

LC-MS Innovations Facilitate Pioneering Testing Capabilities in Forensic and Clinical Toxicology

Germany-based MVZ Medizinische Labore Dessau Kassel GmbH has become an industry leader in developing fast and sensitive methods for drugs of abuse testing using oral fluid and capillary blood samples.

Products: Waters™ Xevo™ TQ-XS Tandem Quadrupole Mass Spectrometer, MassLynx™ Mass Spectrometry Software, Waters ACQUITY™ UPLC™ I Class System, UniSpray™ Ion Source

DRUGS OF ABUSE TESTING AND MONITORING AT MVZ

MVZ Medizinische Labore Dessau Kassel GmbH (MVZ) prides itself on the company's cutting-edge capabilities in drugs of abuse testing and monitoring applications, particularly for intoxication, drug level determination, drug screening for clinical and forensic applications, as well as subsequent confirmatory analysis. Based in Dessau, Germany, the laboratory's 35 employees in its Toxicology department work 24/7 to analyze samples for drugs of abuse, such as analgesics, opiates and opioids (including substitutes), benzodiazepines, and synthetic cannabinoids; as well as therapeutic drugs such as other sedatives, neuroleptics, psychoanaleptics, antiepileptics, antidepressants, antiarrhythmics, and more. The team works with a variety of sample types, including capillary blood, urine, hair, and oral fluid.

MVZ's clients include health clinics, psychiatric hospitals, prisons, specialist psychiatric prisons, and private physician practices working in addiction medicine.

The laboratory's ISO 17025 and ISO 15189 accredited services also help their customers with new psychoactive substances, presenting reliable forensic data in court, monitoring illicit drug use, or analyzing prohibited substances in investigations.

Historically, the forensic and clinical toxicology testing laboratory has mainly relied on urine samples, which can present significant challenges during the collection process, as it must be supervised to avoid an increased risk of sample substitution or adulteration compared to other types of biological samples.



MVZ Medizinische Labore Dessau Kassel GmbH offers cutting-edge capabilities in drugs of abuse and therapeutic drugs testing.

WORKING WITH WATERS

MVZ began its relationship with Waters in 2007 when the laboratory began to invest in LC-MS/MS instrumentation to improve laboratory throughput. The two companies have since worked closely together, as the MVZ team continued to develop innovative methodology required to detect new drug compounds. Over the years, Dr. Michael Böttcher, MVZ's Head of Toxicology, and his team have particularly appreciated the support they've received from Waters. He explains:

"Waters technical engineers can service both their chromatography and MS instrumentation, so we're working with the same people for each. That's very different from our experience with other vendors. When you use equipment from multiple manufacturers, problems can cause a blame game, with one company suggesting the issue is with the other's instrument. There's a tendency to avoid taking responsibility for mistakes in either their instrumentation or their support. With Waters, it's the same company, so they will work to solve the problem, no matter what."



Dr. Michael Böttcher, MVZ's Head of Toxicology, and his team have appreciated the support they've received from Waters since they began working together in 2007.

Under the direction of Dr. Böttcher, the company has developed and optimized groundbreaking methods for oral fluid testing, which is now gaining in popularity, as well as capillary blood testing. Using either a swab or a thumb prick, the sample collection processes of these ground-breaking tests are more easily supervised and can reduce the opportunity for fraud.

"We understood the challenges in traditional urine sample collection and analysis, and we saw an opportunity to develop new testing solutions that address these industry-wide problems. We've worked to develop highly sophisticated methods for oral fluid samples, something that has established us as a leader in the market. We currently receive and test approximately 600-700 oral fluid samples per day, which are analyzed using liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS)."

DR. MICHAEL BÖTTCHER
Head of Toxicology at MVZ

MVZ has invested in Waters analytical instrumentation and software, as well as worked closely with the Waters technical support team, to develop and optimize their pioneering drugs of abuse testing services for oral fluid and capillary blood samples.

LC-MS IN FORENSIC AND CLINICAL TOXICOLOGY

Like many laboratories, MVZ used gas chromatography coupled with mass spectrometry (GC-MS), which was the industry's gold standard during the company's early years. Since that time, LC-MS methods have become more popular as scientists looked for improvements in workflows, particularly increased sample throughput, reduced sample preparation and ease of use, while maintaining the high sensitivity needed for these applications. Those capabilities motivated MVZ's original investments in highly sensitive LC-MS instruments to enable faster identification and quantification of parent drugs and their corresponding metabolites for their customers.

"Originally, we were interested in LC-MS because of its capability to improve our laboratory throughput, giving us better workflows with the sensitivity we needed. LC-MS offered significant advantages for sample preparation, making it much more efficient and cost-effective for us. That's important in a time-sensitive industry like this one. Post-run time is also greatly reduced in LC-MS compared to GC-MS, and data analysis is more efficient."

DR. MICHAEL BÖTTCHER
Head of Toxicology at MVZ

Traditionally, drug tests in forensic laboratories involve a two-step process consisting of an immunoassay screen followed by a confirmatory analysis by GC-MS or LC-MS/MS. For some applications, this process can produce a high number of false positives, and more importantly, miss drugs with negative results. For example, most commercial opiate immunoassays do not detect fentanyl or fentanyl analogues.

LC-MS analysis saves time and costs for companies like MVZ by eliminating presumptive immunoassay analysis and providing detection of all significant drugs present in the sample, as well as quantification of drug concentrations that reflect actual impairment.



It can detect a wide range of drugs and other substances at very low concentrations, which is important in toxicology testing where even trace amounts of a substance may be of interest. Additionally, LC-MS methods can accurately identify and quantify multiple substances in a single sample, which makes it a valuable tool for a multi-targeted screening approach. LC-MS also makes it possible to conduct a quantitative follow-up on drugs with long detection-time windows such as benzodiazepines and THC.

For MVZ's forensic toxicology customers, LC-MS is particularly beneficial because it can provide detailed information about the chemical structure of a substance, which can be used to confirm the identity of a compound and distinguish it from other substances that may be present in the sample.¹ It's also relatively fast and can process large numbers of samples in a short period of time, which makes it well-suited for high-throughput toxicology testing. Dr. Böttcher explains:

"If our clients need tests that will be used in court, for example, we're able to provide them with results from an accredited lab that can prove a specific substance has been detected. We also provide quality control measures to verify the results."



Capillary blood testing offers a new route for drugs testing, as it is more easily supervised and reduces the opportunity for fraud.

PIONEERING TESTING METHODOLOGY

Extensive hands-on experience in forensic and clinical toxicology testing gave MVZ a unique perspective on the challenges in the industry, particularly regarding the disadvantages of the urine sample collection process. As a result, the lab innovated new LC-MS methods that optimized oral fluids testing. That capability has enabled the laboratory to expand its services and attract new customers.

"Urine is the most common physiological fluid used for testing, but the samples must be collected under supervision of a nurse or physician. That puts patients in an uncomfortable situation. Also, it can be challenging to develop new methods for urine testing that can detect new metabolites as drugs are introduced. About 10 years ago we began to research and develop new methods specifically for oral fluids using LC-MS. Now our customers are increasingly interested in testing services for other body fluids, particularly capillary blood and oral fluid."

DR. MICHAEL BÖTTCHER
Head of Toxicology at MVZ

Saliva sample types are non-invasive and can be collected quickly and easily, which makes the testing process more convenient for both the patient and the healthcare provider.² Additionally, oral fluid may be less susceptible to tampering or adulteration, which can be a concern with traditional specimen types such as urine or blood. Some studies have suggested that oral fluid and other sample types may offer improved sensitivity and specificity for certain drugs of abuse, which can make them more effective for detecting and monitoring substance use.³

As MVZ expanded its service offerings, it also needed to maintain the faster workflows that LC-MS provided. So, the company looked to technological advances in LC-MS instrumentation to achieve the increased sensitivity needed for these types of analyses. Dr. Böttcher explains:

"We quickly learned that we needed better sensitivity for oral fluid samples. However, we also found that improved sensitivity could help with our methods for capillary blood samples because the sample sizes were smaller and detection limits were much lower. So, we decided to invest in very sensitive instruments from Waters to keep our sample preparation as simple as possible and to provide our customers with the time-sensitive results they need."

WATERS INSTRUMENTATION AND SOFTWARE

The laboratory's Toxicology department relies on the Waters ACQUITY UPLC I Class system coupled with the Waters Xevo TQ-XS mass spectrometer and MassLynx Software to improve the detection and quantification of the wide variety of drugs and metabolites encountered in routine drug testing.

For example, the wide dynamic range of the system enables the confident detection of highly potent fentanyl compounds at trace levels, in addition to more common drugs present to higher concentrations. The system's speed of analysis, improved selectivity, and optimum analytical sensitivity provides MVZ with the tools needed to achieve results with greater accuracy and efficiency.

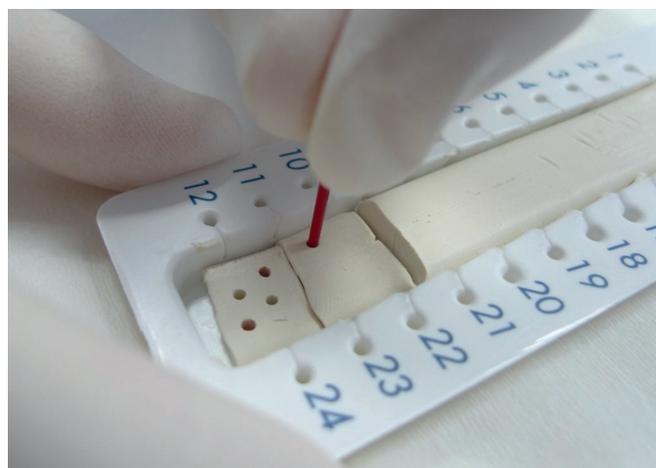
"Of course, the capabilities of LC-MS instrumentation have continued to improve through the years. As the sensitivity of the Waters instrumentation increased, we were able to establish the idea of what we call multi-target screening. Over time, we've expanded this service to include more drug compounds. Today, our multi-target screening in oral fluids can detect up to 73 substances from different classes. In parallel, we did the same thing for capillary blood samples, and we can now detect up to 81 substances."

DR. MICHAEL BÖTTCHER
Head of Toxicology at MVZ

MVZ has found that the Waters UniSpray Ion Source (USI) on the Waters Xevo TQ-XS Mass Spectrometer is an easy and cost-effective way to increase sensitivity. The unique geometry of the USI utilizes several different mechanisms to produce smaller droplets and enhance desolvation. These effects combine to generate a greater number of ions from the same amount of sample when compared to traditional ionization modes, such as electrospray, and typically results in an increase in response across a wide range of compounds. The combination of a broader range of analytes and a potential boost in response give the possibility to consolidate several analysis methods into one, or even just remove the need to change over sources between analyses, saving time and increasing laboratory efficiency.

Additionally, USI also allows the team to use a post-column hydrochloric acid infusion, which is particularly helpful for the sensitivity required in capillary whole blood analysis. For example, glucuronides (which are conjugates of glucuronic acid formed to improve solubility and kidney excretion) as combinations with often-toxic aromatic hydroxyl compounds, are highly responsive to this combination. The improved sensitivity also helps with the short elimination times and half-lives of certain compounds, as well as substances that may be present at very low concentrations, like fentanyls, benzodiazepines, and buprenorphine. That capability has enabled MVZ to expand other services, particularly for capillary blood samples. Dr. Böttcher explains:

"With the addition of the Waters USI to the Waters TQ-XS Mass Spectrometer, we can test from a dried blood spot. We have cutoffs at 0.1 to 1.0 ng/mL. It's been a game changer. Now we can offer capillary blood testing from a simple finger prick, which requires a sample volume of only 20 µL. That makes it very easy to take samples, so anyone can do it and medical professionals are not required to be present in many settings. Plus, with such a small volume, our sample prep time is much faster, and we use less volume of solvents. So, it's also more environmentally friendly and cost effective."



MVZ's multi-target screening can now detect up to 81 substances in capillary blood samples.

NEXT STEPS

Rapid changes in forensic and clinical toxicology require Dr. Böttcher and his team to continuously develop methods for new substances, enabling the company to provide faster and more sensitive drug screening. The team relies on the most up-to-date instrumentation and software to maintain this pace. MVZ is currently considering future investments in new Waters instrumentation for specialized applications as it continues to expand.



Further advances in software, however, are one of the most important technological advances that Dr. Böttcher believes will impact routine drugs of abuse and forensic testing. He sees how advances in machine learning algorithms could allow for more accurate and efficient analysis of test results. Improvements in user interfaces could make software tools easier and more intuitive for laboratory technicians, further streamlining workflows and supporting regulatory compliance. Additionally, the ability to analyze datasets quickly and accurately could help to speed up the interpretation of laboratory results – for example, where each analyte and its associated deuterated standard are measured, an automatic pairing and presentation of a combined set of results would simplify both laboratory process and reporting to MVZ clients.

“We see the advances in software as the key to further innovations in drugs of abuse testing. We’re watching closely as Waters continues to improve its software and will evaluate how these changes can help us further serve our customers and expand our capabilities. We want to build on our pioneering methodology and continue to generate new ideas and solutions in the future.”

DR. MICHAEL BÖTTCHER

Head of Toxicology at MVZ

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