

Minimizing the Variation of Volume Withdrawn from a Container for Injectable Drug Products and Impact to Overfill

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Abstract

Maintaining a system that allows delivery of products with quality attributes appropriate to meet the needs of patients, health care professionals, regulatory authorities and other internal and external customers defines the term "Product Realization."¹ Bridging the therapeutic effect to the regulatory and manufacturing processes will take into account many characteristics of quality as well as prevention of medical errors, controlling of cost and aspects of patient/caregiver satisfaction.

This study demonstrated the consistency of the volume that is withdrawn from a vial when using a vial adapter spike as opposed to user dependant needle penetration. The excess volume² sufficient for withdrawal can be established early in the development process, which in turn contributes to optimizing drug product fill volume along with facilitating improved dosing techniques, ease of patient/caregiver use and ultimately patient satisfaction.

A proactive approach to control withdrawal of the product from the vial and understand the relationship to the end result augments the overall value. The potential benefit of this type of study is to allow special design features to be incorporated into the pharmaceutical development process that will provide rationale for overfill, as well as show a positive impact to patient administration.

Introduction

As concerns for safety in administration of drug products have escalated in recent years, increased scrutiny of administration procedures has occurred. Drug makers have placed greater emphasis on providing the best patient and caretaker experience as well as improving the convenience of drug administration in a highly competitive pharmaceutical market. In addition, many drugs utilized on a regular basis for chronic conditions are beginning to be offered for at-home preparation and administration. Maintaining a consistent dose of drug product to the patient is a critical aspect of patient safety and therapeutic efficacy. In order to ensure sufficient drug product is available in a vial to administer a full dose to a patient, drug makers may include an appropriate volume of overfill in the vial. Drug makers provide up to 30 percent overfill in a single vial,³ which translates into significant additional expense and greater potential for dosing errors. Inadequate overfill results in too little drug product for dosing. Conversely, excess overfill can provide significant residual product that can be abused in a manner that compromises the patient safety and product integrity. Reports of recent lawsuits for purportedly unjustified excess overfill volumes highlight the importance of this issue and will likely increase scrutiny of these practices.

Innovations in the drug delivery market have provided safety administration systems such as a vial adapter, which not only provides the opportunity for needle-free transfer of liquid for reconstitution of lyophilized drug products, but also a means for consistent withdrawal of drug product from a vial. In certain scenarios, consistent withdrawal, by use of a vial

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adapter, has the potential to aid in a reduction in the amount of required overfill and provide a potential for cost savings. This study compares the volumes of liquid withdrawn from a vial using two methods: traditional needle penetration and a vial adapter with spike penetration.

Methods

Three groups of users and two aspiration methods were evaluated. Table 1 depicts the test matrix. Figure 1 provides a schematic of the two aspiration methods. Subjects were provided with instructions for use (IFU), a video presentation and verbal instructions on how to aspirate the liquid using the two methods. Supplies provided were vials containing an average volume of 2.166 mL distilled water, plastic disposable Luer lock syringes, 19 gauge needles, and 13mm vial adapters with siliconized spikes. The experimental groups consisted of 10 certified nurses and 10 hemophilia patients who had not previously used the vial adapter devices. The control group consisted of four experienced lab analysts with previous experience using the vial adapters. A total of 100 aspirations using each method were completed in each subject group. The volume of aspirated liquid was determined by weighing the syringes before and after the aspiration procedure. Nurses were given a nine-minute time limit to complete all 10 aspirations for each method to simulate their actual working conditions.

Table 1. Demographic of test subjects

Aspiration Method	Patients	Nurses (9 minutes)	Lab Analysts (Control)
13mm Vial Adapters	10 x 10 times	10 x 10 times	4 x 25 times
Needle (19 gauge)	10 x 10 times	10 x 10 times	4 x 25 times

Figure 1. Schematic of needle (left) and vial adapter (right) aspiration methods

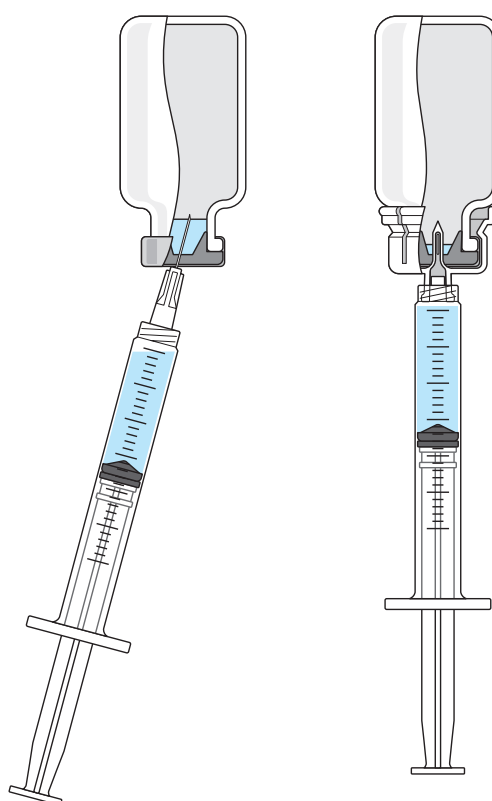


Table 2 provides the average volume withdrawn for each subject group and the standard deviation for all the subjects within that group. Figures 2, 3, 4 and Tables 3, 4, 5 provide the summary statistics for each of the subject groups. The results for the needle and vial adapter penetration were similar for the analyst (control) group. Figure 3 illustrates a more significant difference with withdrawal volume between needle and vial adapter penetration for the nurse subject group. The average volume withdrawn was very similar between the two methods, but the standard deviation was greater using the needle. The patient subject group demonstrated the greatest variability between the needle and vial adapter withdrawal methods. This is illustrated by both the difference in the mean withdrawal and standard deviation, as well as the range of withdrawal volumes shown in Figure 4 and Table 5.

Table 2. Average volume withdrawn and standard deviation for each subject group

	Needle		Vial Adapter	
	Volume withdrawn (mL)	Standard Deviation (mL)	Volume withdrawn (mL)	Standard Deviation (mL)
Lab Analysts	2.04	0.102	2.04	0.025
Nurses	1.98	0.106	1.99	0.057
Patients	1.92	0.237	2.00	0.047

Figure 2. Lab Analysts vial adapter vs. needle withdrawal methods

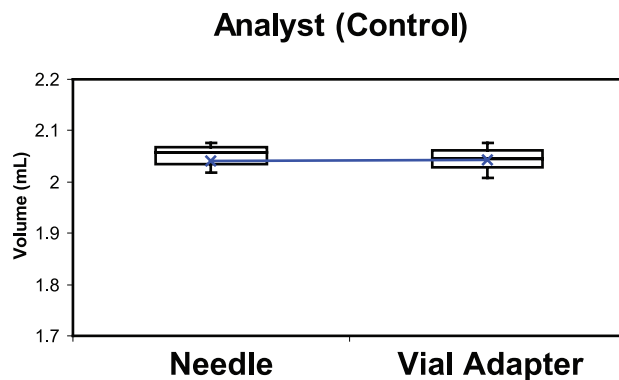


Table 3. Summary statistics for Lab Analysts' use of vial adapter vs. needle withdrawal methods

	Minimum	10%	25%	Median	75%	90%	Maximum
Vial Adapter	1.97	2.01	2.03	2.05	2.06	2.08	2.10
Needle	1.08	2.02	2.04	2.06	2.07	2.08	2.10

Figure 3. Nurses vial adapter vs. needle withdrawal methods

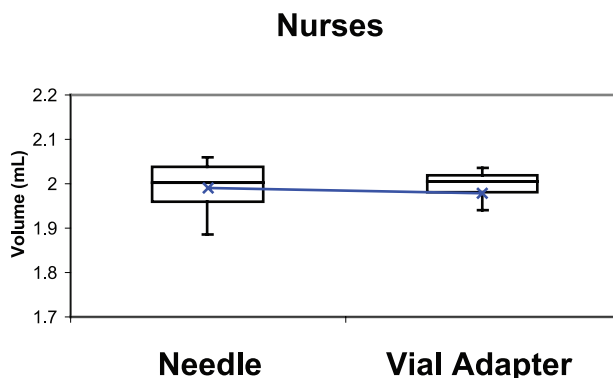


Table 4. Summary statistics for Nurses' use of vial adapter vs. needle withdrawal methods

	Minimum	10%	25%	Median	75%	90%	Maximum
Needle	1.34	1.89	1.96	2.00	2.04	2.06	2.11
Vial Adapter	1.70	1.94	1.98	2.01	2.02	2.04	2.08

Figure 4. Patients vial adapter vs. needle withdrawal methods

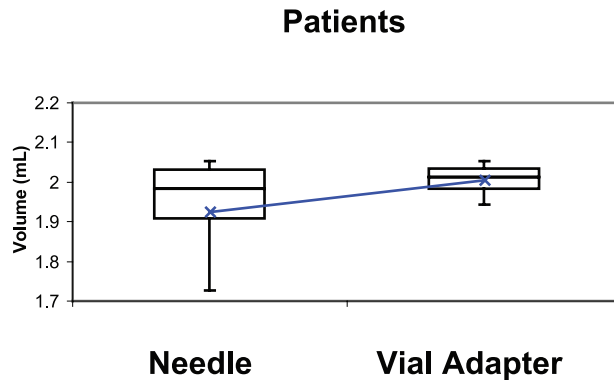


Table 5. Summary statistics for Patients' use of vial adapter vs. needle withdrawal methods

	Minimum	10%	25%	Median	75%	90%	Maximum
Vial Adapter	1.82	1.94	1.98	2.01	2.04	2.05	2.10
Needle	0.24	1.73	1.91	1.99	2.03	2.05	2.10

Conclusions

Overall, the use of the vial adapter resulted in greater consistency for liquid withdrawal than the use of a needle for all experimental groups. From the data provided, it can be inferred that the delivered volume to the patient will be more consistent with the use of a vial adapter than a needle. Planning and management of overfill can be initiated during clinical phases using a vial adapter to make use of the consistency in withdrawal. Reducing risk of inadequate or excessive overfill protects both the patient and the pharmaceutical manufacturer. For a patient or a nurse, the use of the vial adapter provides confidence that they are providing consistent withdrawal, given the ability to administer accurate dosages of drug products using a needle-free device. For a pharmaceutical manufacturer, cost controls associated with overfill practices and the contribution to patient safety as a result of facilitating proper doses may be realized.

References

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West Backstop

West recently launched a backstop for glass syringes as part of its Prefillable Syringe platform portfolio. In addition to the backstop, the portfolio includes products such as plungers, needle shields, tip caps and the Daikyo Crystal Zenith® resin ready-to-use (RU) syringe system.

The West backstop enhances the quick, easy and safe drug delivery provided by prefilled syringes. The backstop functions as a finger-flange extender, which enables better syringe handling during the drug application process. Through the use of the West backstop, accidental withdrawal of the plunger can be prevented through a retaining wall/plate that presents a smaller passageway than the inside diameter of the syringe. Furthermore, the West backstop facilitates the guidance of the plunger rod.

The backstop is assembled onto the syringe after the syringe is filled, the stopper is inserted and the plunger rod is placed. Thus, the normal syringe filling process remains unchanged. The backstop assembly can be accomplished either mechanically or manually. Regarding possible applications, the backstop fits to 1-3mL standard glass syringes barrels as well as 1mL long glass syringes. However, other sizes can be developed on request.

Customers may request samples of the backstop for the 1mL long and 1-3mL standard glass syringes by contacting Technical Customer Support at TCS.Europe-AsiaPacific@westpharma.com or +49 2403 7960.



*If there are any questions or comments, please feel free to contact
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