

## INTRODUCTION

In 1991, the U.S. Occupational Safety and Health Administration encouraged healthcare facilities to "look for engineering controls that make the environment healthier and safer for workers" due to increased needstick injuries among healthcare workers. In April 1992, the FDA issued a needstick safety alert with strong encouragement for the replacement of hypodermic needles with needfree systems or recessed needle systems for accessing IV lines. The FDA indicated that there was no evidence that patient bloodstream infections had increased with the implementation of needfree systems that had been cleared for marketing at that time. These included a protected needle device, split septum/blunt cannula, and a capped luer-activated device.

Since then, numerous reports of increased bloodstream infection rates involving various needfree systems have been published. These reports accompanied the introduction of numerous devices with a wide variety of device designs and mechanical engineering features (Figure 1). It has been suggested that even though several outbreaks of CRBSI have been reported with the use of the early needfree systems device, the use of the newer luer-accessed devices adds additional risk for bloodstream infection. However, multiple potential risk factors for catheter-related bloodstream infection related to needfree device use have been identified, including use of aseptic technique, user competency, frequency of intravenous therapy per disease state, complex therapies, service delivery location, cultural diversity, compliance with manufacturer's instruction for use, and device design.

More recently several institutions have reported increases in catheter-related bloodstream infection rates with a fourth generation of positive fluid displacement luer-activated devices (PFD LAD) designed to prevent retrograde blood flow into the catheter after disconnection of the flush syringe. These findings raise serious questions concerning the safety of all needfree systems—particularly in light of the 2001 congressional passage of The Needlestick Safety and Prevention Act mandating the institutional use of needfree systems. This begs the question - Are we reducing the risk of needstick injury, but at the same time increasing infection risks?

A systematic review including five randomized controlled trials has been conducted recently to determine the effect of the use of needfree closed systems, conventional closed systems or conventional open systems on catheter-related infections in hospitalized patients with intravenous catheters (Niel-Weise BS et al., J Hosp Infect., 2006). It was concluded that there are no objections to using these new systems, but there is insufficient evidence to recommend the needfree closed devices. However, the reviewers also noted that the quality of the trials and the way they were reported were generally unsatisfactory. The ECRI, an independent nonprofit health services research agency, concluded in a special report regarding the concerns of increased infection with LADs that there is not adequate data to justify replacing or removing PFD LADs unless the facility experiences sustained increase of CRBSI associated with the device use (ECRI Accession Number S0129, August 2006).

Clinicians are compelled by federal regulation to use a needfree device on intravenous catheters, but are faced with the selection of a device without assessment of the risk of infection among and between the device designs and comparative evidence of potential risk. The purpose of this in vitro study is to evaluate device design by comparing bacterial transfer from the surface of the connector to injected fluids for multiple commercially available needfree connectors.

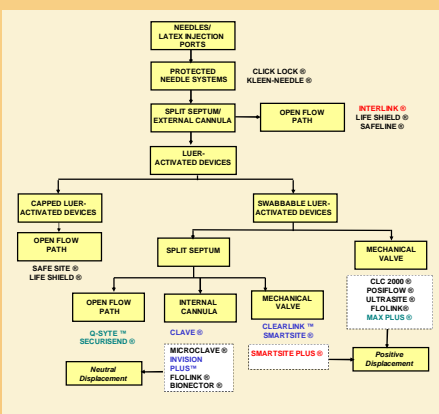


Figure 1. Evolution of needfree connector device design

## METHODS

Nine needfree connector products were tested: Clave® (CV), ICU Medical, Clearlink™ (CL) Baxter, Interlink® (IL) Baxter-BD, InVision Plus™ (IP) Rymed, MaxPlus™ (MP) Medegon Medical, Q-Syte™ (QS) BD, Securisend® (SC) Halkey-Roberts, SmartSite® (SS) and SmartSite Plus® (SP) Alaris-Cardinal. The surface of a connector was inoculated with 10<sup>4</sup> colony forming units (cfu) of *Staphylococcus epidermidis* and dried for 30 min. Then 5 ml of sterile fluid was flushed through the connector at times 0, 2, 4, and 6 h. The number of bacteria transferred (BT) was determined by colony forming unit (cfu) counts in the effluent. These counts were performed by serial dilution in phosphate-buffered saline and spread plating on tryptic soy agar. In each experiment three different connector types were evaluated. For each connector type, 11 connectors were inoculated and 1 served as an uninoculated control. At each time point, 3 connectors in each group were submitted to the flush and count manipulation and 2 connectors served as inoculation checks based on cfu counts for the connector surfaces. Each experiment included CV as the control. The two products tested plus CV formed a set of three products that were compared side-by-side. Each set was repeated 5 times. A diagram of the experimental procedure is shown in Figure 2. This experimental design allowed for assessment of the variability among connectors, among experiments, and among sets so that a comparison of any two products could take into account all relevant sources of statistical variability.

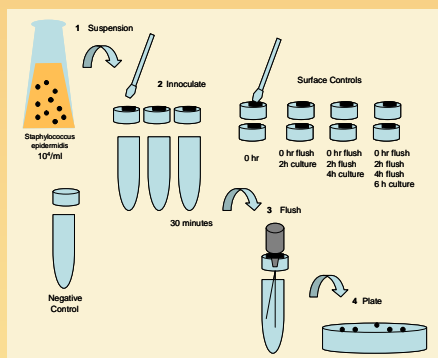


Figure 2. Diagram of test procedure.

## RESULTS

The experiments consistently showed that bacteria contaminating the surface of a connector will appear in the fluid flushed through the connector. Bacterial counts from the surface controls were consistently near the target level of 10<sup>4</sup> cfu per connector and were not significantly different between connectors. Significant differences were observed in flush counts between the different connector designs. These differences were more apparent as the experiments progressed, with the most significant differences after six hours (Figure 3). This was the result of more differences between the mean number of bacteria transferred through the connectors over time. At the 6-hour time point, the products could be segregated into three groups according to the typical BT, 9–28 cfu (CV, SS, CL, IP), 107–224 cfu (MP, QS, SC), and 603–1380 cfu (IL, SP). A stringent significance level was used to compare the connectors (0.0028). As indicated by the p-values in Figure 3, differences between connectors would have been apparent at earlier time points if a lower significance level was chosen. Furthermore, by 6 hours, p-values for significantly different connectors were very low (<0.001) while those for connectors that were not significantly different were often quite high.

## RESULTS (cont'd)

	CV	CL	SS	IP	QS	SC	MP	IL	SP
SmartSite Plus (SP)	<0.001	0.003	0.011	0.021	0.240	0.160	0.410	0.190	
Interlink (IL)	<0.001	0.001	0.003	0.006	0.072	0.045	0.140		
MaxPlus (MP)	<0.001	<0.001	0.052	0.093	0.710	0.530			
Securisend (SC)	0.097	0.048	0.160	0.041	0.790				
Q-Syte (QS)	<0.001	0.029	0.002	0.170					
InVision-Plus (IP)	0.690	0.320	0.740						
SmartSite (SS)	0.570	0.490							
Clearlink (CL)	0.500								
Clave (CV)									
Mean log <sub>10</sub> density:	1.16	0.94	1.29	1.45	2.17	2.03	2.35	3.14	2.78
Geometric mean density:	14	9	19	28	147	108	225	1380	596

	CV	CL	SS	IP	QS	SC	MP	IL	SP
SmartSite Plus (SP)	<0.001	<0.001	<0.001	<0.001	<0.001	0.003	0.390		
Interlink (IL)	<0.001	<0.001	<0.001	<0.001	0.001	0.001	0.019		
MaxPlus (MP)	<0.001	<0.001	<0.001	0.017	0.260	0.350			
Securisend (SC)	0.003	0.006	0.007	0.069	0.840				
Q-Syte (QS)	<0.001	0.011	0.002	0.200					
InVision-Plus (IP)	0.230	0.200	0.210						
SmartSite (SS)	0.240	0.990							
Clearlink (CL)	0.550								
Clave (CV)									
Mean log <sub>10</sub> density:	1.07	1.17	1.17	1.56	1.95	2.01	2.29	3.01	3.22
Geometric mean density:	12	15	15	36	89	102	196	1026	1673

	CV	CL	SS	IP	QS	SC	MP	IL	SP
SmartSite Plus (SP)	<0.001	<0.001	<0.001	<0.001	0.001	0.017	0.077	0.860	
Interlink (IL)	<0.001	<0.001	<0.001	<0.001	0.001	0.023	0.100		
MaxPlus (MP)	<0.001	<0.001	<0.001	0.001	0.074	0.510			
Securisend (SC)	<0.001	0.003	<0.001	<0.001	0.250				
Q-Syte (QS)	<0.001	0.054	<0.001	0.130					
InVision-Plus (IP)	0.380	0.680	0.150						
SmartSite (SS)	0.900	0.300							
Clearlink (CL)	0.085								
Clave (CV)									
Mean log <sub>10</sub> density:	0.96	1.24	0.87	1.39	1.94	2.34	2.58	3.17	3.21
Geometric mean density:	9	17	7	25	86	221	378	1463	1632

Figure 3. Summary of pair-wise comparisons at the 2-hour (A), 4-hour (B), and 6-hour (C) time points. The term "density" denotes the number of viable bacteria that passed through the connector during a simulated use (flush). The geometric mean density was rounded to the nearest integer. A square was shaded grey if, and only if, the two connectors on the row and column for that square had mean log densities that were statistically significantly different at a simultaneous 0.10 significance level, or equivalently, an individual comparison 0.0028 significance level. The number in each square is the individual comparison p-value.

## DISCUSSION

Numerous risk factors for catheter-related bloodstream infections associated with needfree connectors have been proposed. The primary factors are attributed to device design, aseptic device management and frequency of exchange of the connector. Device design, product materials, engineering components and features of the various connectors vary widely among the currently available products. The variability of these designs makes classification and comparisons quite difficult.

The major design components include the access seal or septum configuration (flat, recessed, irregular), mechanism of access to the flow path (external cannula, internal cannula, or mechanical valve), flow path configuration (laminar vs turbulent flow), residual volume, internal surface area and displacement volume (negative, positive or neutral). All of the products in the split septum category allow for the mating luer or cannula to actually pass through the septum for fluid to flow. None of the products in the mechanical valve category has this feature; all of their swabbing surfaces or seals 'become' part of the fluid path when activated.

All the products in the mechanical valve category have a fluid path that relies on moving components. The moving component is in the actual fluid path and must move for fluid to flow. None of the products in the split septum category has a fluid path that relies on moving components. The residual volume left in the connector after flushing and the surface area of the internal compartment affect the number of bacteria retained in the connector. The surface area of material allows for the attachment of organisms and subsequent biofilm formation. Irregular surface area decreases the complete clearance of blood with blood draws or blood product administration. Negative displacement allows residual blood within the catheter, promoting a conditioned surface for bacterial attachment and biofilm formation, and catheter occlusion. The durability of each design component may decrease over time and may increase the potential for bacterial transfer.

The complexity of designs among the available devices makes the common classification of split septum and mechanical valve an oversimplification and an unreliable approach for making clinical decisions. The devices tested in these experiments are color-coded in Figure 1 based on the three groups defined in the results section. Connectors in the lower bacterial transfer range tended to be in the split septum/internal cannula category compared to the mechanical valve and split septum/open flow path system. However, this experiment involved only four flushes without disinfection of the access surface and demonstrates the variability and significant differences among nine different devices. Results may be different with an increased number of accesses over the typical 72–96 hour usage in clinical practice.

## CONCLUSIONS

The observed transfer of bacteria from the surface of needfree connectors to injected fluids underscores the importance of adequate surface disinfection prior to connection. Furthermore, the observed differences between connector products suggest that device design has an important influence on bacterial transfer.