

DuPont Qualicon RiboPrinter® System

APPLICATION PROFILE

Alcon Demonstrates the Value of Accurate Information in Support of Clinical Trials for New Drugs Needing FDA Approval

Alcon, a maker of high-quality eye care products, is using the RiboPrinter® Microbial Characterization System in a variety of ways that demonstrate how much more dependable microbial information can be when state-of-the-art technology from Qualicon™ is used instead of traditional, biochemical methods.

In their comparison study, Alcon's microbiologists characterized 11 ocular isolates of *Corynebacterium* using two different identification methods — API and Biolog. These biochemistry-based tests identified all 11 isolates as *Corynebacterium pseudodiphtheriticum*.

Then the same isolates were analyzed using the RiboPrinter® system. This DNA-based characterization unit grouped 10 of the isolates into four, different pattern groups. The 11th isolate showed a pattern completely different from the other four and grouped separately. This group displayed no genetic relation to the other four RiboPrint® pattern groups indicating that it may not be *C. pseudodiphtheriticum*. The far more definitive and accurate information obtained using RiboPrint® patterns showed the company the exceptional reliability offered by genetics-based testing.

Examining a sterility test failure

The company continued its testing by examining two *Staphylococcus* isolates, one from a sterility test failure and the other from the garment of a line worker. Conventional testing with both a fatty-acid profile obtained using the MIDI system and the biochemistry-based VITEK indicated that the isolates were *S. haemolyticus*. The isolates were indeed *S. haemolyticus*, but ribotyping established them as different strains (see Figure 1). Conventional methods cannot discriminate below the species level to give this type of information.

These results showed that the failed sterility test was not the result of contamination by this worker. The company needed to look elsewhere for its culprit.

Establishing origin of infection

Alcon's study of the RiboPrinter® system information also included an examination of ocular isolates cultured from three patients, two of them at a San Antonio, Texas health facility, another at a Salt Lake City, Utah site.



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RiboPrint® patterns showed that the three patients had been infected with different strains of *Streptococcus pneumoniae*. This information also told researchers that the patients from San Antonio were not infected from the same source, despite being at the same facility.

The pre-and-post therapy RiboPrint® patterns also indicated that in each patient, pre-therapy isolates were identical to post-therapy isolates. This told investigators that the patients had infections from the same bacteria before and after therapy. Consequently, the information also indicated the probability that the therapy was ineffective, not that these patients had suffered a new infection.

Treatment isn't a failure after all

Conversely, a pre-therapy analysis of nosocomial microbes from a conjunctivitis patient showed 40 colony forming units (cfu) of *Staphylococcus epidermidis*. When treatment was finished, conventional biochemical assays determined that the same species was still present, but in even greater concentration — 400 cfu.

However, when the two isolates were characterized by the RiboPrinter® system, the patterns produced showed that there were two different *S. epidermidis*. Consequently, researchers knew that they were not dealing with a therapy-resistant strain of the bacteria but with a new, as yet untreated strain.

This type of information has proven valuable to Alcon in drug trials, when it is important to verify treatment failures. Being able to reverse a trial failure can save the pharmaceutical company the high cost of doing more studies to prove a drug's effectiveness.

Conclusion

Using the RiboPrinter® system to pinpoint sources of contamination and establish the effectiveness of therapy proved to be far more accurate than relying on information from other tests that are not capable of giving as much information, especially information beyond the species level. Using the genetics-based, automated RiboPrinter® system allows Alcon to have greater confidence in the definitiveness of their microbial information.

The company is now able to take action based on information that is reliable. What company would want less?

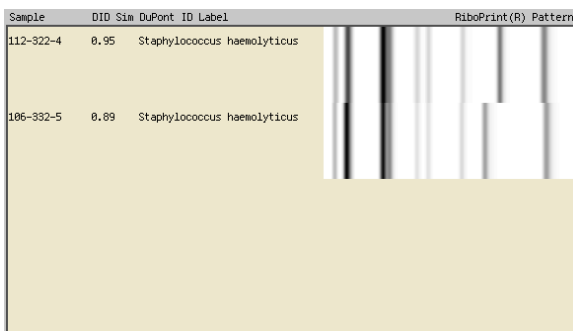


Figure 1. Worker contamination was ruled out when the typing of two *Staphylococcus* isolates — one from a sterility test failure and the other from the garment of a line worker — produced distinctly different RiboPrint® patterns. Conventional tests were unable to discriminate between the two organisms.

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