The BD PhaSeal™ Optima System

Assessment of microbial ingress

Introduction

The aseptic preparation of hazardous drugs is a routine procedure in many hospital pharmacies. Traditionally, injectable hazardous drugs were withdrawn from vials by using a sterile syringe and needle,[1] which carries a risk of needlestick or sharps injury and hazardous drug exposure.[2] Subsequently, drug-vial spike adapters have been introduced to help reduce these risks to healthcare worker safety.[3, 4] While these drug-vial spike adapters allow for reconstitution and multiple withdrawals of a drug from a single entry through a vial septum, they can leave residual drug volume in vials and may not adequately address hazardous drug exposure risk.[2-4] Although such manipulations are typically carried out in a primary engineering control (e.g., biological safety cabinet), repeated vial access through these adapters may introduce environmental contaminants such as microorganisms into the drug transfer system.[1]

Over the past decade, the use of closed system drug-transfer devices (CSTDs) for the preparation and administration of hazardous drugs has become a standard of practice.[1, 2, 5] These devices mechanically prohibit both the escape of hazardous drug or vapor concentration outside the system and the transfer of environmental contaminants, including microorganisms, into the system.[1, 2] Studies that have investigated the potential of CSTDs to maintain the microbial integrity of drug transfer systems have shown that the BD PhaSeal™ System prevents microbial ingress during preparation and storage.[6-10]

The BD PhaSeal™ Optima System is a next-generation CSTD built on the foundation of the BD PhaSeal™ System. It meets the NIOSH definition that a CSTD "mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system, thereby minimizing individual and environmental exposure to drug vapor, aerosols and spills, and prevents microbial ingress for up to 168 hours and 10 penetrations.[*#†]

While previous studies have reported the reduced risk of microbiologic contamination provided by the BD PhaSeal™ System, the aim of the current study was to evaluate the performance of the BD PhaSeal™ Optima System as a barrier to microbial ingress and contamination during simulated preparation and administration of hazardous drugs.[11-13] The assessment included a clinical simulation in which BD PhaSeal™ Optima System Protectors, Connectors and Infusion Adapters (Fig. 1) were exposed to repeated inoculation, disinfection, puncture and flush cycles for 7 days in an International Organization for Standardization (ISO) Class 5 environment.[11-13] The study demonstrates that the BD PhaSeal™ Optima System prevents microbial ingress for up to 168 hours and 10 penetrations.[11-13*#†]

*In an ISO Class 5 environment.
#Bench test results may not necessarily be indicative of clinical performance.
†The ability to prevent microbial ingress for up to 168 hours should not be interpreted as modifying, extending or superseding a manufacturer's labeling recommendations for the storage and expiration dating of the drug vial. Refer to drug manufacturer's recommendations and USP compounding guidelines for shelf life and sterility information.

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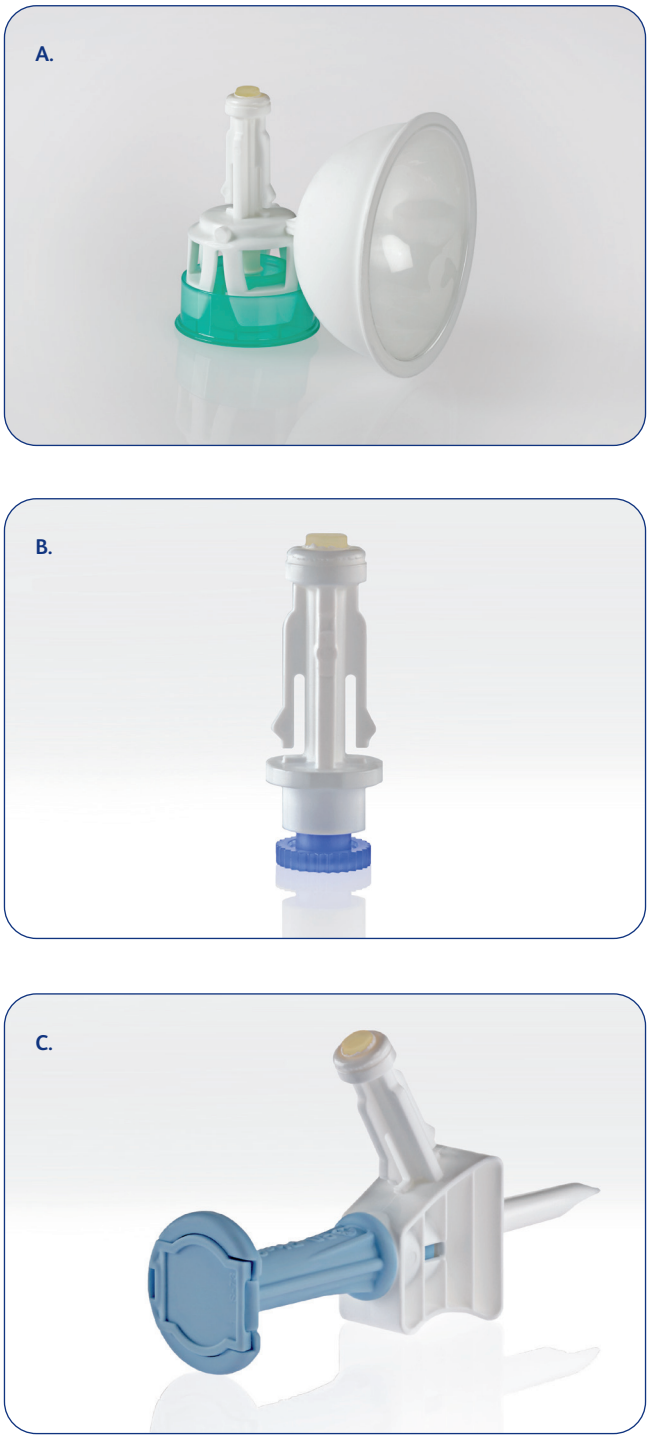


Figure 1. The BD PhaSeal™ Optima System (A) Protector, (B) Connector and (C) Infusion Adapter.

Performance of the BD PhaSeal™ Optima System Protector, Connector and Infusion Adapter[11-13]

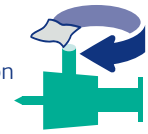
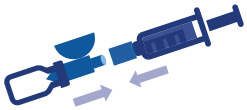
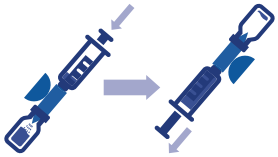
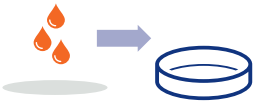
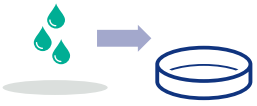
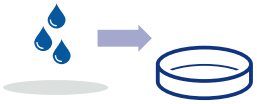
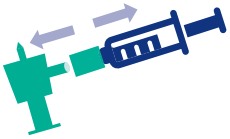
Methods

Three components of the BD PhaSeal™ Optima System were challenged by at least 1 x 10^3 colony-forming units (CFUs) of each of four microorganisms (i.e., *Staphylococcus aureus,* ATCC#6538; *Staphylococcus epidermidis,* ATCC#12228; *Klebsiella pneumoniae,* ATCC#4352 and *Pseudomonas aeruginosa,* ATCC#9027) that were chosen for this study because they are among the most common causative agents of catheter-related bloodstream infection.[14]

The microbiologic integrity of individual BD PhaSeal™ Optima System Protectors, Connectors and Infusion Adapters (N=10 replicates each) was monitored through 10 activation cycles per replicate over a period of 7 days. Each activation cycle consisted of inoculation, disinfection of the CSTD membrane and vial access followed by a saline flush of the system to capture organisms. (Note: four protector activation cycles on Day 7 were combined into one flush to capture organisms.)

The BD PhaSeal™ Optima System Protector was tested for its ability to prevent microbial ingress in vials of simulated drug solutions (Fig. 2A). Another component, the BD PhaSeal™ Optima System Connector, was evaluated for its ability to prevent microbial ingress when connected to an IV line and subjected to a simulated IV push (Fig. 2B). The BD PhaSeal™ Optima System Infusion Adapter was also tested for its ability to prevent microbial ingress when inserted into IV bags (Fig. 2C).

Figure 2. Experimental design of the (A) BD PhaSeal™ Optima System Protector, (B) Connector and (C) Infusion Adapter evaluations. Negative controls were identical to the samples without inoculation. Process simulation controls were run concurrently with the samples without disinfection. Positive recovery controls were conducted by inoculating the device with challenge organisms, then immediately extracting in peptone water, 0.1%, diluting and enumerating the number of microorganisms deposited on the test surface via the plate count method.

A.	B.	C.
1 Inoculate the protector membrane with the challenge microorganism. 	1 Inoculate the connector membrane with the challenge microorganism. 	1 Inoculate the infusion adapter with the challenge microorganism. 
2 Disinfect with an alcohol pad by using a twisting motion with friction for 3 seconds. Let dry for 1 minute. 	2 Disinfect with an alcohol pad by using a twisting motion with friction for 3 seconds. Let dry for 1 minute. 	2 Disinfect with an alcohol pad by using a twisting motion with friction for 3 seconds. Let dry for 1 minute. 
3  Connect a saline syringe equipped with an injector to the disinfected protector.	3  Connect a saline syringe equipped with an injector to the disinfected connector.	3  Connect a saline syringe equipped with an injector to the disinfected infusion adapter.
4  Flush saline through the system, invert and then withdraw.	4 Flush saline through the system and onto a filter. 	4 Flush saline through the system and onto a filter. 
5 Disconnect the syringe from the system and flush the recovered saline through the filter. Retain the protector for further testing. 	5  Rinse the filter, plate on growth medium, incubate and perform plate counts.	5  Rinse the filter, plate on growth medium, incubate and perform plate counts.
6  Rinse the filter, plate on growth medium, incubate and perform plate counts.	6  Disconnect the connector and retain for further testing.	6  Disconnect the infusion adapter and retain for further testing.
7  Repeat by using the original protector but with new injectors and saline syringes.	7  Repeat by using the original connector but with new injectors and saline syringes.	7  Repeat using the original infusion adapter but with new injectors and saline syringes.

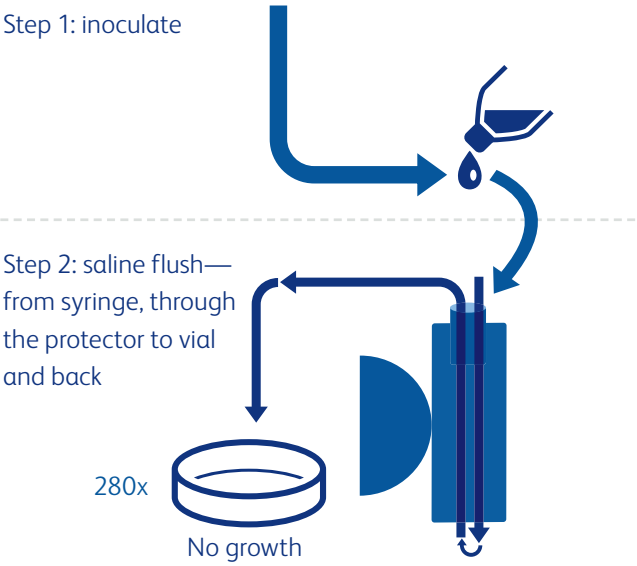
Results and discussion

A total of 280 flushes were performed on the BD PhaSeal™ Optima System Protectors, while 400 flushes each were performed on the Connectors and Infusion Adapters. No CFUs were observed after plating and incubation of any of these saline flushes (Figs. 3 and 4). Results for positive recovery controls, negative controls, and positive process controls were all within acceptance criteria and did not negate the test results.

Figure 3. Performance of (A) the BD PhaSeal™ Optima System Protector and (B) Connector as barriers to microbial ingress. No microbial growth was observed after plating and incubating the saline flushes recovered from these BD PhaSeal™ Optima System components.

A.

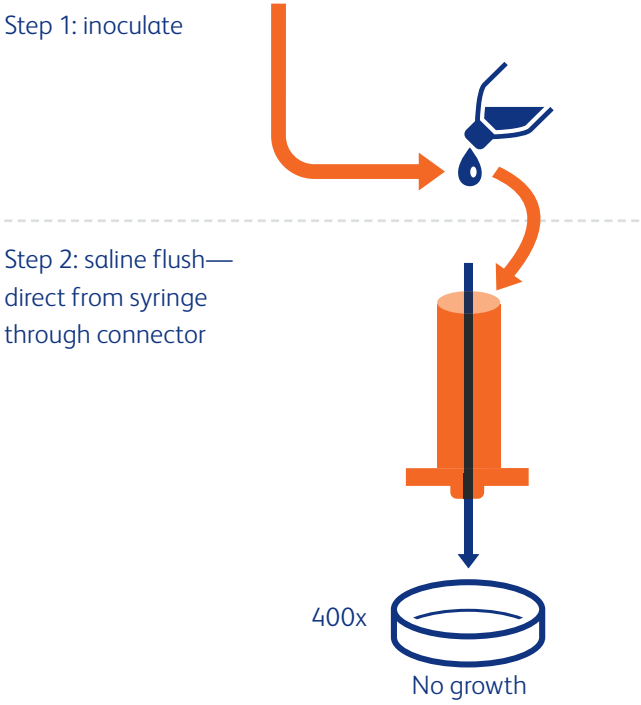
BD PhaSeal™ Optima System Protector	
Organism	Challenge organism concentration applied to membrane (CFU/mL)
S. aureus	1.1 x 10^6–2.6 x 10^6
S. epidermidis	1.2 x 10^6–6.8 x 10^6
K. pneumoniae	3.5 x 10^5–8.8 x 10^5
P. aeruginosa	1.5 x 10^6–5.9 x 10^6



Organism	No. of CFUs recovered
S. aureus	0 of 70
S. epidermidis	0 of 70
K. pneumoniae	0 of 70
P. aeruginosa	0 of 70

B.

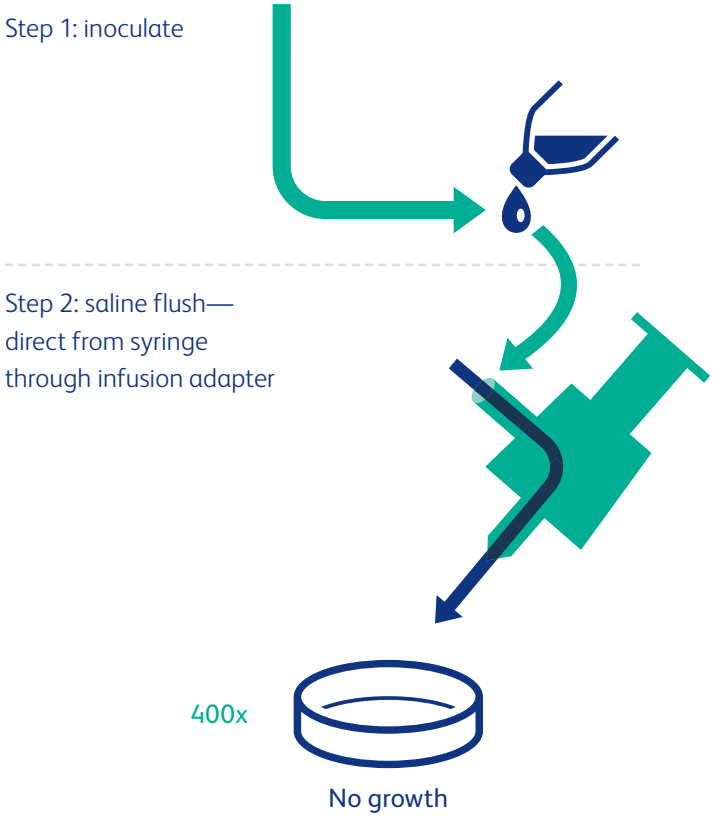
BD PhaSeal™ Optima System Connector	
Organism	Challenge organism concentration applied to membrane (CFU/mL)
S. aureus	9.8 x 10^4–2.3 x 10^6
S. epidermidis	5.0 x 10^5–2.0 x 10^7
K. pneumoniae	4.7 x 10^3–6.1 x 10^6
P. aeruginosa	1.7 x 10^5–2.5 x 10^6



Organism	No. of CFUs recovered
S. aureus	0 of 100
S. epidermidis	0 of 100
K. pneumoniae	0 of 100
P. aeruginosa	0 of 100

Figure 4. The BD PhaSeal™ Optima System Infusion Adapter as a barrier to microbial ingress. No microbial growth was observed after plating and incubating the saline flushes recovered from the BD PhaSeal™ Optima System Infusion Adapter.

BD PhaSeal™ Optima System Infusion Adapter	
Organism	Challenge organism concentration applied to membrane (CFU/mL)
S. aureus	8.8 x 10^4–1.9 x 10^5
S. epidermidis	5.8 x 10^5–1.7 x 10^6
K. pneumoniae	1.6 x 10^5–5.7 x 10^5
P. aeruginosa	2.0 x 10^5–3.0 x 10^5



Organism	No. of CFUs recovered
S. aureus	0 of 100
S. epidermidis	0 of 100
K. pneumoniae	0 of 100
P. aeruginosa	0 of 100

Conclusion

The BD PhaSeal™ Optima System (Fig. 5) prevents microbial ingress for up to 168 hours and 10 penetrations, as demonstrated by the data and results. The Protector, Connector and Infusion Adapter components of the BD PhaSeal™ Optima System can each prevent microbial ingress for up to 10 penetrations and 168 hours for up to 10 transfers of hazardous drugs.[11-13,15 *#†]

Figure 5. The BD PhaSeal™ Optima System family of CSTDs

*In an ISO Class 5 environment.
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