WHITE PAPER

Accuracy Evaluation of the Diana™ Compounding Workflow System

BACKGROUND

The Diana compounding workflow system, manufactured by ICU Medical Inc., is the world's first needlefree, user-controlled automated sterile compounding system for the accurate, safe, and efficient preparation and reconstitution of hazardous drugs. Today, our next-generation, USP ‹800›-compliant system combines tablet-based IV workflow and innovative automation to keep clinicians and patients safe from hazardous drug exposure to chemotherapy preparations, and prevent accidental needlesticks. The system also safeguards the drugs themselves, thanks to a microbiologically and mechanically closed design, which protects the preparation from exposure to environmental contaminants.

PURPOSE

This study was conducted to evaluate the accuracy of the Diana system in a live pharmacy environment in order to verify that the system's fluid-dispensing accuracy was within the manufacturer's stated accuracy claim for volume measurements (±5% error above 5 mL). This study examined data gathered from preparations that required multiple vials, as well as preparations of a selection of drugs commonly prepared in the pharmacy.

INTRODUCTION

The process of measuring medication during the compounding of intravenous medications has inherent variables. Syringe volume graduation markers have been shown to vary by up to ±5%.[1] Human precision in reading the syringe sub-marking measurement is generally considered to be ≥ ±1 mL for fluid volumes drawn in syringes with capacity ≥ 20 mL.[2] Additional human factors such as interruptions, fatigue, and memory lapse are recognized in clinical literature to contribute to preparation errors.[2,3] Finally, manufacturers' diluent IV bags are consistently overfilled, and the overfill varies between the lot numbers of the manufactured products. The standard allowable variation in manufactured pharmaceuticals and compounded preparations is 90 to 110% of the active ingredient.[4,5,6,7] However, because of these combined factors, research suggests that "across the country, 9 of every 100 IV doses that require compounding in the pharmacy contain one or more errors when they are delivered to the nurse."[8]

As a result, the final compounded preparation can inadvertently be out of specification and not meet the required standards. These variations may also contribute to an admixture that differs from the physician-ordered prescription, potentially affecting small therapeutic window situations or contributing to unnecessary drug waste. The Diana compounding workflow system helps take the variation out of the manual drug preparation practice to create an accurate, reliable, and repeatable sterile preparation and safe-handling process.

SYSTEM OVERVIEW

The next-generation Diana system is a syringe pump module controlled by a high-precision stepper motor that facilitates small- and large-volume medication transfers. The system uses ICU Medical's proprietary closed system, fluid transfer components to help reduce exposure to hazardous drugs while preserving the sterility of the preparation. ICU Medical publishes its accuracy specification at the first standard deviation (SD). This means that 68% of the data set will be within the published accuracy range. It also means that 95% of the data set will be within two times the published accuracy range.

The Diana module uses a 20 mL syringe cassette with an integrated stopcock, which can manage the fluid path from the input container to the output container. The cassette technology system can feature either two ChemoLock™ or two Spiros® needlefree closed male luers to facilitate drug transfer between the drug manufacturer's vial and the IV bag or other male luer device connected to the patient IV container.

The Diana system removes the need for gravimetric components to obtain an independent accuracy assessment, a process that can be difficult to maintain due to specific gravities of drugs. Rather, the system provides three methods for independent verification of accuracy: photographic, volumetric, and proprietary sensor technology based on the simultaneous use of a stepper motor and fluid sensor. The stepper motor knows the position of the syringe plunger at all times (both drawing and pulling). While the syringe plunger is pushing, the sensor identifies the presence of fluid. The sensor can detect the presence of fluid over 700 times per mL, allowing the system to accurately monitor the volume of fluid pushed. These independent systems work in concert with each other to provide a system that can effectively and accurately transfer hazardous drugs, with the use of gravimetric scale.

METHODOLOGY

A compounding log from a leading cancer center was obtained to provide data on the accuracy of the Diana system, and clinical volumes were identified for the following drugs:

- Paclitaxel
- Cisplatin
- Fluorouracil
- Methotrexate
- Etoposide
- Carboplatin

TEST PROTOCOL

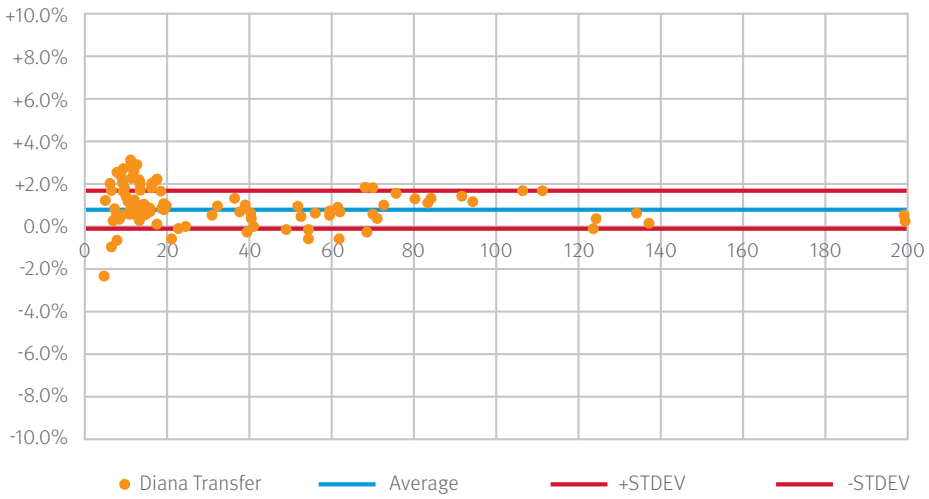
A test protocol was created to perform medication transfers using the Diana system at clinically relevant volumes to determine system accuracy. The specific gravities of the drugs were obtained, and a scale was used to manually determine accuracy (ICU Medical DS2000).

1. Assemble the components:
   - Attach a new Diana cassette to the Diana syringe pump module
   - Attach a bag spike to the empty bag
   - Attach an ICU Medical vial adapter
2. Place the empty container on the scale and press tare
3. Attach the components to the Diana syringe pump module
4. Enter the transfer information into the Diana system
5. Record the photos of the drug vials
6. Initiate the transfer
7. Place the bag on the scale
8. Record the weight
9. Determine the actual volume dispensed by applying the specific gravity to the weight measurement
10. Analyze the resulting data

TEST RESULTS

The Diana system performed better than the published accuracy specifications within all accuracy ranges (Figure 1). The overall average accuracy of the data was 0.8% with a standard deviation of 0.92%, well within the acceptable range of ± 10% as dictated by USP ‹797› and within the stated accuracy claims of ± 5%.

Figure 1. The accuracy of the Diana system at clinical volumes



Accuracy of Preparations by Drug Type

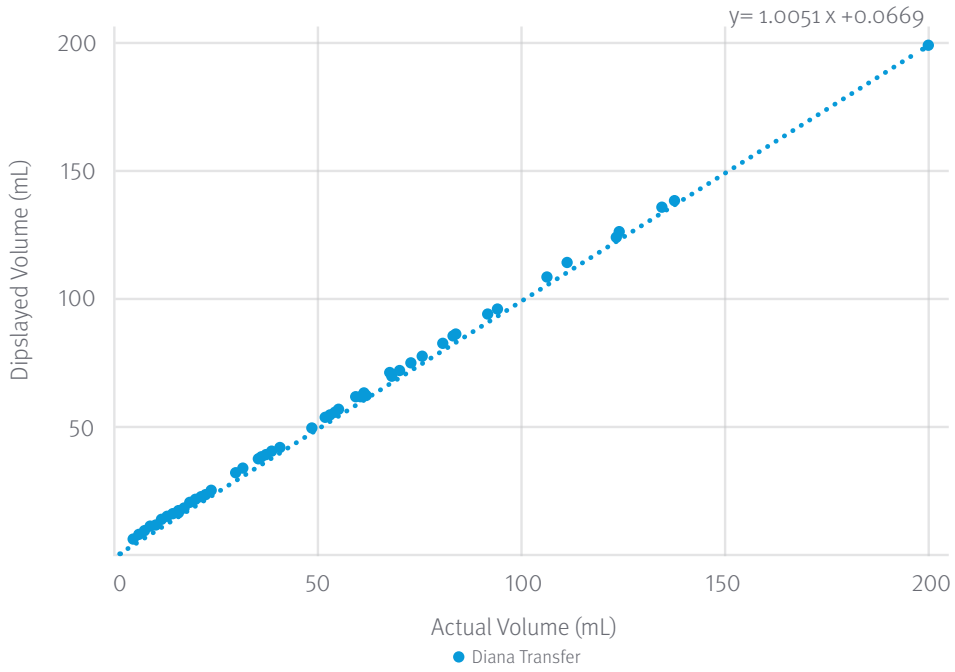
The Diana system provided consistent accuracy when preparing each of the six drugs tested. Drugs with low volumes of data (‹ 10 data points) had higher average accuracy; however, it is expected that if additional data points were captured, Diana would have displayed performance closer to the average performance across all drugs. Each specific drug had an average volume and accuracy of the following:

Drug Type	Average Volume	Accuracy
Paclitaxel	28.36	0.4%
Carboplatin	32.97	0.9%
Cisplatin	95.44	0.2%
Fluorouracil	82.51	1.2%
Etoposide	9.47	1.6%
Methotrexate	9.19	1.0%

Accuracy of Displayed Volume vs. Actual Volume

When compared to actual volumes, the displayed volume of the Diana system has a high degree of correlation (Figure 2.) The data indicates that the displayed volume of the transfer does in fact meets the actual volume delivered.

Figure 2. Displayed volumes vs. actual volumes



CONCLUSION

The Diana compounding workflow system was shown to provide accurate compounding of chemotherapy drugs.

When preparing a variety of common drugs, the system's performance fell within established guidelines of ± 10% and the device's published accuracy specification at the first standard deviation (SD). While this study demonstrates the Diana system's ability to provide consistent accuracy, it is still important to utilize a product trial before implementation to properly gauge the performance of the Diana system and ensure compatibility with site-specific drugs and workflows.

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