

**ASSESSMENT OF CLOSED SYSTEM TRANSFER DEVICES
5-FU DRUG LEAKAGE**

Study Product:

*B. Braun Onguard with Tevadaptor by Teva Medical
BD PhaSeal™
CareFusion VialShield
Equashield
ICU Medical ChemoClave
ICU Medical ChemoLock*

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Study Summary

Title	<i>ASSESSMENT OF CLOSED SYSTEM TRANSFER DEVICES - 5-FU LEAKAGE</i>
Short Title	<i>5-FU Leakage Study</i>
Methodology	<i>CSTDs Connector surfaces tested for drug residuals by wet litmus paper following multiple connector activations and drug transfers</i>
Study Center(s)	<i>Nebraska Methodist Medical Center, Omaha, NE</i>
Objectives	<i>To assess the 'Closeness' of various Closed System Transfer Devices across Liquid Drug Leakage Test</i>
Study Product	<i>B. Braun Onguard with Tevadaptor by Teva Medical BD PhaSeal CareFusion VialShield Equashield ICU Medical ChemoClave ICU Medical ChemoLock</i>

1 Introduction

Recently, the number of marketed Closed System Transfer Device (CSTD) models has increased. Interest in development of a CSTD performance test protocol originated from within the healthcare industry itself, with requests for an independently-developed containment test protocol. Additionally, with the approval of USP chapter 800 mandating the use of closed systems for administration, proper evaluation of CSTD connectors is essential since vast majority of administration procedures involves exclusively the use of CSTD connectors. To date, several leakage studies have been performed to show whether or not different brands of CSTDs are free of leaks, drips, microbeads and drug residuals. However, most of these studies are performed on drug surrogates via a litmus paper, UV light, etc. This protocol will test CSTDs with actual antineoplastic agent Fluorouracil (5-FU).

2 Study Objectives

Objective of this study was to test 6 different CSTD devices to assess how it matches up with their claims of being leak-proof. CSTDs were tested for 5-FU leakage detection.

Table 1: CSTD Study Plan

CSTD Brand	Drug-Litmus Test
Onguard/Tevadaptor	Y
PhaSeal	Y
VialShield	Y
Equashield	Y
ChemoClave	Y
ChemoLock	Y

3 Study Design

The Litmus test was performed per protocol. There were 6 brands of CSTDs evaluated in this study. 10 unique devices from each brand of CSTD were tested. 3 connector membrane or luer activations were made per device with 5 Fluorouracil and drug was transferred back and forth between activations. Following the activations connector surfaces were tested for drug residue.

All devices were allowed to go through 1st membrane activation without any litmus detection. The litmus test was executed on 2nd and 3rd membrane activation.

Note that 5-FU was chosen due to its wide usage in oncology, low cost and good visibility on litmus paper. While 5-FU is in the pH range of 10, if desired the test is expandable with same materials and methodology to test additional drugs in same pH range or in the acidic pH range (preferably pH 2-4). Also, handling and cutting of litmus paper was done with nitrile gloves.

Additionally, only pharmacists or pharmacy technicians skilled in use of the tested CSTDs performed this test in accordance to protocol and manufacturers' directions for use.

4 Supplies Needed

For assessment of Litmus Testing with 5-FU the following supplies were used:

Item	Product Code	Quantity	Lot Number	Expiration Date
PhaSeal Vial Adapter	P50	10	1406009	2019-05
PhaSeal Syringe Adapter	N35	10	1403002	2016-08
Equashield Vial Adaptor	VA-20/2	10	16-20041A	2018-02
Equashield Syringe Unit	SU-10/2	10	16-20053A	2018-02
ChemoClave Genie	CH-77	10	2825364	2019-02
ChemoClave Spiros	CH2000S	10	51-161-SJ	2020-05
ChemoLock Closed Vial Spike	CL-80	10	3055968	2020-05
ChemoLock Injector	CL-2000S	10	3052844	2020-05
CareFusion VialShield	MV0520	10	4215	2017-03
CareFusion Texium	10012241-0500	10	D330920	2016-11
Tevadaptor Vial Adaptor	412111	10	767M13	2020-05
Tevadaptor Syringe Adaptor	412118	10	6874415	2020-05
BD 10mL Syringe	Plastipack	40	4006253	
5-FU - 500mg/10mL	Adrucil	60	31319611B	2017-01
Macherey- Nagel PH 1-14 Universal Indicator Paper (litmus)	90204	Rolls cut to 130 stripes	2041115	NA
Sterile Water for Irrigation	Hospira NDC 0409-7139-09	1	55-501-48-01	2018-07-01
Nonwoven cleanroom wipe: Absorbing pads	Novaplus Contec Np-AMSI0001	12	131010	Mfg Date: 07/2014 *Note: Not Expiration Date

5 Study Procedures

5.1 Negative and positive controls

For the negative control procedural steps are followed:

1. A 5-Flourauracil 10mL vial was capped with a CSTD Vial Adapter
2. A 10ml syringe was attached to a mating CSTD Syringe Adapter (if needed)
3. One piece of litmus paper was dipped at least half of it into sterile water for Irrigation. The wet litmus paper was padded on an absorbing pad to remove excess water droplet.
4. This padded litmus paper was backed with a slight finger press on each membrane of the two mating components of the CSTD system. Sufficient distance was kept on the litmus paper between the two tested membranes. The purpose of rubbing with wet litmus stripe and the two twist motions is to simulate a membrane disinfection procedure with an IPA pad, a quarter turn left and quarter turn right.
5. Immediately a photograph of the negative sample was taken and denote 'L' if no color change was determined and 'y' if color change was determined.
6. Pass criteria for the negative test is if no color change was determined.
7. One negative control test was performed for each brand of CSTD tested.
8. If no color change was determined the negative control vial, syringe and CSTD were deemed appropriate to be used for the litmus drug test.

For the positive control procedural steps are followed:

1. A 5-Flourauracil 10mL vial was accessed and a small amount of the drug was placed on the litmus paper.
2. Pass criteria for the positive test is if color change was determined.

5.2 Study Procedure for Litmus Drug Test

The following procedural steps were followed:

1. A 5-Flourauracil 10mL vial was capped with a brand of CSTD Vial Adapter
2. A 10ml syringe was attached to a mating CSTD Syringe Adapter (if needed)
3. The syringe was attached to the vial.
4. A 7mL of total volume of drug was pulled by the process of Pull-Push-Pull to simulate bubbles removal: pull 4ml, push back 4ml and pull 7ml
5. The vial was inverted upright to reinject 5ml back into the vial (2ml left in the syringe).
6. The two mating systems were disconnected
7. The syringe was attached to the vial and the remaining 2ml was injected from the syringe into the vial.
8. Steps 4 to 6 were repeated.
9. One piece of litmus paper was dipped at least half of it into sterile water for irrigation, then patted dry onto an absorbing pad to remove excess water droplet.
10. The wet litmus paper was backed with a slight finger press on each membrane of the two mating components of the CSTD system. Sufficient distance on the litmus stripe was kept between the two tested membranes. The purpose of rubbing with wet litmus stripe and the two twist motions is to simulate a membrane disinfection procedure with an IPA pad, a quarter turn left and quarter turn right.
11. Immediately photograph of each sample was taken and denote '-' if no color change was determined and 'y' if color change was determined
12. Process steps 7 to 11 were repeated with the same CSTD (for a total of 3 activations)
13. Test were repeated for 9 additional devices within the CSTD category with 9 additional vials of 5-FU
14. Test were completed for 5 additional CSTD brands and results recorded into data collection sheet with image capture

6 Results

The test has been performed without any adverse occurrences. No product or procedure failures were noted. The results are clear and consistent throughout testing of the same CSTD system. The test sensitivity allows clear differentiation between performances of various CSTD systems. Of all the CSTDs brands tested, Equashield brand of CSTD was able to withstand membrane activations and showed 0 leaks. Our expectations that the test is easily replicable by any hospital pharmacy were met. Summary data is presented below:

Brand of CSTD	Failure Rate	Comments
Onguard/Tevadaptor	100%	Major Leaks Detected on All Samples
PhaSeal	30%	Minor Leaks detected on few samples
VialShield	100%	Major Leaks Detected on All Samples
Equashield	0%	No Leakage Detected
ChemoClave	100%	Major Leaks Detected on All Samples
ChemoLock	85%	Minor Leaks Detected on Majority of the Samples

7 Appendices

Appendix I: Data Summary Table for Drug Litmus Test

Appendix II: Onguard/Tevadaptor Data Collection Sheet

Appendix III: PhaSeal Data Collection Sheet
Appendix IV: VialShield Data Collection Sheet
Appendix V: Equashield Data Collection Sheet
Appendix VI: ChemoClave Data Collection Sheet
Appendix VII: ChemoLock Data Collection Sheet






















Appendix I: Data Summary Table for Drug Litmus Test

Device	Onguard/Tevadaptor		PhaSeal		VialShield		Equashield		ChemoClave		ChemoLock	
	1 st Sample	2 nd Sample	1 st Sample	2 nd Sample	1 st Sample	2 nd Sample	1 st Sample	2 nd Sample	1 st Sample	2 nd Sample	1 st Sample	2 nd Sample
1	Y	Y	-	Y	Y	Y	-	-	Y	Y	Y	Y
2	Y	Y	-	-	Y	Y	-	-	Y	Y	-	Y
3	Y	Y	-	-	Y	Y	-	-	Y	Y	Y	Y
4	Y	Y	Y	Y	Y	Y	-	-	Y	Y	Y	Y
5	Y	Y	-	-	Y	Y	-	-	Y	Y	-	Y
6	Y	Y	-	-	Y	Y	-	-	Y	Y	Y	Y
7	Y	Y	-	Y	Y	Y	-	-	Y	Y	-	Y
8	Y	Y	Y	Y	Y	Y	-	-	Y	Y	Y	Y
9	Y	Y	-	-	Y	Y	-	-	Y	Y	Y	Y
10	Y	Y	-	-	Y	Y	-	-	Y	Y	Y	Y
Negative Control	-		-		-		-		-		-	
Positive Control	Y											
Failure Rate	100%		30%		100%		0%		100%		85%	

NOTE: Please denote mark '-' if no color change was detected on the litmus paper otherwise mark 'y' if color change is detected






















*Note additionally that the Litmus Paper that Device 2, sample 1 for Equashield, had a black mark on it. Since the drug discoloration is green and the predefined mark is black, this was ruled as a pass on the test as the discoloration is assigned to the Litmus Paper defect.

Appendix II: Onguard/Tevadaptor Data Collection Sheet

Device	Onguard/Tevadaptor	
	1 st Sample	2 nd Sample
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
Negative Control		
























Appendix III: PhaSeal Data Collection Sheet

Device	PhaSeal	
	1 st Sample	2 nd Sample
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
Negative Control		
























Appendix IV: CareFusion Data Collection Sheet

		CareFusion	
		1 st Sample	2 nd Sample
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
Negative Control			
























Appendix V: Equashield Data Collection Sheet

Device	Equashield	
	1 st Sample	2 nd Sample
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
Negative Control		























Appendix VI: ChemoClave Data Collection Sheet

Device	ChemoClave	
	1 st Sample	2 nd Sample
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
Negative Control		



Appendix VII: ChemoLock Data Collection Sheet

Device	ChemoLock	
	1 st Sample	2 nd Sample
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
Negative Control	