ICU MEDICAL SUPPORTING INFORMATION

Nuitiv™ Clear Needlefree Connector Microbial Ingress

Report of a study commissioned by ICU Medical, Inc. and conducted by Alcami

Background

Studies have found that the incidence rate of central line-associated bloodstream infections in ICUs internationally can range between 0.8 to 4.1 per 1,000 central line days.[1] Needleless devices such as needlefree connectors may increase the patient's risk of bloodstream infections because they facilitate bidirectional fluid flow and have features that may allow entry of microorganisms into the sterile fluid path.[2] Bacterial ingress testing, which is recommended for needleless devices by the US Food and Drug Administration[2], is the evaluation of the ability of a medical device to resist or inhibit the transfer of infectious microorganisms under repeated simulated use conditions.[3]

The Nuitiv Clear needlefree connector features a split septum design that minimizes entry points for microorganisms, a straight fluid path for efficient clearing of medication, blood, and residuals, and a smooth, swabbable surface for disinfection.

Introduction

The purpose of this study was to evaluate the microbial ingress performance of the Nuitiv Clear needlefree connector using an inoculation and activation procedure over a 7-day period.

This supporting information describes the methods, including the types of challenge microorganisms used, the microbial recovery methods, sample size, controls, procedures, including the inoculation methods, the environmental conditions, the validation methods, and the rationales used for these choices.

Methods

Organisms (Four Bacterial Strains)

Organisms chosen for this study include 2 gram-negative and 2 gram-positive organisms, which represent normal microbiological flora found in a clinical setting. The target concentration of 1-5 x 10^3 represents a higher-than-expected microbial contamination load during worst-case clinical use.

Staphylococcus aureus (ATCC 6538)

Staphylococcus epidermidis (ATCC 12228)

Pseudomonas aeruginosa (ATCC 9027)

Klebsiella pneumoniae (ATCC 4352)

Microbial Recovery Study

The microbial recovery study is designed to demonstrate the suitability of the test method by showing microorganisms can be successfully recovered by following the test method in the protocol. This phase of the study was done following the methods below.

The Nuitiv Clear septum was inoculated with an appropriate volume of inoculum to yield one 1-5 x 10^3 colony-forming units (CFUs) of each test organism and allowed to dry for 1 minute at ambient conditions. After drying, the device was placed in 10 mL

of 0.9% sterile saline solution and was mixed using a vortex mixer. The positive control was prepared by inoculating a 10 mL volume of 0.9% saline solution with the same inoculum volume used to inoculate the device, followed by 1 mL aliquots being plated to trypticase soy agar (TSA) and incubated at 30–35°C for 1–2 days.

After incubation, the lab performed the colony counts to determine the percent recovery as

$$\text{Percent recovery} = \frac{\text{CFU recovery fluid}}{\text{CFU inoculum count}} \times 100$$

The acceptance criteria of the percent recovery must be greater than 70%. As seen in Table 1 below, all microbial recovery testing meets this criterion.

Table 1. Microbial Recovery Studies Results

Test Organism	Recovery (CFU/Device)	Inoculum Count (CFU)	Percent Recovery	Meets Criteria
Staphylococcus aureus	2.20×10^3	1.73×10^3	127%	Yes
Staphylococcus epidermidis	2.29×10^4	2.41×10^4	121%	No, S. epidermis concentration 1 log higher than intended. Retested.
Pseudomonas aeruginosa	1.56×10^3	1.41×10^3	111%	Yes
Klebsiella pneumoniae	2.36×10^3	2.21×10^3	107%	Yes
Staphylococcus epidermidis	2.12×10^3	1.94×10^3	109%	Yes

Sample Size

The study evaluated 6 Nuitiv Clear needlefree connector replicates that were inoculated with 4 separate organisms and accessed 35 times.

Procedure

The Nuitiv Clear septum was inoculated in duplicate with an appropriate volume of inoculum to yield one 1-5 x 10^3 CFUs of each test organism and allowed to dry for 1 minute at ambient conditions. The septa were then wiped vigorously in a circular motion for not less than 3 seconds with a 70% isopropyl alcohol (IPA) prep pad and allowed to dry. The device was activated using a syringe with a 10 mL 0.9% sterile saline solution. Fluid was collected in a filter funnel through a 0.45-micron cellulose nitrate filter, rinsed with 100 mL of sterile 0.9% saline solution, and transferred to a plate of TSA. TSA plates were then incubated at 30–35°C for 2–3 days. This process was repeated 840 times (120 activations per day, 20 activations for 6 replicates per challenge organism for 7 days).

Positive and negative controls were performed on day 1 of testing. Positive controls used the same testing protocol but without the 70% IPA disinfection step.

The acceptance criteria of the bacterial ingress study are the following. Negative controls must be negative for the challenge organisms. Positive controls must be representative of the test setup.

Results

Table 2. Staphylococcus Aureus Microbial Ingress Results

Activation		Replicate (CFU/filter)						Inoculum Verification (CFU/Device)
		1	2	3	4	5	6	
Day 1	1–5	0	0	0	0	0	0	1.5 x 10^3 CFU/device
Day 2	6–10	0	0	0	0	0	0	2.1 x 10^3 CFU/device
Day 3	11–15	0	0	0	0	0	0	1.8 x 10^3 CFU/device
Day 4	16–20	0	0	0	0	0	0	1.2 x 10^3 CFU/device
Day 5	21–25	0	0	0	0	0	0	3.2 x 10^3 CFU/device
Day 6	26–30	0	0	0	0	0	0	2.2 x 10^3 CFU/device
Day 7	31–35	0	0	0	0	0	0	3.4 x 10^3 CFU/device
Positive Control Replicate 1 (CFU/Filter)								1 CFU/filter
Positive Control Replicate 2 (CFU/Filter)								1 CFU/filter

Table 3. Staphylococcus Epidermidis Microbial Ingress Results

Activation		Replicate (CFU/Filter)						Inoculum Verification (CFU/Device)
		1	2	3	4	5	6	
Day 1	1–5	0	0	0	0	0	0	2.2 x 10^3 CFU/device
Day 2	6–10	0	0	0	0	0	0	2.3 x 10^3 CFU/device
Day 3	11–15	0	0	0	0	0	0	2.4 x 10^3 CFU/device
Day 4	16–20	0	0	0	0	0	0	2.7 x 10^3 CFU/device
Day 5	21–25	0	0	0	0	0	0	3.7 x 10^3 CFU/device
Day 6	26–30	0	0	0	0	0	0	1.9 x 10^3 CFU/device
Day 7	31–35	0	0	0	0	0	0	2.9 x 10^3 CFU/device
Positive Control Replicate 1 (CFU/Filter)								8 CFU/filter
Positive Control Replicate 2 (CFU/Filter)								301 CFU/filter

Table 4. Pseudomonas aeruginosa Microbial Ingress Results

Activation		Replicate (CFU/Filter)						Inoculum Verification (CFU/Device)
		1	2	3	4	5	6	
Day 1	1–5	0	0	0	0	0	0	1.6 x 10^3 CFU/device
Day 2	6–10	0	0	0	0	0	0	1.8 x 10^3 CFU/device
Day 3	11–15	0	0	0	0	0	0	2.0 x 10^3 CFU/device
Day 4	16–20	0	0	0	0	0	0	1.7 x 10^3 CFU/device
Day 5	21–25	0	0	0	0	0	0	1.8 x 10^3 CFU/device
Day 6	26–30	0	0	0	0	0	0	2.6 x 10^3 CFU/device
Day 7	31–35	0	0	0	0	0	0	1.9 x 10^3 CFU/device
Positive Control Replicate 1 (CFU/Filter)								88 CUF/filter
Positive Control Replicate 2 (CFU/Filter)								46 CFU/filter

Table 5. Klebsiella Pneumoniae Microbial Ingress Results

Activation		Replicate (CFU/Filter)						Inoculum Verification (CFU/Device)
		1	2	3	4	5	6	
Day 1	1–5	0	0	0	0	0	0	3.7 x 10^3 CFU/device
Day 2	6–10	0	0	0	0	0	0	2.3 x 10^3 CFU/device
Day 3	11–15	0	0	0	0	0	0	2.1 x 10^3 CFU/device
Day 4	16–20	0	0	0	0	0	0	2.1 x 10^3 CFU/device
Day 5	21–25	0	0	0	0	0	0	2.3 x 10^3 CFU/device
Day 6	26–30	0	0	0	0	0	0	2.9 x 10^3 CFU/device
Day 7	31–35	0	0	0	0	0	0	2.5 x 10^3 CFU/device
Positive Control Replicate 1 (CFU/Filter)								83 CFU/filter
Positive Control Replicate 2 (CFU/Filter)								79 CFU/filter

Conclusion

The Nuitiv Clear needlefree connector passed the microbial ingress test, and no contamination was found after repeated use, inoculation, and disinfection with 70% IPA. Therefore, the Nuitiv Clear needlefree connector is suitable for use for 7 days on the appropriate vascular access or infusion device.

References

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