer Hospital Infusion and Inpatient Pharmacy at North Carolina Cancer Hospital

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resulting in the cost of waste per drug. For fiscal year 2018 (July 2017-June 2018), the chemotherapy drug budget was $46.8 million. If drug vial optimization had not been utilized, the drug budget would have been $90.6 million.

Since October 2011, monthly quality assurance testing has continued to ensure risk mitigation with the program. This testing is done within pharmacy. Only two plates have shown contamination of single isolates, which were determined by Epidemiology to be user contaminants. With only 2 plates out of 1,680 plates tested showing contamination, the contamination rate is 0.12 percent, which is less than the previous literature contamination rates of 1.86 percent, 1.8 percent, and 0.3 percent.[4-6]

The implementation of drug vial optimization represents an innovative and unique approach to addressing increased drug waste and is the first to be implemented in the United States. The cost savings of greater than $43 million annually—along with the risk mitigation strategy of this initiative—is a best practice that can be modeled at other institutions. OI

Disclosure Statement

Lindsey Amerine served on the Advisory Board for Becton, Dickinson and Company.

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