

# FINAL FDA SAFETY AND EFFICACY TEST – MICROBIAL BARRIER PERFORMANCE

## The new “Swabbable” *InVision-Plus*® Neutral Displacement I.V. Connector System

### 96-Hour Comparative Microbial Barrier Performance Study

Food & Drug Administration (FDA) 510(k) Pre-market Notification Test

Conducted by Nelson Laboratories, Inc., Salt Lake City, UT

New standards and regulatory legislation in I.V. therapy are being directed towards adopting needle-free intermittent injection ports in the workplace such as RyMed Technologies’ new “Swabbable” *InVision-Plus*® Neutral Displacement I.V. Connector System. The clinical purpose for this transition to safer injection ports is to eliminate accidental needle-stick injuries as well as the transmission of blood-borne diseases from patients to healthcare workers. The clinical purpose for RyMed Technologies new “Double Microbial Barrier” internal design is to maintain an effective barrier from pathogen ingress during repeated exposure to microorganisms over an extended period of time.

To prove the safety and efficacy of this new “Double Barrier” design, an extensive microbial challenge study was conducted at Nelson Laboratories, Inc., Salt Lake City, UT to examine the performance of the *InVision-Plus*® System over a 96 hour period of time. The test protocol was developed by Nelson Laboratories, reviewed and approved by the FDA committee prior to the start of the study. The study was conducted under the Good Laboratory Practices (GLP) guidelines of the FDA (21 CFR Part 58). Final test results were filed with the FDA in RyMed Technologies 510(k) pre-market notification application. All raw data are archived at Nelson Laboratories under Date File Number 143165. This summary report is an overview of the study procedures and its results.

## PROCEDURES

The study consisted of repeated contamination of the external septa of the test valves using the common hospital bacterial contaminant *Staphylococcus aureus* and intermittent infusions over a 96-hour period. *Staphylococcus aureus* is useful as a “marker” to quantify contamination levels on the valves. The valves were challenged (average of **7.1 x 10<sup>6</sup> colony-forming units (CFU’s) per mL**) with bacteria by touching each valve with a contaminated gloved finger. This provided a bacterial challenge that is significantly greater than seen in actual use situations. The purpose of this test was to contaminate each valve with an extremely high CFU level of contamination in order to overly-stress the valves and to force a failure. It is by this means that one can truly evaluate how resistant a particular valve design is to downstream contamination. Also, the swabbing procedure was limited to three circular motions in less than 8 seconds; well below recommended hospital protocol. RyMed Technologies believed that this severe challenge would demonstrate their unique “Double Microbial Barrier” design to be a very effective barrier to pathogen ingress under an abnormal clinical environment over an extended period of time.

The *InVision-Plus*® Systems were configured to permit intermittent infusion, capture, and incubation of growth media passed through the valves. The simulated infusions were performed over 96-hours under simulated use conditions. Each infusion consisted of:

- 1) Swabbing the septa’s with 70% isopropyl alcohol (IPA), let dry;
- 2) Administration of the soybean casein digest growth medium and collection of any bacterial contaminant present;
- 3) Flush each test valve with 0.9% saline solution;
- 4) Heparin flush to “lock” the device, and;
- 5) Re-contaminate each valve septum with the bacterium challenge and let sit until the next scheduled simulated infusion cycle.

Step 1 was omitted at the beginning of the test to obtain a negative control. All fluids from each infusion were captured, filtered, and incubated at 30C-35C for 7 days to detect the presence of microorganisms. A total of thirty-three (33) *InVision-Plus*® Injection Ports were evaluated.

**Septum Positive Control:** The septum control was performed once each day of testing to demonstrate the levels of contamination transferred to the test devices.

**Bio-burden Control:** A control was performed to demonstrate the level of survival of *Staphylococcus aureus* on the septa over time. Six (6) *InVision-Plus*® devices were contaminated per protocol. After four hours, the bio-burden on three (3) of each valve was determined. After eight (8) hours, the bio-burden on the three (3) remaining valves was determined.

**Positive Control Units:** The positive control units consisted of three (3) *InVision-Plus*® devices. These were contaminated, but not swabbed with 70% isopropyl alcohol. Positive control units were then tested as normal units on day five.

**Negative Control Units:** A negative control was performed to demonstrate that the test valves were sterile at the start of the study.

## 96 HOUR MICROBIAL BARRIER PERFORMANCE RESULTS:

The total CFU of *Staphylococcus aureus* organisms detected from the *InVision-Plus® Injection Ports* after repeated contamination, alcohol swabbing, and simulated infusion was 237 CFU's out of a possible 75,000 CFU's, or 99.7% effective. The *InVision-Plus® Injection Ports*' new "Double Microbial Barrier" design demonstrated to be an effective microbial ingress prevention barrier.

The ability of the new "Swabbable" *InVision-Plus® Neutral Displacement I.V. Connector System* by RyMed Technologies, Inc. to resist pathogen ingress and migration through the "Double Microbial Barrier" design when severely challenged is clearly demonstrated in the following table:

	RyMed Technologies <i>InVision-Plus®</i>	Positive Control	Negative Control
Total test sample size	33	3/3	0/33
Total CFU's per valve over the 96-hour test period	75,000		
Total CFU's detected over the 96-hour test period	237		
Average CFU's per valve foreach simulated infusion	6,800		
Average CFU's per valvedetected over each infusion	22		
Percentage of the total CFUcontamination NOT allowed passage through the valvesover the 96-hour test period	99.70%		

### CONCLUSIONS

The Nelson Laboratories test data submitted to the FDA by RyMed Technologies, Inc. clearly demonstrated the "Double Microbial Barrier" internal design in the new "Swabbable" *InVision-Plus® Neutral Displacement I.V. Connector System* from RyMed Technologies, Inc. is an effective barrier to pathogen ingress and microbial migration through the barriers and into the catheter lumen.

When using standard disinfection swabbing procedures and a normal clinical environment, the new "Swabbable" *InVision-Plus® Neutral Displacement I.V. Connector System* by RyMed Technologies, Inc. will provide an effective barrier against microbial ingress and microbial migration through the two independent barriers.

NOTE: RyMed Technologies, Inc. selected the ICU Medical CLC2000®, which was newest needle-free injection port system at the time, as the predicate device to compare performance. The CLC2000® did not perform as well as the *InVision-Plus®*. Based on the above test data and the comparison to the results of the predicate device, RyMed received its pre-market 510(k) approval from the FDA in just 43 days from submission of its application.



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Patents #6,113,068; 6,994,315; 6,299,131 and other U.S. and foreign patents pending

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