

Accuracy Evaluation of the Diana™ Hazardous Drug Compounding System

BACKGROUND

The Diana hazardous drug compounding 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. The Diana system was designed to keep patients and clinicians safe from hazardous drug exposure during chemotherapy preparation and may also keep the drugs themselves safe from exposure to outside contaminants thanks to a microbiologically and mechanically closed design that protects the patient preparation from exposure to environmental contaminants while protecting the clinician from both exposure to the drug and accidental needlesticks.

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 (+/- 1 mL error from 5 to 19.9 mL, +/- 3% error from 20 to 49.9 mL, and +/- 2% error at 50 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 and diluent volumes during the compounding of intravenous medications has a number of inherent variables. For example, one study 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.”¹ The standard allowed variation in manufactured pharmaceuticals and compounded preparations is 90% to 110% of the active ingredient.^{2,3,4,5} Syringe volume graduation markers have been shown to vary by up to $\pm 5\%$.⁶ Human precision in reading the syringe sub-marking measurement is generally considered to be $\geq \pm 1$ mL for fluid volumes drawn in syringes with capacity ≥ 20 mL.⁷ Finally, manufacturer diluent IV bags are consistently overfilled, and the overfill varies between the lot numbers of the manufactured products.

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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. Additional human factors such as interruptions, fatigue, and memory lapse are recognized in clinical literature to further contribute to preparation errors.^{7,8} The Diana hazardous drug compounding system helps take the variation out of manual drug preparation practice to create an accurate, reliable, and repeatable sterile preparation and safe handling process.

SYSTEM OVERVIEW

The Diana system is a user-controlled automated compounding system with two syringe pumps (dual channels) that are controlled by two high-precision step motors to facilitate small- and large-volume medication and diluent 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 1st standard deviation (SD). This means that 68% of the data set will be within the accuracy range below. It also means that 95% of the data set will be within two times the published accuracy range.

Channel one uses a 20 mL syringe and cassette device with an integrated dual-valve flow cassette technology system featuring two Spiros® needfree 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). Channel one is mainly used to add hazardous drugs to a patient container (IV bag, syringe, elastomeric pump), or for small-volume fluid transfers.

Channel two is mainly used for transferring diluents, filling elastomeric pumps, reconstituting lyophilized drugs, filling a series of syringes, or performing large-volume fluid transfers. Channel two uses a 50 mL syringe and a dedicated preparation set with a bonded Spiros closed male luer.

METHODOLOGY

Three sites were selected to provide data on the accuracy of the Diana system. There were no changes to their pharmacy workflow during the course of the trial.

In order to efficiently gauge the performance of the Diana system without a serious disruption in workflow, a scale was placed outside of the hood. The technician was instructed to perform the protocol described below and record the results in a compounding log for analysis after the conclusion of the trial.

Data Acquisition Protocol

1. Before performing a measurement, place container on the scale
2. Tare the scale
3. Attach container to Diana
4. Perform preparation using the Diana system
5. Place label in Diana Compounding Log
6. Place container on scale
7. Record weight of bag, NDC code, indication of speed, and any notes

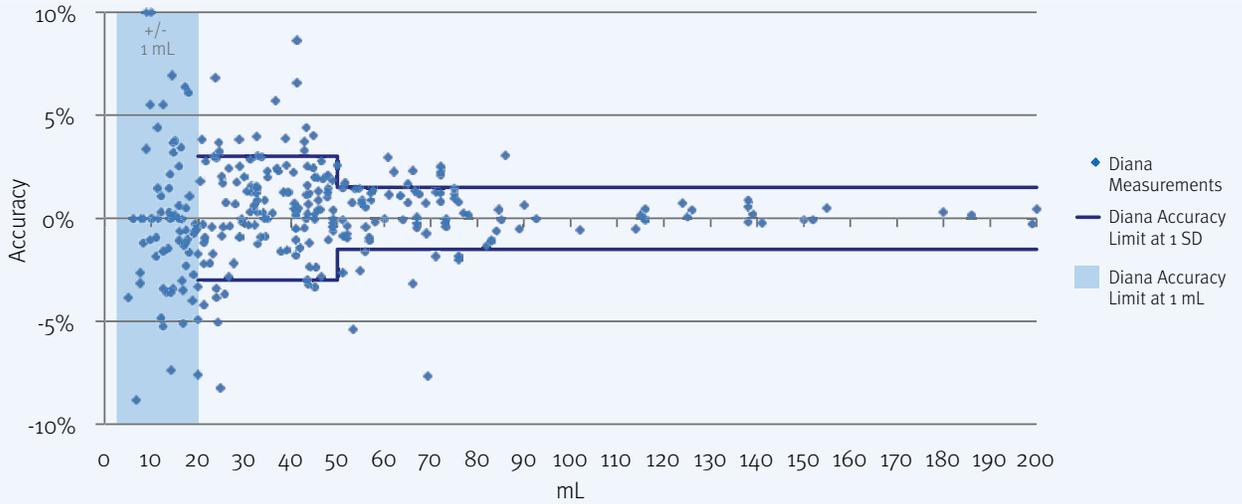
At the conclusion of the trial, data points were omitted from the analysis due to the following:

- › **Technician error** - Error resulted from multiple factors, including failure to follow the steps outlined in the Data Acquisition Protocol Section.
- › **Discarded preparations** - In some cases, refrigerated drugs were shown to cause condensation on the outside of the vial, leading the Diana system to continue to draw fluid. Refrigerated drugs may also cause condensation on the Diana cassette during compounding.
- › **Preparations outside the manufacturer’s intended use** - The data set included data points that fell outside the indications for use as described on the Operator’s Manual.
- › **Inaccurate data points that were verified to be visually accurate** - These inaccuracies were deemed the result of technician error, malfunction, or non-compliance to the data acquisition protocol where the scale was not properly tared at the beginning of a preparation. The technician indicated in the notes section that the compound was visually accurate.

RESULTS

The Diana system performed better than the published accuracy specifications within all accuracy ranges (Figure 1).

FIGURE 1: DIANA SYSTEM PERFORMANCE



Measurement Range	5 to 19.9 mL	20 to 49.9 mL	50 to 999.9 mL
Count	93	186	196
Average Accuracy	-0.35 mL	0.32%	0.11%
Accuracy Range*	0.96 mL	2.39%	1.79%
Accuracy Specification*	± 1 mL	± 3%	± 2%

Accuracy of Preparations Requiring Multiple Vials

The Diana system demonstrated consistent accuracy when preparing medications that required up to four vials. The consistency of data across two, three, and four vials indicates the likelihood of similar accuracy when preparing medications requiring more than four vials.

Vials Used	Average Accuracy	Accuracy Range*	Count of Data Points
2	0.41%	± 2.17%	124
3	0.09%	± 1.64%	10
4	0.05%	± 0.96%	5

*At the 1st Standard Deviation

Accuracy of Preparations by Drug Type

The Diana system provided consistent accuracy when preparing each of the fourteen different types of 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, as is the case with Cytarabine.

The Diana system consistently met the manufacturer's accuracy claims when tested in real-world conditions at three different facilities.

Drug Type	Count	Average
Carboplatin	70	0.22%
Cetuximab	7	0.83%
Cisplatin	70	-0.22%
Cyclophosphamide	27	0.38%
Cytarabine	1	3.82%
Docetaxel	11	0.47%
Etoposide	28	0.14%
Fluorouracil	46	0.49%
Gemcitabine	77	0.96%
Ifosfamide	5	2.05%
Irinotecan	16	0.94%
Oxaliplatin	21	0.77%
Paclitaxel	81	-1.73%
Rituximab	7	0.60%
Total	467*	0.00%

*9 data points were removed as drug type was not determined during the trial

CONCLUSION

The Diana system was shown to meet or exceed the device's published accuracy specification when preparing a variety of common drugs, as well as medication that required multiple vials for a single preparation. While this study demonstrates the Diana system's ability to provide consistent accuracy, it is still important to utilize a product trial before implementation in order to properly gauge the performance of the Diana system and ensure compatibility with site-specific drugs and workflows.

References

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