

Mass Detection Helps CRO Meet the Growing Demand for Outsourced Drug Discovery Services

Waters ACQUITY QDa Mass Detector brings the power of mass detection for purification to Medicilon, helping them meet the growing demand for outsourced services in the pharmaceutical and biotechnology industries

Technology: ACQUITY QDa Mass Detector, ACQUITY Arc System and ACQUITY UPLC PDA Detector

DRUG DISCOVERY AT MEDICILON

As a preclinical contract research organization (CRO), Medicilon serves pharmaceutical and biotechnology customers around the world, with an emphasis on the needs of the U.S. market. Originally founded in 2004, the company offers R&D services from conception through the investigational new drug (IND) application phase.

Headquartered in Shanghai, People's Republic of China, Medicilon occupies more than 400,000 sq. ft. in lab space and employs more than 800 people working on biology, chemistry, and preclinical research applications. The company's customers include some of the biggest names in the industry, including Roche R&D China, Ardea Biosciences, Sunovion Pharmaceuticals (formerly Sepracor), and SK LifeScience.

Medicilon has the largest AAALAC-certified animal research facility in Shanghai and is U.S. GLP and CFDA GLP certified. The company's Chemical Analytical Center provides general analysis and purification services for both internal and external clients, including impurity analysis, method development and purification, and general analytical chemistry.

Pharmaceutical companies entrust CROs like Medicilon with a wide range of projects requiring both scientific expertise and top-of-the-line instrumentation. It's a multi-billion dollar industry, spurred by the increasing complexity and size of clinical trials.

Ms. Zhang Lijuan, Manager of the Pharmaceutical Analysis Team in the Analysis Department at Medicilon, describes her company's role in this rapidly growing marketplace: *"At present, there's a growing need for CRO services, which requires us to invest in more personnel and more instrumentation as we increase our collaboration on projects. We've expanded a lot in a short period of time, growing more every year."*



Medicilon Headquarters, Shanghai.

WORKING WITH WATERS

Waters and Medicilon have worked closely together since Medicilon's launch in 2004, and the CRO has invested in a wide range of Waters instrumentation, particularly for LC-MS analysis, sample preparation and chiral chromatography.

In 2014, Medicilon purchased its first ACQUITY™ QDa™ instrument, fulfilling a need for easy-to-use mass detection to supplement the company's LC-MS analyses. The ACQUITY QDa easily integrated with Medicilon's other Waters instrumentation, which was an extremely appealing benefit. The collaborative relationship between the two companies also was a key factor in the decision, as was Waters' dedication to supporting its customers.

Ms. Zhang said: *"Waters is the first company we will consider for our future needs. They offer both high-quality instrumentation and a quick response time. If we have problems, they're ready to help."*

In partnership with Waters, Medicilon strives to meet the rapidly growing demand for CRO services using the latest in mass detection technology.

GROWING DEMAND FOR CRO SERVICES

CROs fill an important role for pharmaceutical and biotechnology companies. Many large organizations prefer to work with contract labs for some of their analytical needs, particularly for complex techniques that require high levels of training and expertise.

Medicilon has been recognized as one of the top drug discovery CROs in China and is managed by a team of scientists with a wealth of experience in the U.S.-based pharmaceutical and biotechnology industries. The company continues to expand its areas of expertise and service capabilities as more pharmaceutical and biotechnology companies have taken advantage of outsourced integrated drug discovery and development services.

The range of services includes all key aspects of drug discovery – including impurity isolation; impurity identification; isolation and identification of by-products degradation in active pharmaceutical ingredients (API); Q-NMR analysis; and IND package preparation.

Medicilon scientists use a range of analytical techniques to serve their clients, including nuclear magnetic resonance (NMR), liquid chromatography coupled with mass spectrometry (LC-MS), electron affinity (EA), high-resolution mass spectrometry (HRMS), infrared spectroscopy (IR), ultraviolet spectroscopy (UV), and more.

Medicilon also supports its clients with the development and validation of analytical methods in compliance with CP, USP, EMA, and ICH guidelines for:

- water content and residual solvents
- chiral purification
- heavy metals
- structure and purity determination
- high-throughput purification and analysis

Medicilon's Pharmaceutical Analysis Team provides general analysis and purification services for pharmaceutical manufacturing facilities and pharmaceutical companies, as well as some structural confirmations and related tests. It focuses on three key areas:

- impurity analysis and characterization
- development and validation of analytical methods
- general analytical chemistry services

Ms. Zhang explains: "Because the demand for outsourcing business in the market is relatively large and because we have this ability, we also want to expand our business in this area."

To fulfill the growing demand for their services, CROs need to stay on top of the latest instrumentation technology. Medicilon has focused on maintaining its expertise in top-of-the-line analytical instrumentation to meet the needs of its clients. For formulation analysis and original drug analysis, Medicilon scientists have relied on Waters instrumentation, including the company's Alliance™ HPLC systems, SFC preparative systems and ACQUITY UPC²™ systems.

"It's very important to us to acquire and maintain high quality analytical instrumentation from leading companies who can provide the right choices for us."

ZHANG LIJUAN

*Manager of the Pharmaceutical Analysis Team
in the Analysis Department, Medicilon*

Mass detection was particularly appealing for Ms. Zhang's team because of its ability to provide access to mass data without the need for an extensive background in mass spectrometry. She saw an opportunity to tap into the analytical confidence that mass detection brings via the Waters™ ACQUITY QDa Mass Detector.

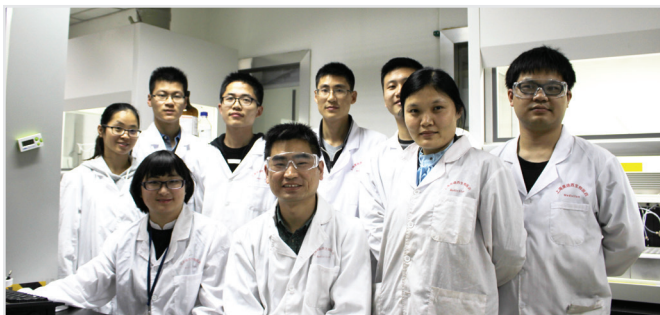
The ACQUITY QDa has dramatically improved the capability of Medicilon's existing analytical or purification systems, providing a simple way to incorporate reliable, versatile mass detection in their laboratories.

Mass detection provides CROs with an easy way to interpret mass data more clearly without the need for extensive training or experience in mass spectrometry. Working in tandem with optical detection, the ACQUITY QDa can significantly reduce the chance that a sample component will go undetected.

Integrating the ACQUITY QDa's cutting-edge technology offered Ms. Zhang's team the ability to enhance the analytical value and productivity of each analysis. Those benefits make a big difference to customers in the demanding CRO services market.

MASS DETECTION FOR DRUG DISCOVERY

The drug discovery field has benefited greatly from the technological advances of liquid chromatography combined with mass spectrometry (LC-MS) and tandem mass spectrometry (LC-MS/MS), making it the analytical tool of choice in the field, particularly to quantify small molecules.



The Pharmaceutical Analysis Team in the Analysis Department at Medicilon, Shanghai.

Medicilon, like many pharmaceutical and biotechnology organizations, uses mass spectrometry (and LC-MS in particular) for specific uses. However, its relative cost, need for experienced personnel, as well as its slow sample preparation restriction and limited throughput, means that it is too costly to work efficiently for analytical purification.

Medicilon saw the potential of using mass detection for purification to alleviate some of the complications of LC-MS while also providing the necessary data to serve their clients' needs. The company integrated the ACQUITY QDa Detector in its laboratories for synthesis after purification; impurity preparation and analysis methods; and analytical purification and preparation of different compounds, such as intermediates, candidate drugs, impurities, metabolites, and various small molecule chemicals.

They've experienced the following benefits as a result.

Resource availability: Typically, Medicilon's LC-MS instruments average between 150 and 200 samples a day. Ms. Zhang estimates each analysis takes about 30 minutes and each instrument can do 60 samples in a day. That means the company's LC-MS instruments are running around the clock.

Ms. Zhang explains: *"We need to use our LC-MS resources wisely, and sometimes we have competing priorities. For example, before we had the ACQUITY QDa, it would take about 10 minutes to get an experiment online. Then it would take about 10 minutes for each sample to get results. Especially for samples that are more complicated, we had to use mass spectrometry for each one to determine which compound was the target. It was a huge workload."*

The ACQUITY QDa Detector reduces the need for LC-MS analysis for certain compounds, thereby freeing up the LC-MS instrumentation for other uses. That improves the laboratory's productivity immediately.

Ms. Zhang elaborates: *"The ACQUITY QDa is very effective for many compounds, particularly those that are not suitable for UV detection. Its major benefit is it can detect mass spectra at the same time without using additional LC-MS analysis, which improves our efficiency."*

Analytical confidence: The ability of the ACQUITY QDa Detector to minimize the risk of unexpected coelutions or components and confirm trace components with certainty was highly attractive to Medicilon.

Mass detection helps the company enhance the analytical value and productivity of each analysis, eliminating the need to run additional assays or time-consuming alternative techniques. Working with the ACQUITY QDa in tandem with optical detection, Medicilon scientists can significantly reduce the chance that a sample component will go undetected.

Ms. Zhang explains: *"Especially for preparations with a relatively low impurity content where the density is high, the data can be collected more accurately. When there are many impurities, there may be deviations if the data is collected by UV. For example, if you analyze a compound with five substances, it's difficult to confirm which one is the target compound. There are too many peaks, and you do not know which peak to collect. We used to have to rely on LC-MS to achieve it. After we integrated the ACQUITY QDa, however, we could see more compounds without using mass spectrometry. Especially when there are impurities, the ACQUITY QDa enables us to see more impurities with lower concentrations."*

Small molecule screening: Typically, Medicilon's test samples are small molecules for active screening, as well as small amounts of custom-made synthetic small molecular compounds with molecular weights ranging from 200 to 700.

Only about 10–20% of these compounds exceed a molecular weight of 1500. The ACQUITY QDa Detector works well with molecular weights of 1250 and lower, so most of the compounds can be identified using faster and more affordable mass detection instead of LC-MS analysis.

Ms. Zhang explains: *"When you look at the molecular weight of these compounds using the QDa, it is clear at a glance. That saves us a lot of time and resources."*

Easy sample preparation: Sample preparation is time consuming, something CRO scientists want to minimize. Easy sample preparation enabled by the ACQUITY QDa Detector streamlines the process for Medicilon's researchers, yet still offers the sensitivity needed for drug discovery methodology.

And that saves a lot of time, which is a valuable commodity in the time-sensitive pharmaceutical and biotechnology industries.

Ms. Zhang explains: *"After completing the analysis with the ACQUITY QDa, we can quickly determine which compounds are of interest, and increase the rate of our sample preparation."*

Easy integration: The easy integration of the ACQUITY QDa Mass Detector into the Analytical Chemistry Center brought affordable mass detection for purification to Medicilon that was also user friendly. That's very beneficial for CROs, which need to adapt quickly.

The ACQUITY QDa integrates easily with Medicilon's current instrumentation in their laboratories, which includes Waters Alliance HPLC systems, SFC purification systems, and ACQUITY UPC² systems. That saved the company a great deal of time in getting the new workflows up and running.

"The Waters ACQUITY QDa is a very good product for us as we work to improve our efficiency and productivity. It's been very helpful."

ZHANG LIJUAN

*Manager of the Pharmaceutical Analysis Team
in the Analysis Department, Medicilon*

Minimal training: In addition to integrating with other instrumentation, the ACQUITY QDa Mass Detector enables any analytical scientist to consistently generate the highest quality mass spectral data routinely with minimal training and with no previous experience of mass spectrometry. It's pre-optimized to work with samples, without the sample-specific or user adjustments typical of traditional mass spectrometers.

Ms. Zhang explains: *"The ACQUITY QDa is relatively simple to use. It can be used directly after opening the machine. Minimal training is required."*

Cost Savings: Medicilon has experienced significant cost savings with the ACQUITY QDa Mass Detector, not only in the purchase price of the instrument, but also in the long-term operational costs.

One of the biggest financial benefits is improved efficiency. Medicilon's goal is to rapidly transform a client's drug discovery program from hit screening to SAR-driven medicinal chemistry in an efficient and cost-effective manner. The indirect savings achieved by using the ACQUITY QDa for certain analyses have a direct effect on the company's ability to meet that goal.

Ms. Zhang says: *"Mass spectrometry is far more expensive. The QDa offers significant advantages because the price is less expensive and it's more convenient to use."*

GROWING DEMAND FOR OUTSOURCED DRUG DISCOVERY SERVICES

The competitive market for CROs like Medicilon is forecasted to grow in the next five years, with the global CRO services market projected to reach USD \$56.34 billion by 2023, up from USD \$39.13 billion in 2018, at a CAGR of 7.6%.¹

That growth will be sustained by growing R&D expenditures, increased outsourcing of R&D activities, and an increasing number of clinical trials. As the demand for CRO drug discovery services grows, so will the need for analytical tools like the ACQUITY QDa Mass Detector to help Medicilon researchers meet that demand and stay ahead of the competition.

Ms. Zhang sees the future of mass detection for purification continuing to expand as more companies discover its ease of use, reduced sample preparation, increased analytical value and fast integration into their existing workflow.

She concludes: *"Analytical tools are something that a laboratory like ours cannot do without. I feel like mass detection for purification is an indispensable tool, and its possibilities in our industry will continue to develop in the future. Many companies currently do not use it, and that's to our advantage."*

References

1. "Contract Research Organization Services (CROs) Market by Type (Discovery, CMC, Preclinical, Clinical Research, Laboratory Services), Therapeutic Area (Oncology, CNS, Cardiovascular), End User - Global Forecast to 2023." *Research & Markets*, February 2018.

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