

## Building Laboratory Capacity to Ensure Cannabis Safety, Quality, and Efficacy

Waters ACQUITY UPLC-MS/MS and Xevo TQ-S micro systems improve pesticide detection for ProVerde Laboratories, helping scientists ensure consumer safety for medical marijuana products

**Technology: Waters ACQUITY UPLC, ACQUITY UPC<sup>2</sup>, and Xevo TQ-S micro MS/MS systems**

### ESTABLISHING TESTING STANDARDS AT PROVERDE LABORATORIES

In 2013, Massachusetts legalized the use of medical marijuana (MMJ), creating a new marketplace in the state. ProVerde Laboratories, Inc. was launched the same year to meet the corresponding need for MMJ testing services, serving as one of the state's first ISO 17025 accredited, full-service analytical testing laboratories specializing in the cannabis and hemp industries.

From its onset, ProVerde was committed to using the latest scientific technologies to yield the most reliable analytical results, while maintaining an environmentally friendly, green approach. Headquartered in Milford, Massachusetts, the company's mission focuses on building lasting relationships with its customers and communities by providing services with reliability, quality, and integrity.

Cutting-edge analytical technology is the core of ProVerde's service offerings. These techniques include liquid chromatography (LC), gas chromatography (GC), and supercritical fluid chromatography (SFC) for method development, batch release testing, research, and consulting services.

These chromatography techniques are coupled with mass spectrometry (MS) detection to achieve the highest possible sensitivity for applications in pharmaceutical, food, materials science, petroleum, and clinical research. Other capabilities include analysis of elemental compositions using inductively coupled plasma mass spectrometry (ICP-MS) as well as screening for microbiological contaminants and pathogens.



ProVerde is the first ISO 17025 accredited lab in Massachusetts.

### WORKING WITH WATERS

ProVerde's founders had a long working relationship with Waters, specifically in pharmaceutical and academic research. The opportunity to build a laboratory from the ground up enabled ProVerde to invest in the highest quality Waters instrumentation available – including ACQUITY™ UPLC™ with Xevo™ TQ-S micro tandem quad MS for pesticide analysis, UPLC, and UPC<sup>2</sup>™ for cannabinoid analysis.



ProVerde Laboratories.

Dr. Hudalla credits his company's relationship with Waters as a key part of its business strategy: "Part of our success is the vendors we choose for instrumentation. That's a major foundational component of what we're able to achieve from a quality perspective."



Dr. Hudalla describes the experience: *"We worked closely with the mother to understand the production of the medicine. She had to produce it herself. We often have to source the product, and we were finding product that was heavily contaminated as we frequently do. These are cumulative toxins, and they are going to have a significant detrimental effect on a 13 month-old child. We were able to intercept it, so the contaminated product wasn't used for the creation of her daughter's medication."*

The experience put a face to the services the company was providing, something that differs significantly from most laboratories in that are conducting pharmaceutical-related research. The ProVerde team became very aware that they held a unique position to ensure consumer safety in the MMJ market.

Dr. Hudalla explains: *"I don't know who's consuming these products. So, I must assume the end user of this product is an infant or someone who has a compromised immune system – someone who may be on chemo who cannot tolerate the toxins that we might find in these products. That lends importance to what we do."*

As a result, today ProVerde executives see the company's role as more than simply a service provider. Dr. Hudalla views his company's services as a way to protect clients from liability by preventing contaminated products from getting into the marketplace. Additionally, the company offers its clients the ability to fix problems by identifying the source of contamination, determining how to remediate it, and ensuring the final product is safe.

Dr. Hudalla describes the company's viewpoint: *"We're on the frontline and see the impact of our work. It's about consumer safety. Our primary goal is making sure that consumers aren't put at risk."*

To do that, ProVerde turned to Waters to ensure it had the best instrumentation available to accomplish its goals.



Dr. Christopher Hudalla, ProVerde co-founder and CSO.

## CUTTING-EDGE ANALYTICAL INSTRUMENTATION FOR CANNABINOIDS AND PESTICIDE TESTING

ProVerde scientists needed to detect and quantify pesticides down to the lowest possible levels, and in the presence of interferences from complex matrices. Large variations in the concentrations of different pesticides further added to this challenge.

Working closely with Waters, ProVerde scientists explored the use of multiple techniques to achieve the most reliable analytical results possible, while maintaining the company's goal for an environmentally friendly, green approach.

### UltraPerformance Liquid Chromatography (UPLC)

From the beginning, ProVerde focused on UltraPerformance LC™ (UPLC) – one of the best techniques for cannabis analysis because of its ability to rapidly quantitate individual cannabinoids. Waters UPLC instrumentation offers the capability to analyze more samples, faster, and with better results.

UPLC is a Waters innovation with re-engineered LC particle technology, column design, injectors, pumps, and detectors. The increased performance of sub-2- $\mu$ m hybrid columns, used in conjunction with Waters ACQUITY UPLC systems delivers mobile phase at high pressures with low dispersion, preserves the chromatographic benefits of such small-particle chemistries – producing sharper and more concentrated peaks.



*"UPLC is a higher-pressure method that is the same as HPLC, but faster and more efficient. It reduced our sample analysis time from 8–9 min to about 3.5 min per sample. That dramatically increased our throughput."*

DR. CHRISTOPHER HUDALLA  
ProVerde Co-founder and CSO

ProVerde scientists also found the ACQUITY UPLC System reduced solvent use without compromising analytical results. That benefit served ProVerde's goal to make as little impact to the environment as possible by minimizing the company's carbon footprint.



“At ProVerde, we think green, and this applies to our technical methodology as well. Our goal is to ensure the most accurate results using the greenest technology – generating less hazardous waste and consuming less energy. When we use UPLC, we generate 60% less hazardous waste per test. Disposal of waste is a significant cost for us. By cutting the cost of disposal in half, it cuts the cost of analysis. It’s a huge cost saving. Plus, UPLC gives us higher throughput, so we can also increase revenue that way.”

DR. CHRISTOPHER HUDALLA  
*ProVerde Co-founder and CSO*

Originally, ProVerde started with one Waters UPLC-MS/MS system in its Massachusetts lab for pesticide analysis and one UPLC-UV for cannabinoid analysis, but the company ended up purchasing three more UPLC-MS/MS systems to keep up with the demand. Today those instruments are churning out data 24/7.

The UPLC instrumentation also helps ProVerde maintain a strong quality control system in this fast-paced environment by enabling the company to perform continuous calibration examinations.

“Waters has been very supportive in helping us optimize our processing methods. When we started, we would identify peaks by their retention time. Now we identify peaks by retention time and their UV spectral absorbance across that peak. We compare that to a library reference.”

DR. CHRISTOPHER HUDALLA  
*ProVerde Co-founder and CSO*



*Pesticide detection for medical marijuana products.*

Dr. Hudalla explains the value of that capability: “Every 20th sample is a QC sample that is designed to determine if the system is performing as it should. I can document that the system is accurately quantitating my cannabinoids, and I’m able to do that in a high-throughput fashion. It’s essential for my business.”

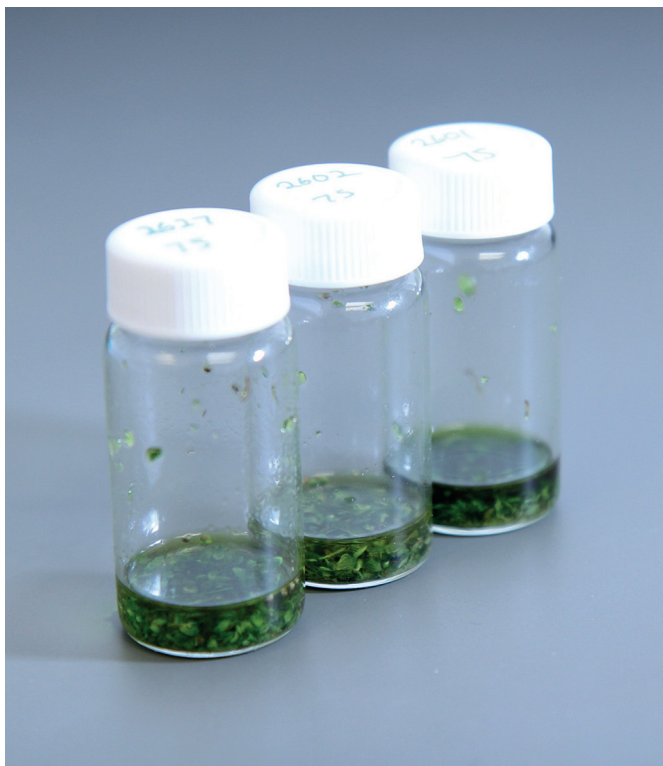
Dr. Hudalla continues to say: “I’ll frequently see products as being marketed as THC-free. Someone is making a cannabidiol (CBD)-based product, and they’re advertising as no tetrahydrocannabinol (THC) in their product. Yet when I test it, I see a THC peak. Not just a peak, because that could just be matrix effect, but the UV absorbance spectrum for that peak matches THC. It has the exact match of weight and absorbance of THC, and it’s enough information to give me confidence that I could defend it in a court of law, if necessary.”

### **UltraPerformance Convergence Chromatography**

ProVerde also performs cannabinoid analysis and potency profiling using the UltraPerformance Convergence Chromatography™ System (UPC<sup>2</sup>) from Waters, using CO<sub>2</sub> as the primary mobile phase component.

The ACQUITY UPC<sup>2</sup> System provides orthogonal selectivity to UPLC since polar metabolites elute later than the parent drug. Coupling UPC<sup>2</sup> with electrospray ionization and MS analysis can be a powerful and complementary technology in cannabis applications.

Waters’ ACQUITY UPC<sup>2</sup> Technology represents one of the fastest, most reliable, and robust technologies available for chromatographic testing. At the same time, UPC<sup>2</sup> enables a dramatic reduction in the use of organic solvents, minimizing the amount of hazardous waste generated, making it one of the most environmentally friendly testing methodologies available and thus maintaining ProVerde’s commitment to ‘green’.



*ProVerde specializes in medical marijuana testing.*

While UPC<sup>2</sup> is a relatively new addition to MMJ testing methodology, it's a good match for cannabis analysis because of the large number of cannabinoids found in samples, which typically fall between 80–100. Waters UPC<sup>2</sup> Technology can separate and quantify all the major cannabinoid compounds, providing a more detailed, accurate profile of a marijuana extract.

This information allows dispensaries to issue proper doses and recommend the right cannabis strain for customers. For example, CBD is a component of marijuana that has been shown to help reduce seizures in children with epilepsy. But dispensaries want to ensure these products do not have THC, the psychoactive ingredient found in cannabis.

Dr. Hudalla explains: *"Children respond exceptionally well to high amounts of CBD, but you don't want to give them too much THC. You don't want to have your kid inebriated."*

### Mass spectrometry

ProVerde uses UPLC with tandem mass spectrometry (UPLC-MS/MS) to screen for and quantitate pesticides – helping to ensure that compounds used during cultivation do not make their way into final consumer products. ProVerde develops matrix-specific pesticide preparation steps before analyzing products on Waters UPLC-MS/MS instrumentation.

The Xevo TQ-S micro Mass Spectrometer offered ProVerde a significant increase in sensitivity with no reduction in selectivity. Meaningful information was obtained for a greater number of components across a larger population of samples, giving a more complete picture for improved understanding and more confidence in results – two important benefits for the company.

That data also helps Dr. Hudalla and his team when accuracy is vital, such as verifying product marketing and packaging information.

### Triple quad for pesticide testing

The variety of matrices for MMJ products is a significant challenge for ProVerde scientists. Again, the company's relationship with Waters proved fruitful when they discovered new analytical techniques could help address these issues – this time with UPLC coupled with the Xevo TQ-S mass spectrometry for pesticide testing, to ensure products are safe.

When analyzing MMJ samples, it can be difficult to separate pesticides in certain instances when they are eluting with cannabis resin components (such as THC) that are present in very high levels and cannot be separated by any reasonable cleanup.



*"Being able to use different approaches gives us increased confidence in the results. If we have a potential matrix effect, we can turn to complementary analytical technology to get the information we need."*

DR. CHRISTOPHER HUDALLA  
*ProVerde Co-founder and CSO*

ProVerde found UPLC worked well for detecting contaminants in MMJ samples when coupled with the Xevo TQ-S micro Mass Spectrometer. The company's scientists found the increased sensitivity of the Xevo TQ-S micro instrument enabled them to quantify and confirm trace components at lower levels in the most complex samples.

## ADVANCING MMJ TESTING CAPABILITIES

MMJ is a new and emerging market in both the United States and throughout the world, and ProVerde sees a future that taps into the power of cutting-edge analytical technology and scientific expertise to ensure product quality and safety – just like in related industries such as pharmaceuticals, food, beverages, and dietary supplements.

As the MMJ market evolves, ProVerde and Waters plan to continue to work together to ensure consumer safety, in addition to meeting the growing need for regulatory compliance testing services. ProVerde's investment in the most advanced Waters analytical instrumentation is a key component of the company's long-term strategy to build trustworthiness and credibility in this emerging industry.

Dr. Hudalla summarizes the importance of the relationship between ProVerde and Waters to his company's approach:



**"Instrumentation is the most critical component of our business. Waters equipment is a foundational portion of our testing platform."**

DR. CHRISTOPHER HUDALLA  
*ProVerde Co-founder and CSO*

# Waters

THE SCIENCE OF WHAT'S POSSIBLE.™

Waters, The Science of What's Possible, Xevo, UltraPerformance LC, UltraPerformance Convergence Chromatography, ACQUITY, UPLC, and UPC<sup>2</sup> are trademarks of Waters Corporation. All other trademarks are the property of their respective owners.

©2018 Waters Corporation. Produced in the U.S.A. August 2018 720006394EN PM-PDF

Waters Corporation  
34 Maple Street  
Milford, MA 01757 U.S.A.  
T: 1 508 478 2000  
F: 1 508 872 1990  
[www.waters.com](http://www.waters.com)