An extended use microbial challenge of NeutrArt® Needle-free Neutral Valve

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Introduction

Central-venous-catheter-related bloodstream infections (CRBSIs) are an important cause of hospital-acquired infections associated with morbidity, mortality, and cost. Amongst, different measures implemented to reduce the risk for CRBSI, preventive strategies based on inhibiting micro-organisms originating from the skin or catheter hub from adhering to the catheter involve utilization of needle-free valves (also called needleless connectors). Numerous elements have been ascribed to the level of the infection risk associated with needle-free connectors and incorporate the adequacy of sanitization of the infusion ports. It has additionally been proposed that surface disinfection of needle-free connectors is not intuitive which may lead to non-compliance. In this study, the microbial barrier properties of the NeutrArt® split septum needle-free valve (NFV) was demonstrated in several microbial challenges. An independent test laboratory was commissioned to conduct the study[i].

Materials and Methods

Table 1. Number of devices used vs organisms

Microorganism	Test	Positive control	Negative control
Staphylococcus epidermidis, ATCC #12228	6	3	3
Staphylococcus aureaus, ATCC #6538	6	3	3
Klebsiella pneumoniae, ATCC #4352	6	3	3
Pseudomonas aeruginosa, ATCC #15442	6	3	3
Candida Albicana, ATCC #10231	6	3	3
Escherichia coli, ATCC #11229	6	3	3
Candida Glabrata, ATCC #60406	6	3	3

Actuation of each test device was performed each day, for 7 consecutive days, for each microorganism. Each actuation included the following steps in this order: disinfection, inoculation, disinfection, access and flush. Between testing days, devices were stored in sterile 50ml conical tubes at 36 ± 1°C. On the final day of testing, 1 additional actuation was performed, as “Final Actuation”.

Each test device was swabbed with a fresh 70% IPA + 2% chlorhexidine prep pad using a circular motion on and around the septum of the valve for 25 – 30 seconds for disinfection. Following disinfection, each device was allowed to dry ambiently for ≥ 1 minute.

A 0.01 ml aliquot of the prepared inoculum was placed directly onto the septum of the valve and was allowed to dry ambiently for ≥ 1 minute. Following the inoculation dry time, the disinfection was performed a second time.

A sterile syringe filled with 10 ml of sterile PBS was connected to the valve via the luer lock.

The full volume in the syringe was flushed through the valve. On day 7 of actuations, following completion of the 5 actuations, 1 additional actuation was performed for each device. Each test device was swabbed with a fresh 70% IPA prep pad using a circular motion on and around the septum of the valve for 25 – 30 seconds. Following disinfection each device was allowed to dry ambiently for ≥ 1 minute. A sterile syringe containing 10 ml of Soybean Casein Digest broth with 5% fetal bovine serum was connected to the valve via the luer lock. The full volume in the syringe was

flushed through the valve and was filtered through a 0.45 µm membrane filter. The filter was then placed on sterile solidified growth agar and incubated at 36 ± 1°C for 5 – 7 days.

Three positive and three negative control devices were included for each test microorganism. Both positive and negative controls were treated in the same manner as test devices, however, no disinfection was performed on positive controls following inoculation and no inoculation was performed on negative controls. Actuation of the control devices was performed 5 times each day, for 7 consecutive days, for each microorganism. On the final day of testing, 1 additional final actuation was performed.

Sterility and Viability controls were performed on each day of testing, for the media used that day.

After incubation, number of organisms on the membranes for each treatment length and challenge organism was measured by viable count.

Table 2. Inoculum enumeration results for testing conducted against Test Microorganisms

Microorganism	CFU/ device inoculum	CFU / Device Recovered		
		Test	Positive control	Negative control
S. epidermidis	1E+03	0.00E+00	4.5E+03	0.00E+00
S. aureaus	1E+03	0.00E+00	3.8E+03	0.00E+00
K. pneumoniae	1E+03	0.00E+00	4.9E+03	0.00E+00
P. aeruginosa	1E+03	0.00E+00	3.3E+03	0.00E+00
C. albicans	1E+03	0.00E+00	4.4E+03	0.00E+00
E. coli	1E+03	0.00E+00	4.3E+03	0.00E+00
C. glabrata	1E+03	0.00E+00	5.4E+03	0.00E+00

Results and Discussion

Test samples were subjected to a use simulation which followed the FDA guidance requirements.[ii]

All positive controls had positive assays confirming the viability of the challenge organisms for the duration of each test period. The total mean log10 CFU per untreated NFV internal surface effluent for all experiments was ≥3. These results provided evidence that a single activation of the NFV valve is sufficient to transfer viable cells from the external septum surface of the NFV into the lumen of the device.

6 non-inoculated, sterile NFVs (negative control) were processed to recover and quantify any organisms on NFV effluent, using the standard recovery protocol. All negative controls had negative assays confirming the absence of the organism in samples not inoculated with challenge organism. (Table 2). This also proved the sterility of the methodology.

No bacterial growth was detected on all connectors tested for the 7 microorganisms studied.

The media used in the study was confirmed to be sterile. The viability control for the test microorganisms was pure and demonstrated adequate growth of the target microorganism.

Conclusion:

No bacterial growth was observed for the test valves under conditions described above for a period up to seven days. In clinical use, NeutrArt® needle-free valve prevent contamination of the fluid path by microorganisms. Microbial Ingress. NeutrArt® needle-free neutral valve when used with an adequate disinfection procedure, maintains its microbial barrier properties over a 7-day period and can be used to prevent catheter hub infection.

[i] Report no: YUEF-İKTAL 0169 – 24 July 2020

ii Guidance for Industry and FDA Staff: Intravascular Administration Sets Premarket Notification Submission [510(k)]. 2008