

Evaluation of the Clave[®] technology and resistance to microbial ingress

BACKGROUND

The Centers for Disease Control and Prevention (CDC) estimates approximately 250,000 incidents of Catheter Related Bloodstream Infections (CRBSIs) occur annually in the United States.¹ Although attributable mortality due to CRBSIs is not clear, these infections have been associated with higher costs, mortality rates, and number of hospital days.^{1,2} Microbial ingress is among the circumstances that risk the safe use of catheters.

The Clave is a microbiologically and mechanically closed needlefree connector that features reversed split-septum technology, which incorporates an internal blunt cannula and a split-septum to seal off the fluid path. The internal blunt cannula creates a unique dedicated internal fluid path such that the housing, outside of the silicone seal, and outside of the administration device never come in contact with the fluid path.

The U.S. Food and Drug Administration (FDA) classifies needlefree connectors as class II medical devices that require clearance from the agency in accordance with the published guidance document Intravascular Administration Sets Premarket Notification Submission [510(K)].³ This document requires that all new needlefree connectors seeking approval to include a microbial ingress study as part of the submission. While only new devices seeking approval are required to conduct this study, ICU Medical independently contracted with Nelson Laboratories of Salt Lake City, Utah, to perform the required testing with the Clave. The results are reported herein.

PURPOSE

Intravenous (IV) therapy is the primary route for therapeutic regimens in the acute care setting. Nearly all hospitalized patients have some type of vascular access device inserted to support their treatment. As reliance on the IV pathway has increased, the potential for accidental needlestick injuries has led to the creation of luer-activated needlefree connectors. These devices are used to connect catheters, administration sets, and/or syringes to deliver IV therapy. Unfortunately, placement of a vascular access device increases the risk of a bloodstream infection. In fact, approximately 87 percent of bloodstream infections are associated with the presence of some type of intravascular device.⁴ There are two primary portals for bacterial ingress into the bloodstream through a catheter: the first is the insertion site, and the second is the hub, which is used to administer fluids and medications. The need to effectively prevent bacterial ingress through the needlefree connector is paramount in helping to prevent bloodstream infection.

In compliance with FDA guidance, microbial ingress testing evaluates a product's design and its ability to resist the passage of microorganisms under a simulated use model. The intent of this study is to demonstrate that the device will act as a barrier to intraluminal bacterial contamination under normal use. Specifically, microbial ingress testing should demonstrate that if the device were disinfected by manual scrubbing using a standard disinfectant, then the subsequent connection using a sterile device would not transmit bacteria. The FDA recommends testing new devices under extreme use conditions, such as repeated insertions into the female luer or split-septum and static insertion over a period of hours.

Development of the methods and protocols in this study were based on the 2008 FDA guidance, including a test period of 72 hours and the testing of at least four different bacteria, including Gram negative and Gram positive strains.

MATERIALS AND METHODS

In order to assess whether the septum of the Clave connector can be effectively disinfected with 70 percent isopropyl alcohol (IPA) and maintain a physical barrier to bacteria, a protocol was developed and executed by Nelson Laboratories of Salt Lake City, Utah, using four bacterial strains:

- › Staphylococcus epidermidis, ATCC #12228
- › Staphylococcus aureus, ATCC #6538
- › Klebsiella pneumonia, ATCC #4352
- › Pseudomonas aeruginosa, ATCC #9027

Twenty-four test samples were prepared in addition to eight negative control samples and eight positive control samples. Each sample device was subjected to five inoculations/disinfections/activations per 24-hour period for 3 days. After the 15th activation, two additional activations were performed: one 4-hour “extended activation” and one final activation, in which 10 mL of soybean casein digest broth (SCDB) with 5% deactivated bovine serum albumin was flushed through the device.

Over a 3-day period, this experiment utilized artificial contamination of the Clave septum with an inoculum level of at least 10³ organisms to simulate extreme-use conditions. Each sample was subjected to inoculation and allowed to dry for at least 1 minute, followed by standard hospital disinfection procedure using a 70% IPA prep pad and wiping vigorously in a circular motion for 3 seconds. This entire process was completed five times per 24-hour period. After each engagement, injectate through the connector was collected and tested for the presence of the challenge microorganisms.

Positive controls included in this study were inoculated with the same number of organisms as the test samples, but were not subjected to the disinfection process prior to activation. Negative controls included in this study were not inoculated with any of the challenge organisms, but were subjected to the same disinfection and activation processes as the sample units. All negative control samples were negative for ingress of any of the challenge organisms.

RESULTS

Of the four bacterial strains, the data indicates that zero colony-forming units (CFUs) of each test organism passed through the septum of the Clave needlefree connector for all 17 activations to which each of the 24 test samples were subjected. (See summary table.)

Test Organism	Extended Activation (CFU)	SCDB Flush (CFU)	Positive Control Log Reduction
Staphylococcus aureus	0	0	3.2
Staphylococcus epidermidis	0	0	3.7
Klebsiella pneumoniae	0	0	2.4
Pseudomonas aeruginosa	0	0	3.2

CONCLUSIONS

In all cases, the microbial barrier of the Clave needlefree connector effectively prevented microbial ingress when inoculated with at least 3 logs of organism and challenged under simulated extreme-use conditions, including repeated inoculation on the outer surface of the septum, disinfection, and activation over a period of 3 days. Furthermore, the results confirm the Clave microbial barrier meets the requirements delineated by the 2008 FDA guidance document Intravascular Administration Sets Premarket Notification Submissions [510(k)]. The Clave may be considered an effective tool in the prevention of catheter hub contamination and intraluminal bacterial colonization.

1. Blot SI, Depuydt P, Annemans L, et al. Clinical and economic outcomes in critically ill patients with nosocomial catheter-related bloodstream infections. *Clin Infect Dis* 2005;41:1591-1598.
2. Centers for Disease Control and Prevention. Reduction in central line-associated bloodstream infections among patients in intensive care units—Pennsylvania, April 2001–March 2005. *MMWR Morb Mortal Wkly Rep* 2005;54:1013-1016.
3. Guidance for Industry and FDA Staff: Intravascular Administration Sets Premarket Notification Submission [510(K)]. 2005.
4. Ryder, M. Catheter-related infections: It's all about biofilm. *Topics Adv Pract Nurse Journal*. 2005 [cited 2006 Sept 11]; 5(3). Available www.medscape.com/viewarticle/508109.