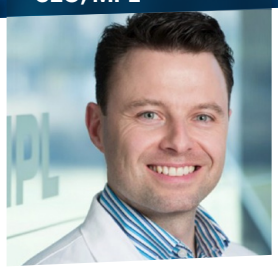

**Stefan Karl**
**CEO, MPL**



**Mikrobiologisches Prüflabor GmbH, Innsbruck, Austria**

# Expert Insights

## The MALDI Biotyper® enables increased throughput and reliability in pharmaceutical microbial testing

Specialized microbial testing is essential in drug development, where bacterial and fungal contamination can pose a serious threat to drug efficacy and patient safety, requiring painstaking, time-consuming and potentially costly follow up action.

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**Working with Bruker**

Specialist pharmaceutical testing laboratory, the MPL – Mikrobiologisches Prüflabor in Innsbruck, Austria, has switched to Bruker's MALDI Biotyper® sirius System to support accurate and robust microbial testing in a high throughput workflow.

*"It used to take anywhere between four hours and 20 hours to perform reliable identification testing for product release; more if additional sample preparation activity was needed, which could easily add one or two extra days. Bruker's MALDI Biotyper® sirius System has brought the process down from days to minutes – literally a few minutes per sample."*

## Detecting microbial contamination

Throughout the drug development and manufacturing processes, the potential for bacterial and fungal contamination of raw materials, operator clothing, production facilities and finished products poses a serious threat to drug efficacy and patient safety.

Many active pharmaceutical ingredients (APIs) and excipients support microbial growth. This microbial contamination can occur at any stage in the pharmaceutical supply and production chain, where it can lead to drug degradation and subpotency, and, worse, can cause serious harm to vulnerable patients.[1] In a landscape where drug developers are under extreme pressure to cut drug development time, safety and speed are of the essence.

In this highly regulated sector, manufacturers must establish rapid and robust microbial monitoring and contamination control strategies as part of current good manufacturing practice (cGMP). Fast and efficient product release testing and environmental monitoring are critical. Due to the complexity, this is often outsourced to expert laboratories, such as MPL – Mikrobiologisches Prüflabor in Austria.

## Validated testing

MPL offers validated microbiological analysis and release testing for the pharmaceutical industry, conducted according to the current regulations defined by the European Pharmacopeia (EP) international ISO standards, the United States Pharmacopeia (USP) and by the European Medicines Agency (EMA), all within the cGMP umbrella.

Stefan Karl, CEO at the MPL – Mikrobiologisches Prüflabor explains:
*"We offer both sterile and non-sterile product testing. In the non-sterile manufacturing environment, frequently there needs to be an absence of certain potentially harmful microbes, such as Escherichia coli (E. coli) or Salmonella, so during the analytical test we need to make sure that these germs are not present. Here, we need to confirm that we can exclude a specific type of bacteria or fungus, so the Bruker MALDI Biotyper® sirius System supports our analysts in drawing the right conclusions. In the sterile manufacturing line, pharmaceutical and biopharmaceutical manufacturers need to confirm whether the product is free of microorganisms throughout the manufacturing process, as contamination can be introduced at different stages. A sterile product is often only terminally sterilized at the end of the production process, and still needs to be tested before sterilization, where it is essential that the analysis returns a confident and accurate result."*

Stefan continues: *"Just like in environmental monitoring programs, our customers need to know what kind of contamination exists, so that from the microbiological perspective, we can clearly outline the direction in which improvements need to be made in production."*

When bacterial or fungal isolates are found in a production facility, it is essential to identify the organism rapidly and reliably at species level. Accurate identification supports tracking, trend reporting, and setting up a reliable data log to inform future preventative methods.

## A new alternative to sequencing

Genomic techniques are considered a high-end solution in microbial identification. Identifying potential contaminants using this approach, based on polymerase chain reaction (PCR) and deoxyribonucleic acid (DNA) or ribosomal ribonucleic acid (rRNA) sequencing for detection and identification of potential contaminants ensures raw materials and finished products comply with specification.

Sequencing, however, is time consuming and a greater financial burden. Additional identification testing typically takes five to ten hours, plus further sample preparation is required in some instances – which can quickly add up to a delay of one or more extra days before a product can be released. In this time-critical, high-cost environment, a better solution at a comparable quality level is needed that offers the same high level of data quality and data integrity.

## Microbial analysis - a next generation solution

MPL's new flagship microbial identification workflow uses the Bruker MALDI Biotyper® sirius System, that is based on Matrix-Assisted Laser Desorption/Ionization Time-Of-Flight Mass Spectrometry (MALDI-TOF MS). It is recognized as a fast, reliable and cost-effective microbiology method for microorganism identification starting from colony material on agar plates.

Stefan outlines why MPL chose to switch from classic phenotypic methods to the prototypic mass spectrometry-based method: *"Since we were founded in the early 1990s, as Austria's first privately owned microbiological laboratory, we have always been a business that is not afraid to innovate – which is not always the case in the pharmaceutical environment. The Bruker solution and partnership approach ticked all the right boxes. Together with Bruker, and our partner Charles River Laboratories, we opted to implement a MALDI-TOF identification solution for our clients. We now have a fully operational, validated workflow with the Bruker MALDI Biotyper® sirius System and the Accugenix® database, which is very much oriented towards the needs of the life science and pharmaceutical industry. Its speed is impressive. We have taken analysis time down from hours, sometimes days, to minutes."*

The MALDI Biotyper® workflow delivers validated results within minutes from a small amount of culture. The quality of identification plus its speed, the ability to run multiple sample tests in parallel, and to repeat samples in short times, has brought down identification time to around two minutes per sample, representing a considerable – and highly valuable – time saving in the drug development environment, where every hour's delay can potentially add substantial cost.

The system is flexible for medium or high-throughput workloads, and is further enhanced at MPL by the validated and highly maintained Accugenix® reference database of more than 16,000 entries for bacteria and fungi, made up of Bruker's high quality library and the significant Charles River in-house library, which together ensure reliable and accurate results.

Stefan outlines why MPL chose to collaborate with Bruker: *"Bruker is a highly valuable partner. They continuously work on improving their instruments and, from a technical perspective, we can rely on rapid support – it really is first class. This is important for us as a laboratory involved in release testing of products, where we need to limit instrument downtime as much as possible."*

*"The technical support that we receive from Bruker really is first class. They are very quick in responding to issues, which is very important for us to deliver the excellent service our pharmaceutical customers rely on."*

## Supporting environmental monitoring

Another fast growing area of microorganism identification on species level in the pharmaceutical industry is in environmental monitoring. Water especially is a potential source of microbial contamination, as it is used throughout many raw material and drug product manufacturing processes – and can be a significant ingredient itself in many injectable and oral drugs.

Stefan continues: *"Pharmaceutical manufacturing falls under the EU GMP guideline, which requires environmental monitoring programs where samples are cultured and analyzed. Microorganism identification of the pharma microbiome per product and per production line is a critical part of that. The pharmaceutical industry must conduct environmental monitoring, and we can utilize the MALDI Biotyper for microbial identification."*

## Fungal identification

Fungal contamination is also a key area in pharmaceutical testing, where contamination can arise from airborne sources or from the workforce. Although less common than bacterial contamination in terms of customer sample numbers, it can have a major impact on the manufacturing process, the product, and the patient.

Identifying molds and multicellular fungi is one of the most challenging aspects of microbiology, and fungal contamination is under increased scrutiny as contaminated pharmaceuticals could lead to outbreaks of severe fungal diseases in the community.[2]

Filamentous fungi, in particular, are notably difficult to identify. Stefan highlights the issue: *"The identification of fungi is completely different from bacterial identification – it is much more difficult. In many laboratories across the globe this is a fully manual, and therefore highly subjective, non-standardized, process. The MALDI-TOF workflow together with the Accugenix database introduces standardization of analysis. So there is much less room for error compared to even the best manual work and interpretation, because we now have a standardized system that allows us to run these tests and cross-check with morphological and microscopic interpretation."*

For next-generation fungal testing, Bruker has introduced the Mycelium Transfer (MyT) procedure with easy direct fungi transfer. After isolating mycelium, the MBT HT Filamentous Fungi Module rapidly identifies filamentous fungi down to the species level. The workflow introduces a standardized approach, combining an extensive reference library with advanced software that supports automation of mass spectral acquisition and analysis to deliver accurate identification.

## A changing analytical landscape

The trend towards outsourcing is set to continue in the pharmaceutical sector, who use specialist service partners to reduce overheads, benefit from expert advice, minimize in-house performance risk for routine microbial monitoring, and accelerate the process of bringing new drugs to market.

Stefan concludes: *"The pharmaceutical landscape is changing rapidly. There is far more analytical testing required under current regulations and, because of this, the need to outsource specialist testing is increasing accordingly. The industry will see continued globalization of outsourcing, both to keep pace with demand and ensure a standardized approach. The state-of-the-art technology we use that offers consistent analysis, high throughput and accurate results will help streamline costs and increase efficiencies to bring safe and effective drugs to market more rapidly. We look forward to a continued successful partnership with Bruker."*

For more information about MPL – Mikrobiologisches Prüflabor GmbH, please visit https://www.mpl.co.at/
For more information about the Bruker MALDI Biotyper® sirius System, please visit https://www.bruker.com/en/products-and-solutions/microbiology-and-diagnostics/microbial-identification/maldi-biotyper-sirius-system.html


### References

[1] Parenteral Drug Association (PDA): Microbial Control of Raw Materials Used In Pharmaceuticals, October 2022. Accessed June 2024. https://www.pda.org
[2] Ahmed MAEE, Abbas HS, Kotakonda M. Fungal Diseases Caused by Serious Contamination of Pharmaceuticals and Medical Devices, and Rapid Fungal Detection Using Nano-Diagnostic Tools: A Critical Review. Curr Microbiol. 2023 Nov 17;81(1):10. doi: 10.1007/s00284-023-03506-7. PMID: 37978091; PMCID: PMC10656328.

**Stefan Karl and his team from MPL**

Not for use in clinical diagnostic procedures.
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