

An In Vitro Comparison of Microbial Ingress Into 8 Different Needleless IV Access Devices

ABSTRACT

There are conflicting reports of the effect needleless intravenous access devices have on rates of catheter-related bloodstream infection. The aim of this study was to identify any differences between the rates of microbial ingress into 8 different devices following contamination. Each type of device was subjected to a 7-day clinical simulation that involved repeated microbial contamination of the injection site and decontamination followed by saline flushes. Significant differences in the number of microorganisms associated with each device were detected in the saline eluates. Three positive-displacement mechanical valves were associated with the ingress of significantly fewer microorganisms compared with other devices.

Key words: in vitro, infection risk, microbial ingress, needleless device

BACKGROUND

Needleless intravenous (IV) access devices that attach to catheter hubs were initially introduced into clinical practice to reduce the risk of IV catheter-related needlestick injuries.¹ However, these devices can provide a conduit for the ingress of microorganisms. There have been varying reports on the rates of catheter-related bloodstream infection associated with these devices, including an increase in incidence following a change from split-septum devices to mechanical valves.²

The Centers for Disease Control and Prevention has subsequently recommended that when needleless systems are used, a split-septum valve may be preferred over some mechanical valves.³ Furthermore, the Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America advised that positive pressure needleless connectors with mechanical valves should not be used before a thorough assessment of risks, benefits, and education regarding proper use.⁴

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The authors have previously undertaken randomized clinical studies assessing microbial contamination associated with the use of needleless IV access devices in comparison with standard ports.^{5,6} These demonstrated that there was no potential increased infection risk associated with the use of these devices as compared with standard luers.

The objective of the current study was to ascertain whether different needleless IV access devices, including positive-displacement valves, provide a similar physical barrier to prevent the ingress of microorganisms when microbiologically challenged under simulated controlled clinical conditions.

METHODS

Needleless IV Access Devices

The needleless IV access devices evaluated in this study are shown in Figure 1 and include CareSite (CS) (B. Braun Medical, Inc.); MaxPlus Clear (MP) (CareFusion, Inc.); MaxGuard (MG) (antimicrobial silver device, CareFusion, Inc.) [positive-displacement mechanical devices]; Clave (CL) (ICU Medical, Inc.); V-Link (VL) (silver antimicrobial device, Baxter Healthcare Corp.) [negative-displacement devices]; MicroClave Clear (MC) (ICU Medical, Inc.); Bionector (BN) (Vygon) [neutral displacement devices]; and Q-Syte (QS) (Becton Dickinson) [split-septum luer access device].

Clinical Simulation of Needleless IV Access Devices

This work was carried out by a National Health Service (NHS)-employed clinical research scientist in a contain-

ment level 2 laboratory. The devices were subjected to 7 days of clinical simulation as outlined in Figure 2. An overnight culture of *Staphylococcus aureus* National Collection of Type Cultures (NCTC) 6571 on blood agar was used to prepare a 1×10^5 CFU/mL suspension in phosphate-buffered saline (containing 10% [v/v] horse blood). The injection site of 24 of each type of needleless IV access device was then inoculated with 10 μ L (containing 1×10^3 CFU) of viable *S. aureus*. These were left to dry at room temperature for 30 minutes. The inoculum was applied to the injection sites before cleaning to mimic repeated IV access in a busy clinical scenario, such as in theater or intensive care. The injection sites then were decontaminated using a 70% (v/v) isopropyl alcohol wipe (Sani-Cloth 70% IPA, PDI).⁴ For 12 of each type of device, the antiseptic wipe was firmly applied to the injection site and rotated through 180° 3 times over 5 seconds; for the remaining 12 of each type, through 180° 15 times over 15 seconds. The antiseptic subsequently was allowed to dry for 30 seconds. The clinical simulation included decontamination of the devices before the first flush and following the last flush in each round of activations. The antiseptic was allowed to dry for 5 minutes before the next inoculation with microorganisms. The activations in each round were completed consecutively. The same administration set was used for each needleless IV access device for the first 4 days to mimic static insertions, after which a sterile set was used for the remaining 3 days.³ The male luers on the administration sets were capped with sterile luer plugs between each use.

Three positive and 3 negative controls for each device type were also included. The positive and negative controls were subjected to clinical simulation but without any decontamination or microbial inoculation,



Figure 1 Needleless IV access devices evaluated. From left to right: CS, MG, MP, CL, VL, BN, MC, and QS. (Courtesy of the authors.) *Abbreviations:* IV, intravenous; CS, CareSite (B. Braun Medical Inc.); MG, MaxGuard (CareFusion Inc.); MP, MaxPlus Clear (CareFusion Inc.); CL, Clave (ICU Medical Inc.); VL, V-Link (Baxter Healthcare Corporation); BN, Bionector (Vygon); MC, MicroClave Clear (ICU Medical Inc.); QS, Q-Syte (Becton Dickinson Infusion Therapy Systems Inc.).

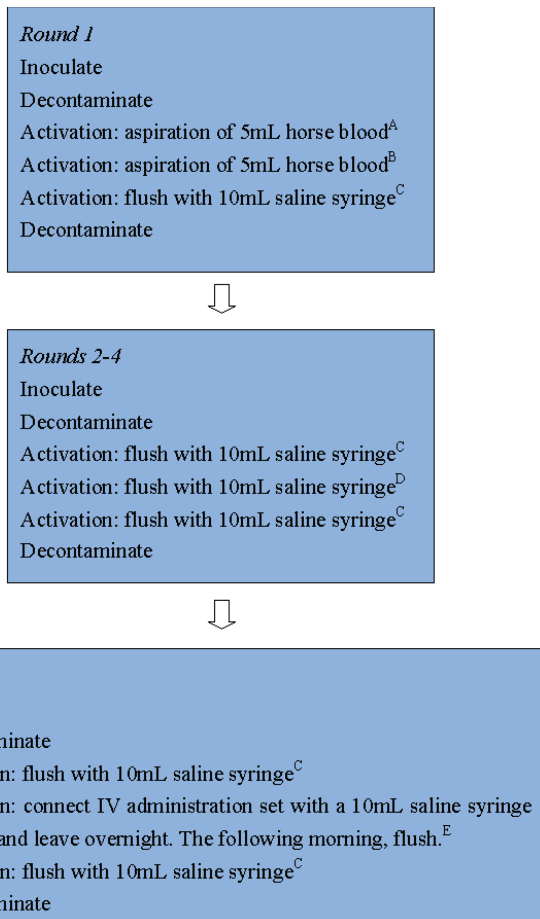


Figure 2 Outline of clinical simulation carried out daily for 7 consecutive days. To mimic: ^Adiscard of blood before sample collection; ^Bblood sample collection; ^Ca line flush; ^Dbolus drug administration; ^Ea static insertion, ie, continuous infusion.

respectively. For every 7 days of clinical simulation performed, the same number of each type of device was studied to ensure that they were subjected to the identical inoculum. The study resulted in a total of 15 male luer insertions and activations of each needleless IV access device every 24 hours and 105 over the 7-day period. The frequency of use of all the needleless IV access devices evaluated in this study was within the manufacturers' guidelines except for the QS, which the manufacturers recommend should be used only for up to 100 activations. Indeed, there are no national or international guidelines on the frequency of device replacement beyond changing no more frequently than every 72 hours and to follow manufacturers' recommendations.³

Collection and Processing of Microbiological Specimens

All saline eluates from each 24-hour period were collected and pooled in a sterile container containing an equal volume (130 mL) of double-strength Dey and Engley neutralizing broth and stored at 4°C. The

neutralizer had been evaluated previously when it was confirmed that it nullified the effect of silver and was noninhibitory against *S. aureus* NCTC 6571 (AL Casey et al, unpublished data). Each 24-hour pooled eluate was filtered through a 0.45- μ m membrane filter under vacuum. The filter papers were aseptically transferred to individual chromogenic agar plates (chromID *S. aureus* [Biomerieux]). Each administration set male luer tip used to access the needleless IV access devices was imprinted onto a chromogenic agar plate once, following completion of use. All plates were incubated in air for 48 hours at 37°C, and the number of CFU was determined.

Statistics

The Kruskal-Wallis test was used to analyze CFU counts. If $P < .05$, the Dunn posttest was performed on each pair of connectors being compared. Analysis of the number of administration sets contaminated with *S. aureus* was performed with the Fisher exact test, applying a Bonferroni correction for pairwise comparisons. Comparison of the 2 decontamination regimens was undertaken using the Mann-Whitney test.

RESULTS

Microbial Ingress Through the Needleless IV Access Devices

All negative control devices had associated negative cultures. The median CFU counts in the eluate from positive control were 282, 218.5, 379, 742.5, 1001, 663, and 864.5 on days 1 to 7, respectively. The median CFU counts in the daily pooled saline eluate for each of the devices over the 7-day period with the 5-second cleaning regimen are shown in Figure 3. Significant pairwise comparisons of the devices across the 7 days of use are given in Table 1. Following 7 days of use, significantly fewer microorganisms were detected in the eluates collected from the MG and MP compared with the BN, MC, and VL. In addition, fewer microorganisms were detected in the eluates collected from the MP than the CL.

The median CFU counts in the daily pooled saline eluate for each of the devices over the 7-day period with the 15-second cleaning regimen are given in Figure 4. Significant pairwise comparisons of the devices using this extended cleaning regimen across the 7 days of use are shown in Table 2. Following 7 days of use, significantly fewer microorganisms were detected in the eluates collected from the CS, MG, and MP compared with the VL. In addition, fewer microorganisms were detected in the eluates collected from the MG and MP than the BN, MC, and QS.

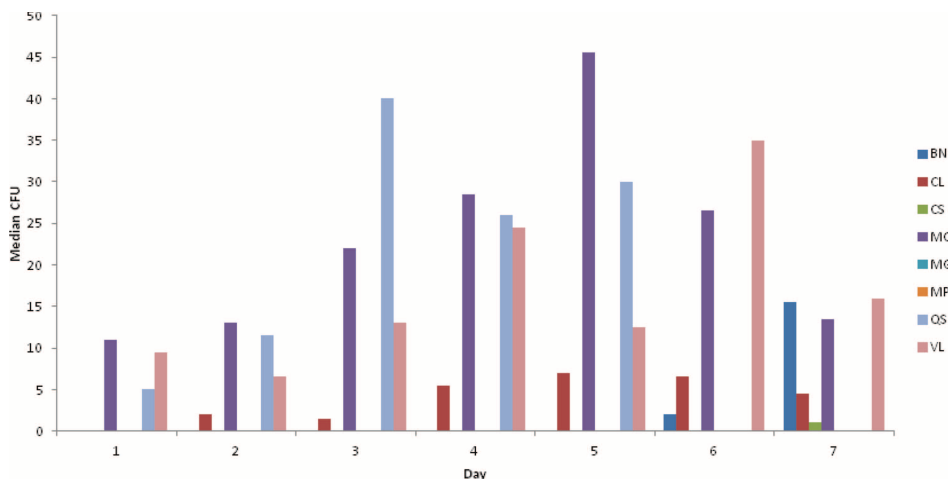


Figure 3 Median CFU of *Staphylococcus aureus* recovered from each daily saline eluate of 8 different needleless IV access devices over 7 days of simulated clinical use with a 5-second cleaning regimen (n = 12). Abbreviations: BN, Bionector; CFU, colony-forming unit; CL, Clave; CS, CareSite; IV, intravenous; MC, MicroClave Clear; MG, MaxGuard; MP, MaxPlus Clear; QS, Q-Syte; VL, V-Link.

Overall, 225 out of 357 (63%) administration set male luer lockers were contaminated with *S. aureus* NCTC 6571 regardless of cleaning regimen. Significantly fewer administration sets were contaminated with *S. aureus* in the CS (0%), MG (0%), and MP (0%) groups than the

MC (39.6%) (all $P < .0001$), CL (20.8%) (all $P = .0006$), BN (29.2%) (all $P < .0001$), and VL (41.7%) (all $P < .0001$) groups. Furthermore, significantly fewer administration sets were contaminated in the QS (0%) group than the MC ($P = .0003$) and VL ($P < .0001$)

TABLE 1

Significant Differences Among 8 Different Needleless IV Access Devices in Regard to the Number of CFU of *S. aureus* Recovered From the Saline Eluate Over 7 Days of Use With a 5-Second Cleaning Regimen (n = 12)

| Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|-------------------------|---------|---------|---------|---------|---------|---------|---------|
| Significant differences | BN < QS | BN < MC | BN < MC | BN < MC | BN < MC | CS < MC | MG < BN |
| | BN < VL | BN < QS | BN < QS | BN < VL | CS < CL | CS < VL | MG < MC |
| | CL < VL | BN < VL | BN < VL | CS < MC | CS < MC | MG < MC | MG < VL |
| | CS < MC | CS < MC | CS < MC | CS < QS | MG < CL | MG < VL | MP < BN |
| | CS < QS | CS < QS | CS < QS | CS < VL | MG < MC | MP < MC | MP < CL |
| | CS < VL | CS < VL | CS < VL | MG < MC | MG < VL | MP < VL | MP < MC |
| | MG < VL | MG < MC | MG < MC | MG < QS | MP < MC | | MP < VL |
| | MP < MC | MG < QS | MG < QS | MG < VL | | | |
| | MP < QS | MG < VL | MG < VL | MP < MC | | | |
| | MP < VL | MP < MC | MP < MC | MP < QS | | | |
| | | MP < QS | MP < QS | MP < VL | | | |
| | | MP < VL | MP < VL | | | | |

Kruskal-Wallis test was $P < .0001$; therefore, the Dunn posttest was performed on each pairwise comparison. Significant differences were classified as those where $P < .05$. A < B indicates that needleless IV access device A resulted in a significantly lower CFU count than needleless IV access device B.

Abbreviations: IV, intravenous; CFU, colony-forming unit.

**TABLE 2**

Significant Differences Among 8 Different Needleless IV Access Devices in Regard to the Number of CFU of *S. aureus* Recovered From the Saline Eluate Over 7 Days of Use With a 15-Second Cleaning Regimen (n = 12)

| Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|-------------------------|---------|---------|---------|---------|---------|---------|---------|
| Significant differences | BN < QS | CS < QS | CL < VL | CL < VL | CS < BN | CS < BN | CS < VL |
| | CL < QS | CS < VL | CS < VL | CS < BN | CS < VL | CS < VL | MG < BN |
| | CL < VL | MG < QS | CS < QS | CS < VL | MG < BN | MG < BN | MG < MC |
| | CS < QS | MG < VL | MG < QS | MG < BN | MG < MC | MG < VL | MG < QS |
| | CS < VL | MP < QS | MG < VL | MG < QS | MG < QS | MP < BN | MG < VL |
| | MC < QS | MP < VL | MP < QS | MG < VL | MP < BN | MP < VL | MP < BN |
| | MC < VL | | MP < VL | MP < BN | MP < MC | QS < VL | MP < MC |
| | MG < QS | | | MP < QS | MP < QS | | MP < QS |
| | MG < VL | | | MP < VL | | | MP < VL |
| | MP < QS | | | | | | |
| | MP < VL | | | | | | |

Kruskal-Wallis test was $P < .0001$; therefore, the Dunn posttest was performed on each pairwise comparison. Significant differences were classified as those whereby $P < .05$. A < B indicates that needleless IV access device A resulted in a significantly lower CFU count than needleless IV access device B.

Abbreviations: IV, intravenous; CFU, colony-forming unit.

groups. Some of the QS devices could not be activated before the 7-day time point had been reached. This was due to the inability to insert a male luer into the device's injection site after they had been used for various time periods.

Overall, there was no significant difference between the median number of CFU recovered following a 5- and 15-second decontamination regimen (64.74 vs 96.1 CFU, respectively, $P = .84$).

CONCLUSIONS

This study was undertaken to investigate potential differences in infection risk associated with needleless IV access devices under controlled laboratory conditions and to negate some of the variables in previously reported clinical observations. The devices selected for evaluation are frequently used in clinical practice and represent the spectrum of types available. The needleless IV access devices were evaluated in line with US Food and Drug Administration (FDA) microbial ingress testing recommendations.^{7,8} Only *S. aureus* was tested because of the complexity of the investigation undertaken in this

study. One additional element in this study was added to the FDA test. This involved blood aspiration through the devices that mimicked blood discard and sampling, commonly carried out in clinical practice.

In this laboratory-based study, differences in the number of CFU of *S. aureus* detected in the saline eluates collected after passing through the various needleless IV access devices were demonstrated. The positive-displacement mechanical valves—CS, MG, and MP—were associated with ingress of significantly fewer microorganisms compared with several of the other devices tested. This may have been related to the design and, in particular, to the topography of the injection sites of these devices, which in turn may have influenced the efficacy of the decontamination process.

The positive displacement devices were correspondingly associated with significantly fewer contaminated administration set male luers than the other devices tested, which supports the conjecture that the injection site designs may be easier to decontaminate.

Interestingly, despite decontamination of the needleless IV access devices before attachment of administration sets, more than half of all the male luers were contaminated with *S. aureus* following insertion into

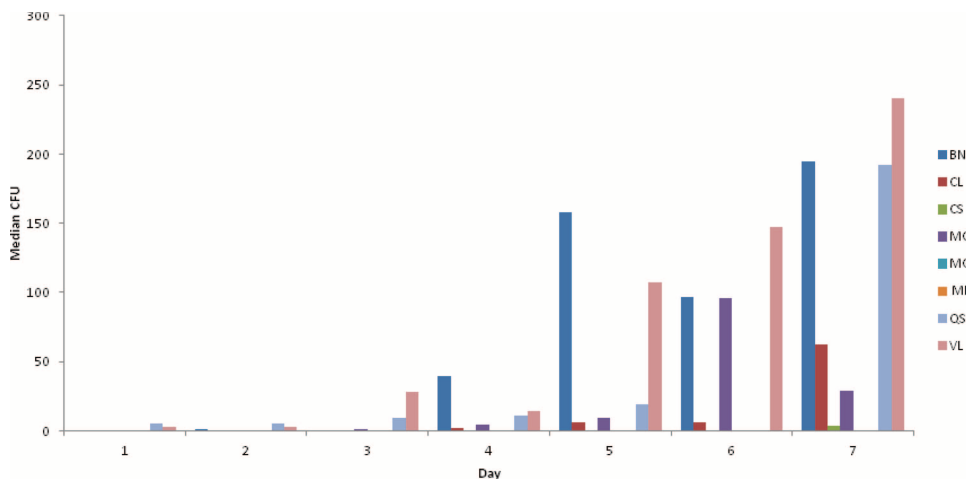


Figure 4 Median CFU of *Staphylococcus aureus* recovered from each daily saline eluate of 8 different needleless IV access devices over 7 days of simulated clinical use with a 15-second cleaning regimen (n = 12). Abbreviations: BN, Bionector; CFU, colony-forming unit; CL, Clave; CS, CareSite; IV, intravenous; MC, MicroClave Clear; MG, MaxGuard; MP, MaxPlus Clear; QS, Q-Syte; VL, V-Link.

the devices. This again may reflect microbial contamination of elements of the needleless IV access devices, which are not easily decontaminated. These findings suggest that the repeated insertion of the same male luer, such as associated with an administration set into the injection site, should be discouraged in clinical practice as microorganisms from a contaminated male luer subsequently may be introduced into a sterile needleless IV access device.

The differences in median CFU counts recovered from the eluates from the needleless IV access devices may also be related to a number of other factors in addition to cleaning efficacy of the injection sites, including the priming volume. Significantly fewer CFU were recovered from needleless IV access devices with relatively large priming volumes, such as MP, than those with small priming volumes, including the BN. However, there is only limited information on the effect on infection risk of laminar versus turbulent flow in needleless IV access devices and leakage of fluid into interstitial space (outside of the normal fluid pathway).⁹ The authors did not investigate this specific factor in the current study.

The results may also reflect differences in pressure and mechanical technology. It has been suggested that negative- and positive-displacement mechanical needleless IV access devices, because of their complex design, may be susceptible to contamination.² However, this proposal is based on retrospective observational clinical data in which staff training and device cleaning was not fully defined. In comparison, in a recent observational study, rates of bloodstream infection were found to remain at zero regardless of whether a neutral- or positive-displacement valve was used.¹⁰ The replacement of a neutral-displacement valve with a positive-displacement device (the MP) has also been reported to result in a reduction in central line-associated bloodstream infections in pediatric cardiac intensive care unit patients.¹¹

In line with these observations, in this controlled laboratory study, in which a strict defined cleaning regimen was employed, the positive-displacement devices were not associated with increased CFU numbers. Previous in vitro studies have also demonstrated a significantly reduced ingress of bacteria through specific types of devices.¹²⁻¹⁴ However, it is difficult to make direct comparisons of results because testing conditions were different from those used in our study. Indeed, there is great variance in methodology among in vitro microbial ingress studies. In comparison with our evaluation, some of these previous studies have tested the devices for shorter periods¹²⁻¹⁴; used a higher bacterial inoculum¹²⁻¹⁴; conducted fewer activations^{12,14}; inoculated with microorganisms fewer times^{12,14}; and omitted the decontamination process.¹²⁻¹³ We designed this study to encompass what we considered was a realistic clinical scenario following, where available, the manufacturer's guidance for device use.

In this current study, the devices were also evaluated following either a 5- or 15-second cleaning of the injection site. Manufacturers' advice on decontamination of needleless IV access devices is variable. All the manufacturers of the devices tested in this study recommend decontamination with an appropriate antiseptic before each access. However, only 4 of the 8 product instructions for use state that the user should allow the antiseptic to dry, 3 recommend decontamination of the device following each use, and 2 suggest that the devices should be cleaned for at least 15 seconds. The devices in this study were evaluated to encompass all the defined instructions for use. For example, all devices were decontaminated before and following each set of activations; the antiseptic was allowed to dry; and the authors tested devices that were decontaminated for 15 seconds. This follows the new epic3 national evidence-based guidelines for preventing health care-associated infections in NHS

hospitals in England, which have recommended that catheter hubs be cleaned for a minimum of 15 seconds and allowed to dry before accessing the system.¹ There is conflicting opinion regarding whether a 5-second alcohol scrub of needleless IV access device ports is sufficient.¹⁵⁻¹⁸ In this study, there were significant differences between the needleless IV access devices with regard to microbial ingress following both cleaning schedules. Indeed, overall there was no significant difference between the median number of CFU recovered following a 5- and 15-second decontamination regimen. This may suggest that for certain devices even an extended cleaning regimen such as 15 seconds may still be insufficient to remove microbial contaminants from the injection ports, possibly because of the topography of the injection port. This also suggests that 5 seconds' decontamination is sufficient for certain devices with an injection site topography conducive to decontamination, which is supported by previous findings.¹⁷

Concern has also been raised as to whether in clinical practice these devices are cleaned adequately, with variable approaches taken and limited supporting evidence.² In vitro it has been demonstrated that the addition of chlorhexidine to alcohol wipes provides residual antimicrobial activity on needleless IV access devices for up to 24 hours.¹⁹ Furthermore, the recent epic3 guidelines recommend 2% chlorhexidine gluconate in 70% isopropyl alcohol for decontamination of access ports.¹ The efficacy of alcohol-impregnated injection-site protectors also has been demonstrated both in vitro and in vivo, albeit in combination with implementation of a neutral displacement device.²⁰ There are also limited published data on the efficacy of silver impregnated/coated needleless IV access devices. A recent in vitro study demonstrated that following blood exposure, the antimicrobial activity of 3 silver-coated or -impregnated devices was significantly reduced.²¹ Interestingly, a silver-impregnated device evaluated in this study (MG) did not demonstrate superior efficacy when compared with its identical but nonantimicrobial counterpart (MP). On the basis of this evidence, it may be prudent to consider the use of chlorhexidine-alcohol wipes or antiseptic-impregnated injection-site protectors in addition to rather than as a replacement for standard cleaning.

The significance of the findings in this controlled laboratory study needs to be elucidated in the clinical scenario also under defined conditions, including the use of a correct clamping procedure and a clearly defined decontamination process applied before and after each access. Because injection port designs that are conducive to optimal decontamination may be beneficial, a study on the topography of needleless IV access devices before and after clinical use needs to be considered and the findings correlated to product design and clinical performance.

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REFERENCES

1. Loveday HP, Wilson JA, Pratt RJ, et al. epic3: national evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. *J Hosp Infect.* 2014;86(suppl 1):S1-S70.
2. Jarvis WR, Murphy C, Hall KK, et al. Healthcare-associated bloodstream infections associated with negative- or positive-pressure or displacement mechanical valve needleless connectors. *Clin Infect Dis.* 2009;49(12):1821-1827.
3. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis.* 2011;52(9):e162-e193.
4. Marshall J, Mermel LA, Classen D, et al. Strategies to prevent central line-associated bloodstream infections in acute care hospitals. *Infect Control Hosp Epidemiol.* 2008;29(suppl 1):S22-S30.
5. Casey AL, Worthington T, Lambert PA, Quinn D, Faroqui MH, Elliott TS. A randomized, prospective clinical trial to assess the potential infection risk associated with the PosiFlow needleless connector. *J Hosp Infect.* 2003;54(4):288-293.
6. Casey AL, Burnell S, Whinn H, Worthington T, Faroqui MH, Elliott TS. A prospective clinical trial to evaluate the microbial barrier of a needleless connector. *J Hosp Infect.* 2007;65(3):212-218.
7. Anonymous. Guidance for industry and FDA reviewers on the guidance on premarket notifications for intravascular administration sets. 2005.
8. Anonymous. Guidance for industry and FDA reviewers on the guidance on premarket notifications for intravascular administration sets. 2008. <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070850.pdf>. Accessed November 14, 2014.
9. Hadaway L, Richardson D. Needleless connectors: a primer on terminology. *J Infus Nurs.* 2010;33(1):3-11.
10. Logan R. Neutral displacement intravenous connectors: evaluating new technology. *JAVA.* 2013;18(1):31-36.
11. Costello JM, Forbes Morrow D, Graham DA, Potter-Bynoe G, Sandora TJ, Laussen PC. Systematic intervention to reduce central line-associated bloodstream infection rates in a pediatric cardiac intensive care unit. *Pediatrics.* 2008;121(5):915-923.
12. Ryder M, Fisher S, Hamilton G, Hamilton M, James G. Bacterial transfer through needlefree connectors: comparison of nine different devices. Presented as a poster at: Society for Healthcare Epidemiology of America conference; 2007; Baltimore, MD.
13. Ryder M, James GA, deLancey Pulcini E, Bickle L, Parker AE. Differences in bacterial transfer and fluid path colonization through needlefree connector-catheter systems in vitro. Presented as a poster at: The Society for Healthcare Epidemiology of America conference; 2011; Dallas, TX.
14. Chernecky C, Waller J. Comparative evaluation of five needleless intravenous connectors. *J Adv Nurs.* 2011;67(7):1601-1613.
15. Menyhay SZ, Maki DG. Disinfection of needleless catheter connectors and access ports with alcohol may not prevent microbial entry: the promise of a novel antiseptic-barrier cap. *Infect Control Hosp Epidemiol.* 2006;27(1):23-27.
16. Smith JS, Irwin G, Viney M, et al. Optimal disinfection times for needleless intravenous connectors. *JAVA.* 2012;17(3):137-143.

17. Rupp ME, Yu S, Huerta T, et al. Adequate disinfection of a split-septum needleless intravascular connector with a 5-second alcohol scrub. *Infect Control Hosp Epidemiol.* 2012;33(7):661-665.
18. Simmons S, Bryson C, Porter S. "Scrub the hub": cleaning duration and reduction in bacterial load on central venous catheters. *Crit Care Nurs Q.* 2011;34(1):31-35.
19. Hong H, Forbes Morrow D, Sandora TJ, Priebe GP. Disinfection of needleless connectors with chlorhexidine-alcohol provides long-lasting residual disinfectant activity. *Am J Infect Control.* 2013;41(8):e77-e79.
20. Sweet MA, Cumpston A, Briggs F, Craig M, Hamadani M. Impact of alcohol-impregnated port protectors and needleless neutral-pressure connectors on central line-associated bloodstream infections and contamination of blood cultures in an inpatient oncology unit. *Am J Infect Control.* 2012;40(10):931-934.
21. Chernecky CC, Waller JL, Jarvis WR. In vitro study assessing the antibacterial activity of three silver impregnated/coated mechanical valve needleless connectors after blood exposure. *Am J Infect Control.* 2013;41(3):278-280.