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Efficient *Burkholderia cepacia* complex identification in pharmaceuticals

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The *Burkholderia cepacia* complex is a group of gram-negative bacteria known for contaminating non-sterile, water-based pharmaceutical products. This has led to several incidents, causing recalls of both over-the-counter and prescription medications. To prevent such issues, the FDA recommends not only stringent manufacturing practices and robust water system management but also continuous monitoring of the microbial count. Bruker's MALDI Biotyper® aids in this monitoring process, leading to substantial cost savings and fewer recalls.

Recently, the FDA issued a warning to manufacturers of non-sterile, water-based pharmaceutical products about the ongoing contamination risk posed by *Burkholderia cepacia*.[1] Formerly known as *Pseudomonas cepacia*, the group includes over 20 closely related species of opportunistic gram-negative bacteria, and it is more accurately referred to as the *Burkholderia cepacia* complex (Bcc). While these bacteria generally pose minimal risk to healthy individuals, they can cause severe respiratory infections in those with specific health conditions, such as compromised immune systems or chronic lung diseases.[2]

There is a well-documented history of recalls involving both over-the-counter (OTC) and prescription medications due to Bcc contamination. The first recalls occurred in the 1980s and early 1990s, including incidents involving povidone-iodine, prompting the FDA to warn the industry about these risks. Despite advances in control systems

and cleaning procedures, there have been recent recalls of products like topical antiseptics, topical analgesics, cherry-flavored suspending bases, and oral antiseptic rinses.[1] These recalls are particularly concerning because the products are often used in hospitals to treat patients who are especially vulnerable due to their medical conditions.

Bcc has become a major contaminant mainly because of its ability to survive in nutrient-poor conditions, thrive in aqueous environments, form biofilms, and develop resistance to antibiotics and antiseptics. Remarkably, *Burkholderia cepacia* can metabolize organic matter in low-nutrient environments and even use certain disinfectants, such as quaternary ammonium compounds, which are commonly used for microbiological control in production facilities.[3] This adaptability means that even products compliant at the time of release can become contaminated if a low initial level of microbial contamination proliferates over time after release.

To prevent such contaminations, it is crucial to maintain strict control over raw materials, ensure validated cleaning processes for work environments, equipment, and facilities, adhere to good manufacturing practices (GMP), and conduct appropriate microbiological testing on finished products. Until recently, there was no specific testing guidance for *Burkholderia cepacia* complex bacteria in non-sterile products in the USA or Europe. The current recommendation now is to use *Burkholderia cepacia* selective agar (BCSA) in a standardized protocol to confirm the absence of Bcc in at-risk products. Although all known Bcc bacteria can grow on this medium, so can some non-Bcc bacteria, necessitating confirmation through the identification of suspected colonies.

Phenotypic identification methods, including biochemical analyses, are challenging for Bcc species due to the close phenotypic similarities between them, the variability in trait expression depending on the culture's physiological conditions, and the limitations of available identification solutions. Genotypic methods such as WGS require a significant time and cost investment next to high levels of technical expertise. However, MALDI-TOF MS offers pharmaceutical microbiologists a rapid, cost-effective and easy method for identifying microorganisms based on their unique proteomic fingerprints. Bruker's MALDI Biotyper boasts an extensive reference library covering 4,320 species and additionally a Security-Relevant (SR) Library that covers 12 highly pathogenic species across 10 genera, such as *Burkholderia*. Implementing this technology can result in significant cost savings and reduced recalls.

References

1 https://www.fda.gov/drugs/drug-safety-and-availability/fda-advises-drug-manufacturers-burkholderia-cepacia-complex-poses-contamination-risk-non-sterile

2 di Cello F, Bevivino A, Chiarini L, Fani R, Paffetti D, Tabacchioni S, et al. Biodiversity of a *Burkholderia cepacia* population isolated from the maize rhizosphere at different plant growth stages. Appl Environ Microbiol. 1997;63(11). https://doi.org/10.1128/aem.63.11.4485-4493.1997

3 Hendry S, Steinke S, Wittstein K, Stadler M, Harmrolfs K, Adewunmi Y, et al. Functional Analysis of Phenazine Biosynthesis Genes in *Burkholderia* spp. Appl Environ Microbiol. 2021;87 (11). https://doi.org/10.1128%2FAEM.02348-20

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