Efficacy of the Q-FLO™ Universal Male Luer Lock Device for Vapor Containment During Compounding and Administration of Hazardous Drugs

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INTRODUCTION

One of occupational safety risks to healthcare workers around the world is routine exposure to hazardous drugs, through the preparation and administration of these drugs to patients. Hazardous drugs ("HD"s) include many classes of drugs, ranging from cancer chemotherapy (antineoplastic drugs), antiviral drugs, hormones, some bioengineered drugs and others. HDs provide a significant health risk due to their harmful mutagenic, carcinogenic, teratogenic, as well as reproductive toxicity[1] . Several international organizations have recommended the use of closed system drug transfer devices ("CSTD"s) as an important safety measure for use in drug preparation and administration. CSTDs are intended to facilitate the transfer of drug from one reservoir to another, and may be used throughout the drug handling chain from compounding in the pharmacy, to patient dose administration at the bed side. An important feature of CSTDs is that they limit the potential for aerosolizing drug contamination and exposing workers to inadvertent needle sticks, both of which reduce the likelihood of occupational exposure to HDs. CSTDs are designed to mechanically prohibit the transfer of environmental contaminants into the drug transport and delivery system, as well as to prevent the escape of HDs or vapor concentrations outside of the same system[2].

Given these significant toxic exposure risks in the hospital environment, new regulations governing the handling of hazardous drugs in health care settings were published by the United States Pharmacopeial Convention in 2016. These standards, known as USP General Chapter are a legally enforceable set of guidelines that apply to the transport, storage, handling and administration of hazardous drugs.

As CSTDs have proliferated in the infusion device industry, and a wide range of designs and performance characteristics have emerged, there has been a significant need in developing a single performance test standard by which the effectiveness of each CSTD can be measured objectively for its ability to restrict drug mass (vapor or liquid) from crossing the system boundary and escaping into the environment. To this end, the US National Institute for Occupational Safety and Health (NIOSH) has published a draft protocol, entitled "A Vapor Containment Performance Protocol for Closed System Transfer Devices Used During Pharmacy Compounding and Administration of Hazardous Drugs" which has yet to be finalized, and is still undergoing review and revisions. However, in the absence of any other established performance test protocol to evaluate CSTDs, this draft protocol is often used and cited for the evaluation of CSTDs and their performance merits. This white paper is a report on the evaluation of a novel CSTD, the Q-FLO™ Universal Closed Male Luer device using the NIOSH vapor containment protocol, referenced above. Q-FLO™ is among the newest closed male luer ("CML") devices that have entered the market, and it offers the following key features and benefits:

- **Closed, No Drip, Valve Connector**, preventing drips and spillage and surface contamination upon connecting and disconnecting the device,
- **Universally Inter-Compatible** with the leading brands of female luer locks, including SmartSite™, Clave®, and MicroClave®. This inter-compatibility offers hospitals and healthcare providers with more freedom to source the different components of their CSTD systems, without getting locked into using a single branded CSTD system.

- **Completely Swabable** at the distal end of the connector, with flat smooth surface allowing for true friction disinfection during pre-access swabbing.

- **Visual Indicator.** The Q-FLO™ is the only product of its kind to offers a clear, color coded, visual indicator confirming the status of the connection. This important feature facilitates the ease of use of the Q-FLO™, and gives the healthcare worker added confidence regarding proper use of the device during connection and disconnection. Flow is turned on through a full rotation of the Q-FLO™, which results in an audible "snap", as well as the appearance of the Visual Indicator, confirming that the flow is on in the line.

- **Passive 'Fool Proof' Safety System** seals off the flow twice, during the rotation used to disconnect the Q-FLO™; this safety measure helps prevent exposure to hazardous compounds even when there is high fluid pressure in the line;

- **Low Residual Volume.** The internal volume for the Q-FLO™ is substantially smaller than all other competing connectors (less than 0.045 mL) minimizing the volume of fluid that is wasted within the CSTD connection, and more importantly, minimizing the volume of hazardous fluids that need to be contained in the process.

- **High Performance.** The Q-FLO™ is designed as a neutral bolus valve connector, with a higher flow rate than the competing closed system connectors of its kind, higher tolerance for pressure during connecting and disconnecting, with proven effective microbial ingress barrier for the fluid path, and lower internal residual volume.

- **Safe Material Composition**. The Q-FLO™ is Latex, and DEHP free, making it an ideal connector for the entire spectrum of chemotherapy and nuclear medicine drugs.

The main objective of this study is to compare and contrast Q-FLO's performance, as a CML, in quantitatively assessing the combined liquid, aerosol, and vapor containment, as compared to two of the leading commercially available CML brands, namely Becton Dickenson's Texium™, when used with the SmartSite™, and ICU Medical's Spiros®, when used with the Clave®. Given Q-FLO's universal inter-compatibility, in each case Q-FLO's performance was measured when used with the respective branded female luer lock system; in other words, Texium™ + SmartSite™ was compared to Q-FLO™ + SmartSite™, and Spiros® + Clave® was compared to Q-FLO™ + Clave®. This ensured a direct comparison of the efficacy of Q-FLO™ in vapor containment in each of the above leading systems that are in current use in the hospital setting.

MATERIALS AND METHODS

The protocol used in this study closely follows the draft protocol published by NIOSH[3], which provides a methodology for evaluating the containment performance of CSTDs for a designated challenge agent. The protocol evaluated four CSTD system configurations using administration manipulations performed with a known challenge agent (70% isopropyl alcohol [IPA]) inside a custom environmental test chamber. Environmental Test Chamber The environmental test chamber was

Figure 1: *Photograph of the modified Secador® Techni-dome® Test Chamber*

a customized Secador® Techni-dome® 360 Large Vacuum Desiccator (Bel-Art Products, Pequannock, NJ), as shown in **Figure 1** above.

The Secador® Techni-dome® is a sphere with a 52.1 cm inner diameter, that separates at its horizontal equator into equal lower and upper halves. We customized the sphere with a 30 cm extension ring, fitted with 20 cm glove ports and installed between the lower and upper sphere halves. The addition of the extension ring converted the round Techni-dome® sphere into a cylinder with hemispherical ends. This modification also provided for a larger volume to carry out the administration manipulations. This test chamber was used to evaluate the escape of the challenge agent into the closed environment of the chamber using a highly sensitive gas analyzer.

Detection Instrument

The specific IPA detection instrument ("IPA Detector") used was a Miran SapphIRe Infrared Analyzer Model 205A (Thermo Electron Corporation, Franklin, MA), hereafter referred to as Miran SapphIre (see **Figure 2 on the next page.**).

Figure 2: *Photograph of the Miran SapphIRe Infrared Analyzer Model 205A*

The Miran SapphIRe was chosen, since it was the identical detector to that which was used by the NIOSH investigators, capable of providing a specific response to IPA, with a detection limit that is moderately low (0.3 ppm when calibrated and operated using the long pathlength with an 8.852 wavelength in IPA detection mode). The Miran SapphIRe measured IPA vapor concentrations from the environment within the test chamber once every second and recorded the data in parts per million, ppm.

The IPA Detector had the following specifications for IPA vapor detection: accuracy of ± 10% of the reading; range up to 100 parts per million (ppm); and a minimum sampling flowrate of 10 L/min when the sampling hose was attached to the discharge port of the environmental test chamber. The IPA Detector was required to be within the manufacturer's recommended factory-level calibration period. Results of the test protocol was used to compare containment performance across multiple CSTD systems to include:
a) Texium™ + SmartSite™,
b) Q-FLO™ + SmartSite™,
c) Spiros® + Clave®, and
d) Q-FLO™ + Clave®.

Based on testing performed within NIOSH laboratories, a maximum leak performance threshold of 1.0 ppm of IPA vapor was determined to be a feasible performance value when measured in accordance with the procedures spelled out within the protocol outlined below.

Test Chamber Preparation

The test procedures involved first measurement of the background concentration of IPA vapor inside the room. If room concentrations exceeded 4 times the IPA detector's LOD, the source of the IPA vapor was identified and removed, and the room was reventilated. Then the actual background concentration of the IPA vapor inside the room was recorded. The task specific components were then placed inside the environmental test chamber, and the chamber was closed, and the IPA detector's sampling hose was then attached to the chamber's outlet port. AT that point, it was assessed if the test chamber background concentrations were below the instrument's LOD, and if so, then the testing was started. If the measured concentration inside the environmental test chamber exceeded the room background concentration, as well as the instrument's LOD, then a connection leak or surface contamination was suspected, and as such the experiment was halted, the environmental test chamber removed and the test components were inspected and replaced as needed. The procedure was then repeated and the experiment was only started when the environmental test chamber showed room background concentration of the IPA vapor.

Test Sample Set up and Preparation

Supplies were prepared and assembled in advance, prior to placement in the environmental test chamber. This preparation included the assembly of needle free IV sets ("IV Set"s) as shown in **Figure 3,** next column.

Figure 3: *Photograph of the needle free T-Connector sets connected to syringes (no CMLs shown). SmartSite™ female luer lock device is shown on the left and Clave® on the right.)*

This procedure involved bonding of 4 inches of mini-bore tubing to each of the T-Connectors at the Bond Pocket with UV adhesive. Then female luer was bonded to tubing pocket with UV adhesive. Assemblies where then exposed to UV light until cured. The female luer locks (SmartSite™ and Clave®) were connected to the female luer, and the male luer on the T-Connector was capped. The sets were then tested for leaks and occlusion.

The syringe preparation involved the transfer of 10 mL of the 70% IPA into two of the syringes. The syringes were then connected to the female luer of the T-Connector on the Needle Free IV sets.

Any residual IPA was then wiped off and allowed to dry in a well ventilated area for 60 minutes. Finally air was expelled from each of the 10 mL syringes, and each of the CMLs to be tested (Q-FLO™, Texium™, or Spiros®) was then attached to a separate 10 mL syringe. All test supplies were then placed on a tray, as presented in **Figure 4,** next page.

Figure 4: Photograph of syringes with connected Q-FLO™, Spiros® and Texium™ CML's, in respective order, from left to right.

Administration Test Procedure

For the Spiros® + Clave® system, the Spiros CML was connected to the Clave IV set. 10 mL of IPA was pulled from the IV Set with the syringe attached to the Spiros, simulating pulling dose from a vial or bag. For simulating the IV push, the syringe attached to the Spiros was used to inject into the IV Set. The pull and push was then repeated. Then the Spiros was disconnected from the Clave. The IPA Detector was then monitored to measure any IPA expelled. The IPA Detector is expected to increase and then return to its baseline value. The highest IPA level reading, in parts per million, was observed and recorded. This cycle took approximately 60 to 120 seconds. This test procedure was performed five (5) times and the reading for each time was recorded. A test procedure identical to the above was then carried out for the Texium™ + SmartSite™, the Q-FLO™ + Clave®, and the Q-FLO™ + SmartSite™ systems. Data Compilation The IPA Detector's LOD, maximum detection, and sampling flow rate was recorded, as well as the room background concentrations of IPA. The calibration status of the IPA Detector was also noted in the log of the data collected. The average IPA detected in parts per million was calculated, tabulated, and plotted using Microsoft Excel software, for each of the systems tested. Standard deviation in the measured values were designated as error bars in the data plot.

RESULTS

The graph shown in **Figure 5** (next column) summarizes the data obtained in this study.

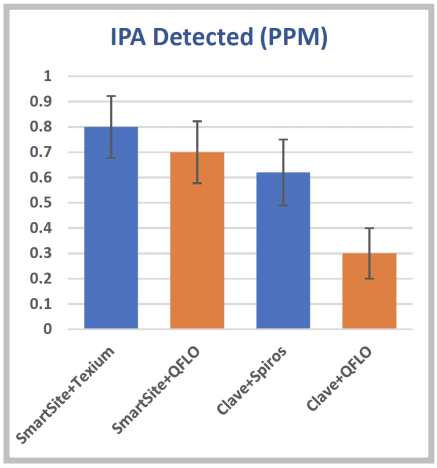

Figure 5: Comparison of vapor containment effectiveness using SmartSite™+Texium™, SmartSite™+Q-FLO™, Clave®+Spiros®, and Clave®+Q-FLO™ systems.)

The data clearly illustrates that the systems that included Q-FLO™ provided better vapor containment than the systems that used the intended branded CML (Spiros® for the Spiros®+Clave® system, and Texium™, for the Texium™ +SmartSite™ system).

DISCUSSION

The results obtained in the current study are confirmatory and supportive of prior leak testing studies conducted by the authors, including litmus blotter tests, which validated strong sealing of the fluid when the Q-FLO™ is switched off and disconnected, resulting in a dry disconnect in every application. These consistent findings could be attributed to the sequential valving system that is the principle of operation of the Q-FLO™ CML, which seals off the flow of fluid or aerosols well in advance of disconnecting the Q-FLO™ from its adjoining female luer lock device.

The protocol used in the current study mirrored the test assembly, supplies, and detection system used in the NIOSH Vapor Containment draft protocol referenced. The current protocol, however, differed from the NIOSH vapor containment draft protocol, to limit the tasks for testing vapor containment mostly to the tasks that are representative of typical drug administration applications, versus drug compounding applications. The tasks tested, as noted in the Materials and Methods section above, involved connecting of the CML to the corresponding female luer lock device, repeated IV push and pull operations, followed by a disconnecting of the CML from the adjoining female luer lock device, to assess the release of aerosolized drug in this process. The results found confirm that the Q-FLO™ CML is highly effective in improving vapor containment in the systems tested. Future studies can be directed at evaluating the efficacy of the Q-FLO™ CML for vapor containment in a compounding setting, as well as the efficacy of the Q-FLO™ CML for administration of drugs using other commercially available systems.

CONCLUSIONS

The Q-FLO™ Male Luer device represents a novel new entrant in the landscape of CSTD's available to healthcare professionals to ensure safety from inadvertent exposure to hazardous drugs. The results of the current study, using NIOSH's vapor containment protocol, confirms the efficacy and superiority of the Q-FLO™ for vapor containment, during hazardous drug administration, when used in conjunction with the commercially available SmartSite™ and Clave® female luer lock devices.

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FOOTNOTES

1 Howard J. Preventing occupational exposure to antineoplastic and other hazardous drugs in health care settings, the National Institute for Occupational Safety and Health (NIOSH) Publication Number 2004-165, Cincinnati; 2004. Available at: http://www.cdc.gov/niosh/ docs/2004-165/pdfs/2004-165.pdf

2 NIOSH [2004]. NIOSH alert: preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2004-165

3 A Vapor Containment Performance Protocol for Closed System Transfer Devices Used During Pharmacy Compounding and Administration of Hazardous Drugs. CDC/NIOSH Web site. www.cdc.gov/niosh/docket/review/docket288/default.html. Accessed May 11, 2016.