

pH Liquid Integrity Test of FDA-Cleared ONB Closed-System Transfer Devices

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BACKGROUND

Healthcare workers who handle hazardous drugs are at risk for occupational exposures resulting in adverse events including skin rashes, stillbirths, spontaneous abortions, and certain cancers.¹ Closed-System Transfer Devices (CSTDs) are specifically designed to reduce this risk.² Since 1999, six CSTDs have received FDA 510(k) clearance. In 2012, the FDA established a new category for CSTDs under an ONB code to better categorize products that are intended to be used for safe handling. Today, only two CSTDs have received FDA clearance for the new ONB code: PhaSeal[®] (Becton, Dickinson and Company, Franklin Lakes, NJ) and the newly 2013 cleared ChemoLock[™] (ICU Medical, Inc, San Clemente, CA) systems.

HISTORY OF LITMUS TESTS AND CSTD'S

2007 Leakproof Connection Integrity Test For Devices Intended for Handling Hazardous Drugs.³

- › Spiros[™] & Clave[®] by ICU Medical Inc., B. Braun OnGuard[™] Vial Adaptor & Syringe Adaptor by Teva Medical Ltd., Alaris SmartSite[®] Vented Vial Access Device & Texium[™] Male Luer by Cardinal Health, and PhaSeal Protector & Injector Luer Lock by Carmel Pharma.
- › Results: PhaSeal was the only system with no leakage observed after 10 manipulations.

Using a closed-system protective device to reduce personnel exposure to antineoplastic agents.⁴

- › Showed that personnel exposure to cyclophosphamide (CP) and ifosfamide (IF) decreased after 6 months of implementation of PhaSeal. 24-hour urine samples were collected from 8 employees including pharmacists, pharmacy technicians, and nurses working full-time in a chemotherapy drug infusion center and pharmacy. 6 of 8 had positive urine samples for CP and 2 of 8 were positive for IF before implementation. 0 of 8 were positive after 6 months of implementation.

The FDA ONB Code (last updated November 1, 2013)

- › Definition: Reconstitute and transfer antineoplastic and other hazardous drugs in healthcare setting indicated to reduce exposure of healthcare personnel to chemotherapy agents in healthcare setting.
- › Three criteria must be met: 1) no escape of hazardous drug or vapor concentration, 2) no transfer of environmental contaminants, and 3) prevention of microbial ingress.

WHAT IS CHEMOLOCK?

CSTD cleared in 2013

- › Needlefree system that passively aids in both needlestick injuries and exposure to cytotoxic chemicals
- › One-step connection process with an audible click that sounds when syringe successfully connects to the vial
- › Air pocket chamber located inside drug vial that collects any air vapor that may escape

WHAT IS PHASEAL?

First CSTD, cleared in 1999

- › Contains enclosed needle within syringe connector
- › Three-step connection process: "Push, Turn, Push"
- › Large air pocket chamber alongside vial adaptor that collects any air vapor that may escape



Photo 1. ChemoLock system



Photo 2. PhaSeal system

OBJECTIVES

To evaluate the liquid containment of the two FDA ONB code-cleared CSTDs, PhaSeal and ChemoLock, in comparison to the traditional needle and syringe method for drug transfers at varying pH's. To mimic the full-scale pH of hazardous drugs by using the following pH buffers as a substitute for active drug: pH 4.0, pH 7.0, and pH 10.0.

Hazardous Drug	pH from MSDS
Bleomycin	4.5-6.0
Carboplatin	5.0-7.0
Cytarabine	7.6
Davarbazine	3.0-4.0
Epirubicin	3.0
Fludarabine	7.2-8.2
Irinotecan	3.5
Methotrexate	8.5

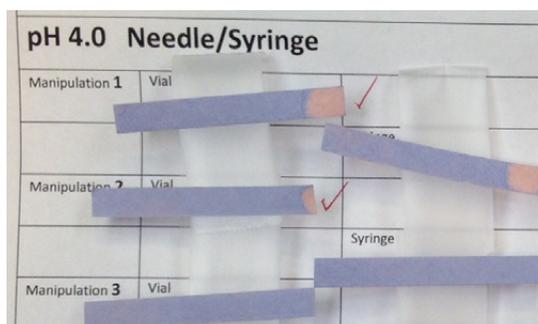


Photo 3. Litmus paper results for needle and syringe method

METHODS

For each ONB CSTD and needle and syringe method: Ten 1 mL transfer manipulations with each of the three pH buffers.

- › Disconnected vial and syringe after each manipulation and tested both connection endpoints with litmus paper.
- › Connection endpoints were cleaned and allowed to dry with sterile alcohol if previous manipulation resulted in litmus paper color change.
- › Each syringe connector and vial adaptor was used in ten consecutive manipulations without being changed, in accordance with the FDA-cleared limitations of the devices.
- › The test was performed in duplicate by pharmacy residents from The Nebraska Medical Center and from Nebraska Methodist Hospital in Omaha, Nebraska.

RESULTS

Visible leakage occurred with 1.7% of PhaSeal System and 43% with traditional needle and syringe method. (Table 1). No leakage was observed with the ChemoLock system by ICU Medical.

	PhaSeal			ChemoLock			Needle and Syringe		
	pH 4.0	pH 7.0	pH 10.0	pH 4.0	pH 7.0	pH 10.0	pH 4.0	pH 7.0	pH 10.0
Total Color Changes	1	1	0	0	0	0	22	17	13
Total Manipulations	20	20	20	20	20	20	20	20	20
Percent of Litmus Tests with Leakage	1.7% (2 of 120)			0% (0 of 120)			43% (52 of 120)		

CONCLUSION

The data suggests that CSTDs are necessary for safe preparation of hazardous drugs as the needle and syringe method failed to contain all three pH solutions within the transfer process. The PhaSeal product improved solution containment but had two failed manipulations in a relatively small sample size. The ChemoLock product had no litmus paper color changes and no visible droplets evident during manipulations. The currently FDA-cleared ONB CSTD systems demonstrated containment of acid, base, and neutral solutions when compared to the traditional needle and syringe method.

References

1. Powers, Luci A. Closed-System Transfer Devices For Safe Handling of Injectable Hazardous Drugs. Pharmacy Practice News. June 2013; 1-16.
2. National Institute for Occupational Safety and Health. NIOSH alert: preventing occupational exposure to anti-neoplastic and other hazardous drugs in healthcare settings. www.cdc.gov/niosh/docs/2004-165/
3. Jorgenson, JA. Leakproof Connection Integrity Test for Devices Intended for Handling Hazardous Drugs. The University of Utah. 2007.
4. Wick C, Slawson MH, et al. Using a closed-system protective device to reduce personnel exposure to antineoplastic agents. Am J Health-Syst Pharm. 2003; 60:2314-2320.

* Texium/SmartSite is marketed as a closed system, not a CSTD.