

Antimicrobial efficacy of the LifeShield™ CLAVE® Connector using silver-saturated fluid path elements

Background

Contamination of vascular access devices remains a substantial risk to patients in today's healthcare environment. The CDC estimates that there are a minimum of 250,000 incidents of catheter-related bloodstream infections (CRBSIs) annually in the United States.¹ Those patients that develop CRBSIs may incur extended hospital stays and an increased risk of long-term health effects and mortality. The treatment of CRBSIs carries substantial cost to the healthcare provider, placed at an average cost of \$56,000 USD per incidence.² The Centers for Medicare Reimbursement (CMS) recently identified CRBSIs (also defined as "Vascular Access Device-Related Infection"), as one of the listed preventable medical errors. CMS enacted a ruling in October of 2008 that will result in reimbursement for the treatment of CRBSIs to cease in their fiscal year of 2009.

In a 1996 Special Communication, Pearson et al, identified two primary points of entry for bacteria in a central venous catheter: the extraluminal, or dermal entry point for the catheter, and the intraluminal, or hub of the catheter through which clinicians administer fluids and medications. This report went on to suggest that the hub is the more likely culprit for bacterial entry when the catheter dwell time exceeds 10 days.³ In 1993, the LifeShield CLAVE Needle-Free Connector was developed to protect the hub and intraluminal pathway of catheters. The LifeShield CLAVE is a microbiologically and mechanically closed connector which permits access to the catheter via use of a needle-free luer lock connection. The LifeShield™ Antimicrobial CLAVE® is a device that incorporates silver-saturated fluid path elements, which are housed in the traditional LifeShield CLAVE design. The LifeShield Antimicrobial CLAVE has been developed to reduce bacterial contamination on the swabbing surface and in the fluid path, which serves as the portal for entry to the catheter. This paper discusses the evolution of the needle-free connector market since the introduction of the LifeShield CLAVE, how the unique design of the LifeShield CLAVE can positively impact the prevention of bacterial colonization of the catheter, and, lastly, the findings of investigations that demonstrate a greater than 4-log reduction in both gram-negative and gram-positive bacteria in an all new LifeShield Antimicrobial CLAVE.

Introduction: The Evolution of Needle-Free

Central venous catheters (CVCs) are widely used in healthcare today to facilitate the treatment of patients at inpatient hospital facilities, outpatient clinics and even in patients' homes. While these catheters are often providing life-saving fluids and medications, they are also associated with serious infectious complications. In a recent study, Safdar and Maki found that preventative measures used at the catheter insertion site were largely unsuccessful at reducing CRBSIs. Their conclusion supports that as much as 60% of CRBSIs likely originate from the intraluminal pathway, or through the catheter hub.⁴

Protection of the catheter hub is solely accomplished by use of a capping device, most commonly known as a needle-free connector (NC), coupled with specific nursing protocols for handling that NC. The introduction of the first stand-alone NC that did not require needles or cannulas for IV access was the LifeShield™ CLAVE® Connector in 1993. Since then there have been as many as 20 different NCs introduced in the United States, including devices that exhibit positive pressure, and, most recently, neutral NCs such as the LifeShield™ MicroCLAVE®.

The incentive for companies to develop NCs after the LifeShield CLAVE came with the onset of recommendations to use devices which aid in the prevention of needlestick injury, ultimately becoming a Federal OSHA Mandate in 2000 known as the Bloodborne Pathogens Standard. While use of these devices resulted in substantial gains towards the reduction of needlestick injury for healthcare workers, their designs did not incorporate robust infection control features which might protect the catheter from contamination, and, therefore, the patient against potential CRBSIs.

In the late 90s, reports started coming out about NCs causing an increase in CRBSIs, which were ultimately linked to capped NCs. Since then, the market has become almost exclusively capless, or what are now known as one-piece, swabable NCs. Swabable implies that if you use a 70% Isopropyl swab to wipe the injection site of an NC, bacteria will be removed such that the access point for the intraluminal pathway of a CVC is protected. The majority of today's market uses a one-piece swabable NC, with the LifeShield CLAVE Connector being the largest stakeholder.

More recent reports linking swabable NCs with an increase in CRBSIs started surfacing circa 2005. Since then, there have been a number of public statements and terms used in published works that implicate certain features such as "positive pressure" or "mechanical valve" as being associated with CRBSIs. Yet, despite attempts by certain investigators and the promotional efforts of particular device manufacturers, no single design feature or broad classification can be used to indict a device as the culprit behind an increase in CRBSIs. Each NC has a very unique design with complex componentry, functions and features that make up the finished device. It is therefore necessary to consider each device as a whole, and not as a single feature or classification. Further to this concept, it was recently recommended by Mermel and Marschall that NCs should "involve fail-safe engineering advances aimed at further mitigation of the risk of infection in the complex hospital environment in which they are used."⁵

In addition, no single feature, including an antimicrobial additive, is capable of significantly reducing CRBSIs in isolation of robust infection control policies and practices. The NC is only a component in the infection control bundle, which also includes such important practices as the care and maintenance of CVCs and the protocols associated with handling the NCs used to protect them.

The LifeShield CLAVE Connector

The LifeShield CLAVE was developed in the early 90s as a microbiologically and mechanically closed connector. Its primary intent was to replace the popular pre-slit blunt cannula systems of the time. Clinicians were asking for a simplified system that didn't require multiple parts and pieces to use. The LifeShield CLAVE design simply took the once external blunt cannula and integrated it into the split septum, so one could access with any standard male luer. Further, while the LifeShield CLAVE has undergone numerous incremental improvements over the last decade, the reversed, split-septum technology remains as the foundation of its design today.

The LifeShield CLAVE is the most widely used and published NC on the market today. Various studies have shown that terminating the use of the LifeShield CLAVE in favor of alternative NCs has resulted in a temporal increase in CRBSIs.^{6,7} Results demonstrated that upon returning to the LifeShield CLAVE, the facility was able to return to its baseline infection rate or better. Other studies have shown that the LifeShield CLAVE will independently reduce catheter hub colonization on central venous catheters.⁸ Catheter hub colonization is a recognized and acceptable surrogate endpoint for CRBSI development.⁸ Additionally, a comparative *in vitro* study found that the LifeShield CLAVE was the least likely of nine other commercially available NCs to permit the transfer of bacteria into the fluid path.⁹ The heart of the LifeShield CLAVE design is the reversed, split-septum technology, which provides the dedicated internal fluid path. This feature can be found in all variations of the LifeShield CLAVE, including the LifeShield MicroCLAVE, the Y-CLAVE and the LifeShield™ Antimicrobial CLAVE®.

The LifeShield Antimicrobial CLAVE

The LifeShield Antimicrobial CLAVE was developed to provide another tool in the fight against CRBSIs. While the reversed, split-septum technology of the LifeShield CLAVE remains the key factor for the prevention of catheter contamination, the antimicrobial additive provides additional benefit. This premise is based on the notion that if the injection site and fluid path, which are constantly exposed to manipulation, include a feature to combat bacterial contamination, then subsequent contamination of the intraluminal fluid path may be limited.

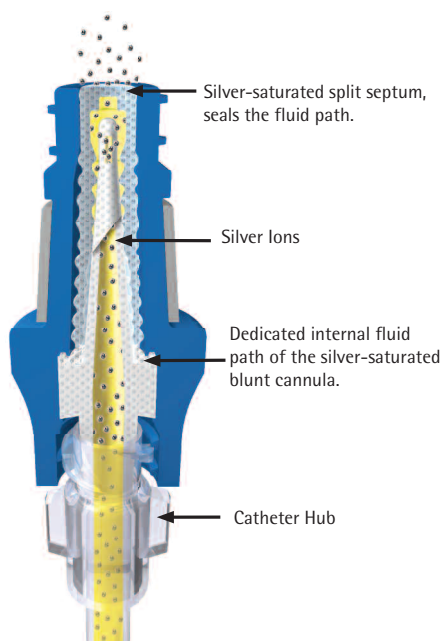
Methods

An exhaustive development program was completed to determine the best agent with the greatest efficacy and least risk, as well as a method of manufacturing to ensure proper release and distribution of the agent in the clinically important components. This research determined that the following attributes are required:

- The agent must be widely accepted in clinical practice and have no measurable incidence of adverse reactions in patients.
- The agent must be integral to the componentry and not an add-on or coating that has the risk of wearing off.
- The agent must demonstrate clinical efficacy of greater than a 4-log kill factor for gram-negative and gram-positive bacteria.
- The agent's efficacy must be established for a 96-hour period, in accordance with CDC guidelines, when subjected to a simulated-use model.

All components which have communication with the fluid path of the LifeShield CLAVE were considered. These include the internal blunt cannula and split septum. The housing is not in communication with the fluid path, and, therefore, was determined to be outside the scope of consideration. Two proprietary formulations of ionic silver that are compatible with the unique LifeShield CLAVE components were selected. These formulations were integrated into the materials of the split septum and the internal blunt cannula. This process of integration ensures complete saturation of the component and even distribution throughout, while also providing scratch-resistant antimicrobial protection over the useful life of the device. This proprietary process allows for the proper "elution" of the silver ions so that they can exit the component and enter the fluid path where any bacteria present will be exposed to the silver ions.

LifeShield™ Antimicrobial CLAVE®: Internal Fluid Path Operation



In order to establish antimicrobial efficacy, the FDA was consulted regarding their draft publication, Premarket Notification [510(k)] Submissions for Medical Devices that include Antimicrobial Agents (2007). It was determined that efficacy testing must be done on a finished device in a simulated-use model. Four organisms were selected for study to represent commonly found bacteria in the healthcare environment. Efficacy was required for a period of 96 hours, as that is a minimum use life common to NCs.

The four organisms used in this testing were:

- *Staphylococcus aureus* (ATCC #6538)
- *Staphylococcus epidermidis* (ATCC #35984)
- *Klebsiella pneumoniae* (ATCC #4352)
- *Pseudomonas aeruginosa* (ATCC #9027)

Procedures

For a 96-hour period, the fluid path of each study device was inoculated with a 5-log concentration of the specified organism. Total bacterial counts were measured at four unique time points over the 96-hour period. This model was selected to demonstrate the durability and efficacy of the antimicrobial agent for the useful life of the device.

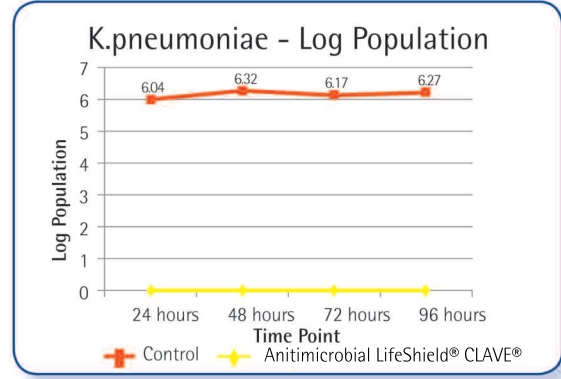
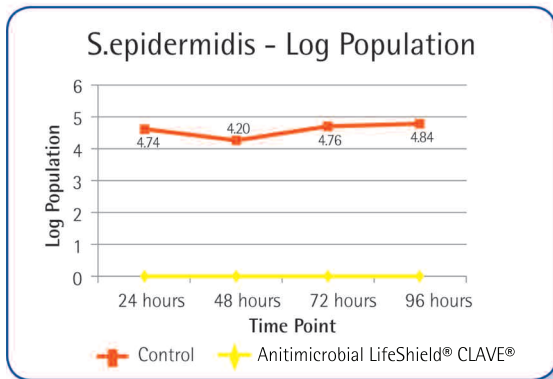
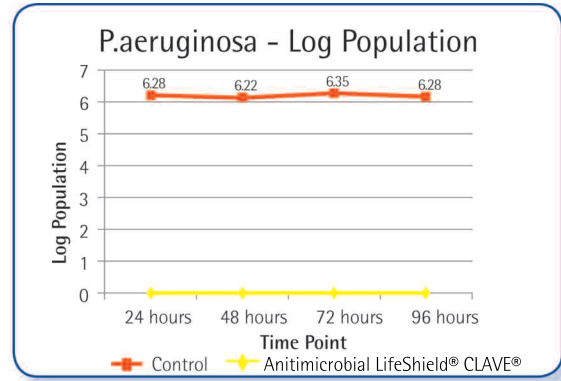
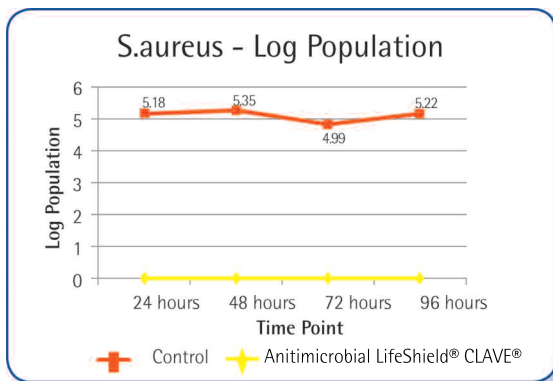
Antimicrobial efficacy was measured in terms of total log reduction in bacterial counts. LifeShield Antimicrobial CLAVE test devices and standard LifeShield CLAVE control devices were used for each bacterial model. The reduction was calculated by comparing the inoculated count to the number of bacteria recovered from the study devices at various time points. The following charts show the antimicrobial efficacy of the LifeShield Antimicrobial CLAVE as compared to the standard LifeShield CLAVE for each of the test microorganisms over time.

Conclusions

For all four bacterial strains, there was a significant reduction in the total bacteria counts on the Antimicrobial LifeShield™ CLAVE® devices for the simulated model of repeated contamination. The LifeShield™ Antimicrobial CLAVE® was capable of providing a minimum 4-log kill factor, or 99.99% efficacy, against all four strains of bacteria at various time points.

In all cases, the LifeShield Antimicrobial CLAVE was effective at significantly reducing the number of bacteria for an extended 96-hour use life. The proprietary ionic silver formulation and mode of integration into the finished device was proven to be effective in a worst-case model.

The LifeShield Antimicrobial CLAVE can limit bacterial colonization of the catheter; however, the internal fluid path design and proper adherence to an infection control bundle remain important for limiting CRBSIs.



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Reduction in colonization or microbial growth on the device has not been shown to correlate with a reduction in infections in patients. Clinical studies to evaluate reduction in infection have not been performed.

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