

DuPont Qualicon RiboPrinter® System

APPLICATION PROFILE

Drug developers can't leave identification of potentially lethal organisms to chance

The safety of future users is second to nothing when pharmaceutical companies begin clinical trials of new products. When one company discovered a tough-to-identify organism in their formulation for a new asthma inhaler, their only choice was to halt the trials until definite answers could be found. The RiboPrinter® Microbial Characterization System had those answers.

The clinical trials for the new inhaler had reached their final stages when quality control managers of a major pharmaceutical company realized the problem. There was no mistaking the presence of a bacterial organism in their formulation, a bronchodilator most often used by asthmatics.

The company's own investigation into the mystery failed to consistently identify the organism and offered little information about the source of contamination. Conventional plating on non-selective agar had produced two different *Pseudomonas* identifications. At this advanced stage of clinical trials, there was a sense of urgency surrounding the problem. Every day that the problem went unsolved was another day lost in bringing the product to market.

Ribotyping the Isolates

Running out of options, researchers turned to the Qualicon RiboPrinter® microbial characterization system for answers. Within eight hours they had a name for their contaminant and an idea of how big their problem was. *Enterobacter cloacae* was the organism and the risk it posed to users was so great that the trial was halted. Clinical literature warned that this was an organism notorious for its highly immunogenic lipopolysaccharide (LPS) protective coating. The LPS could produce violent and perhaps lethal allergic reactions, including anaphylactic shock. This was an especially nasty and risky discovery in a product intended for hypersensitive asthmatics.

The problem was compounded when it was learned from information in the public domain that simply killing the organism wouldn't inactivate the LPS, a hearty shell able to withstand harsh treatment. The organism had to be avoided, researchers concluded. Finding the source of the organism itself was the key.



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Strain Differentiation

By examining RiboPrint® patterns (Figure 1) of organisms isolated from both the product and its environment, it became clear that there were several different strains of *Enterobacter cloacae* present in the ingredients for the formulation. However, only one of these strains was winding up in the product. RiboPrint® patterns of pre-processing organisms from the formulation's ingredients quickly showed that the contaminating organism was being introduced to the product by food-grade lactose used as the inert carrier for the inhaler's active ingredient.

Phenotypic tests could not have discriminated between the variety of strains present. None of these less definitive methods would have been able to provide the unfaltering genetic fingerprint of the organism that ultimately directed investigators to its source.

Solutions

To solve their problem and resume clinical trials, the pharmaceutical company merely switched to a higher grade of powdered lactose because those in research had little faith in the likelihood of identifying and ridding the product of the organism. But with accurate, fast and reproducible information, the problem was solved and the clinical trial process could proceed with confidence that the company had both perfected its product and protected themselves against a potentially lethal problem.

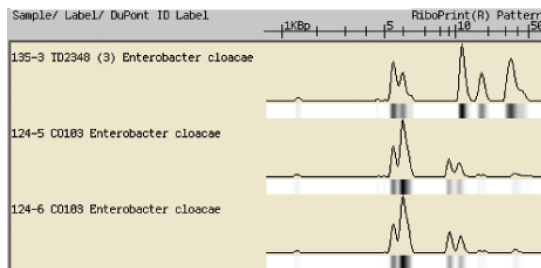


Figure 1. RiboPrint® patterns of *Enterobacter cloacae* found in the finished product (124–5) and the lactose used as the inert carrier for the inhaler's active ingredient (124–6) clearly match. Notice how distinct they are from another *E. cloacae* strain (135-3) also found in the formulation but not in the inhaler.

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