

Risk-based Approach Supports Migration of Legacy Methods for Eurofins BPT Toronto

Eurofins BioPharma Product Testing division assessed the Waters ACQUITY Arc HPLC System for the migration of legacy methods in a regulated environment to ensure consistency and deliver improvements to customer service and commercial capabilities

Technology: ACQUITY™ Arc™ HPLC System, Empower™ Chromatography Data System

BIOPHARMACEUTICAL PRODUCT TESTING AT EUROFINS

With 36 facilities in 19 countries, Eurofins BioPharma Product Testing (BPT) division delivers a comprehensive scope of Good Manufacturing Practice (GMP) testing services for some of the world's largest pharmaceutical, biopharmaceutical, and medical device companies.

Eurofins BPT has a global footprint of more than 185,000 m². The organization's network of GMP laboratories operates under the same strict quality procedures, LIMS, and centralized billing system across its 36 locations worldwide.

Eurofins BPT Toronto, located in Ontario, Canada, provides chemical, microbial, stability, and sterility testing on a vast array of products ranging from raw materials to finished products. The company focuses on delivering accurate, reliable, and timely results to its clients, and is proud of its strong emphasis on customer service.

The Chemistry Lab can offer method development, optimization, validation, and transfer, with state-of-the-art instrumentation to allow both qualitative and quantitative analysis to determine the chemical makeup of samples, and allows for a diverse portfolio of testing methods in their respective applications.



Eurofins BPT Toronto has had a long-standing partnership with Waters, however this collaborative project brought a new component to the relationship.

WORKING WITH WATERS

Eurofins BPT Toronto and Waters™ recently worked together to evaluate the Waters Arc HPLC system's ability to replicate existing liquid chromatography (LC) methods, without compromising data quality or requiring changes to the original method.

Eurofins BPT Toronto has had a long-standing partnership with Waters as a vendor, however, this collaborative project brought a new component to the relationship for both companies.

As a contract research organization (CRO), Eurofins BPT Toronto continuously evaluates its operations to ensure it can meet customer demand in a timely and cost-efficient way.

Working with Waters, the team saw an opportunity to apply a modern, risk-based approach to method migration and to understand the impact of introducing state-of-the-art technology for their legacy methods.

As a CRO, Eurofins BPT laboratories offer a broad range of methodologies under GMP authorization, ISO 17025 accreditation and ISO 9000 certification. All analyses are performed according to European and British Pharmacopeia (EP and BP), United States Pharmacopeia (USP) and Japanese Pharmacopeia (JP), as well as specific customer methods.

“Eurofins BPT employs around 8,900 people in 36 laboratories around the world. Our infrastructure is highly harmonized, including a networked LIMS system across all locations. We serve our clients here in Canada, but we can also send work to other intercompany laboratories if a customer needs something that’s very specialized. We are truly a global operation. I always tell our clients that we can test almost anything, either here or in our sister labs.”

DR. DOUGLAS TURK

Business Unit Manager, Eurofins BPT Toronto



Mr. Uttam Ghosh is the Department Head of R&D and Validation at Eurofins BPT Toronto.

ASSET MANAGEMENT

As part of an ongoing program to manage and update their analytical portfolio, Eurofins BPT Toronto formed a collaboration with Waters to assess the risk and impact around introducing modern HPLC technology for their validated analytical test methods. The goal of the project was to ensure that the lab’s potential switchover from its aging HPLC systems to Waters Arc HPLC or ACQUITY UPLC™ H-Class PLUS instrumentation on Empower CDS would be seamless, while ensuring data equivalency and regulatory compliance.

WORKING WITH WATERS

Dr. Douglas Turk, Business Unit Manager at Eurofins BPT Toronto, explains:

“We do analytical method migration and method transfers all the time, whether it’s from an internal lab or it’s from a client’s method that they want validated or transferred to our facility. Waters approached us because they were interested in seeing what was involved in the migration of an assay on a HPLC platform in a GMP lab. The fact that we had the opportunity to evaluate a new HPLC system from Waters was enticing, but ultimately we wanted to see how the instrument would perform with the migration of legacy methods in a regulated environment.

“We were interested in seeing the performance of the Waters Arc HPLC system because newer machines typically don’t have as many issues. Our clients want results, and they want their work done on time. They’re not going to understand why their assay is delayed because the HPLC is down, and we need to migrate a method to a new HPLC system. We want machines that don’t break down because if we repeat an assay three times due to equipment issues, that’s time when we’re not running another method. For us, it’s a productivity issue and a turnaround time issue. But it’s also a customer satisfaction issue with the quality of our work. The best way to achieve those things is to have a solid method on a good platform.”

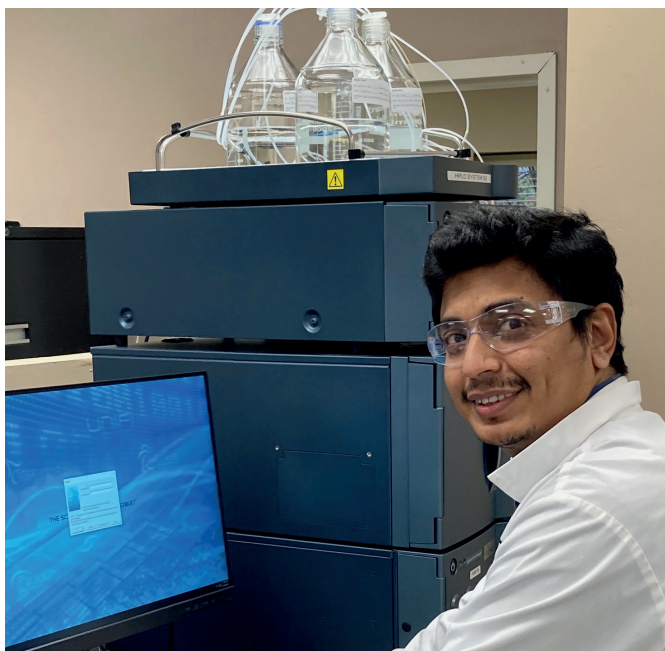
“ We’re always interested in how a vendor like Waters can support us in our instrument acquisition and turnover so we can maintain our instrumentation needs, particularly when repairing or replacing older equipment that’s out of date.”

DR. DOUGLAS TURK

Business Unit Manager, Eurofins BPT Toronto

Poorly functioning older instrumentation in any laboratory can affect downtime, which means an organization is losing money every time an instrument goes down or isn’t performing well. Additionally, such delays and frustrations can potentially damage a company’s reputation for high-quality customer service. Dr. Turk explains:

“There is always an issue with older machines breaking down, repairs, service calls, maintenance. Our approach to instrumentation replacement and selection is a ‘fit-for-purpose’ approach: if our business is growing, we monitor our business needs and supply to meet growth. We also access the CAPEX available across four different business units on site (BPT is one of four groups on site) so if BPT does not have the budget, we are lucky to have four budget pots for the business units on site.”



The risk-based analysis project between Waters and Eurofins BPT Toronto was developed to ensure the lab’s switchover to Waters ACQUITY Arc HPLC would be both seamless and compliant.

RISK-BASED ANALYSIS – VALUE FOR EUROFINS BPT TORONTO AND FOR ITS CLIENTS

Risk assessment is a key element of the quality by design approach and was used in this case to proactively identify the actions needed to ensure the performance of validated analytical procedures on the new LC system.

Using risk-based analysis, laboratories can ensure a smooth method migration between analytical platforms without the need to revalidate. Revalidation is often an extremely time-consuming and expensive effort for CROs like Eurofins BPT Toronto. The data extracted from this approach can also inform decision-making on replacing aging legacy instruments, when comparing cost-in-use with the technical advantages of modern instrumentation in applications like routine quality control (QC) analysis. Dr. Turk explains:

“As a CRO, a number of our assays are based on historical methods that our client has been using for many years. They’re often reluctant to change because these older assays are an important component of their legacy submissions to the regulatory agencies but advances in analytical technology and method development can help them in the long run with time and cost efficiencies. That’s the advantage of taking a risk-based approach, where you’re measuring the potential impact of instrument performance and method transfer before making that decision.”

The process starts prior to the purchase of new technology with a risk assessment of how instrument differences could impact validated procedures, followed by the design of experiments, to determine the severity of the potential impact.

Even if the eventual results support the equivalence of the two instruments without the need for control strategies, completing this level of due diligence ensures confidence in the performance of the new instrumentation. Risk-based analysis is designed to help users:

- Understand considerations to make when purchasing or upgrading LC assets
- Focus on the relevant performance/technical aspects of the instrument specifications
- Predict the impact of a new instrument on the analytical procedure performance
- Proactively prevent issues due to instrument differences by making allowable¹ instrument adjustments to align the differences
- Demonstrate instrument suitability

Ultimately, risk-based analysis helps organizations minimize the variability due to the instrumentation or the methodology.

RETURN ON INVESTMENT

For a CRO, replacing old instrumentation or introducing new technology must meet the company's need for return on investment.

To mitigate the risks of an aging instrumentation base, Eurofins BPT Toronto will look to new technology that can keep pace with customer demands and laboratory throughput, while also considering analytical needs and compliance demands.

Additionally, there's a risk to the laboratory's ability to produce high-quality reportable data – a vital component to any company that works with regulatory agencies. The ever-evolving regulations are a key consideration for the CRO when evaluating both the performance and the value of new instrumentation.

“ We do not compromise on quality, regardless of the type of testing the client requires. We always adhere to regulatory agency guidelines and validation processes. So, whether it is method validation, method transfer, or method verification, we follow all the pertinent regulatory requirements. Every time we've been audited by regulatory agencies, there were no questions with either our validation parameters or our procedures. Evaluating quality was an essential factor for us with this risk-based analysis project.”

MR. UTTAM GHOSH

Department Head of R&D and Validation,
Eurofins BPT Toronto

PROJECT RESULTS – PROVING EQUIVALENCE

The joint project between Waters and Eurofins BPT Toronto followed specific steps in the risk-based analysis process. The complexity of such risk-based studies depends upon the type and extent of differences between instruments and the level of necessary adjustments or controls required to mitigate any potential risk. The phases of the project included:

- Installation of the ACQUITY Arc HPLC System, and running Waters instrument suitability and other necessary tests to ensure the system is in operable condition

- Comparison of the specifications of the customer's current system vs. ACQUITY Arc HPLC System
- Development of risk assessments and control strategies for an isocratic method
- Demonstration of instrument performance comparability with an isocratic method by running reference standards and samples
- Development of risk assessments and controls strategies for a gradient method
- Demonstration of instrument performance comparability with a gradient method, following the same process as above
- Determination whether the ACQUITY Arc HPLC performance is equivalent and does not contribute to method migration failures, with added controls as determined in the risk assessment

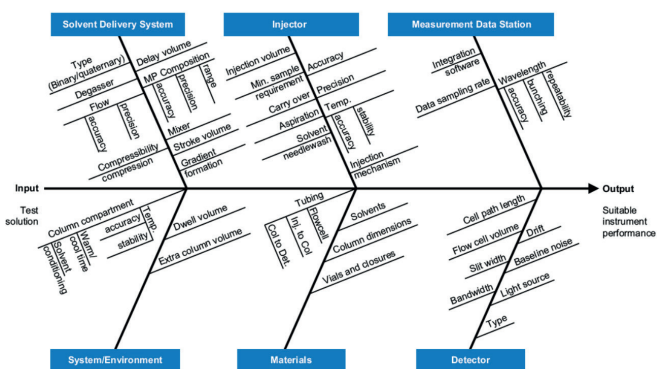


Figure 1. Ishikawa diagram (fishbone) used to identify LC and material-related aspects that could potentially introduce variability into the output of an analysis.

Dr. Turk describes his perspective on the experience:

“If you are a practical person, you might just go right to the result to look at how your method performed on one platform vs. the second platform. However, if you do that, you don't gain the knowledge from comparing the two systems throughout the process. It's beneficial to go through the whole progression in some detail at least the first time. The lessons learned will be useful when considering the replacement of any piece of equipment.”

The risk-based analysis determined if the ACQUITY Arc HPLC System could easily migrate existing methods and reviewed the instrument's ability to achieve equivalent test results without compromising method integrity or changing validated conditions.

Dr. Turk describes the equivalency testing process:

“The whole quality by design process was a learning curve for us. For the comparative testing, we set up our existing equipment and the new Waters ACQUITY Arc HPLC System with the same column, the same injections, the same mobile phase, and the same prep for both instruments. We were running the tests on the same day, so there’d be no issues with mobile phase differences, sample stability or column performance. Everything remained identical as much as possible.”

“ We set the instrument comparison targets at 1% difference in the RSD and 3% difference in the absolute retention times. I’m not worried about an absolute retention time being different if I have a standard that I run it against. But, from a method transfer perspective, if the SOP says 2 minutes plus or minus point 2, and you’re at point 5, that’s not equivalent. So that’s where the ACQUITY Arc HPLC System could be beneficial. The response to the detector was more than adequate, signal to noise was good, and the reproducibility of the injections was spot on. The ACQUITY Arc HPLC System performed very well.”

MR. UTTAM GHOSH

Department Head of R&D and Validation, Eurofins BPT Toronto

WHAT’S NEXT?

The completion of the risk-based analysis for the Waters ACQUITY Arc HPLC System demonstrated to Eurofins BPT Toronto that Eurofins BPT Toronto could migrate methods with confidence from its aging assets to the Arc HPLC in a GMP environment, and that the performance of the methods are comparable on the Arc HPLC. Mr. Ghosh describes his suggestion for future tests:

“The recent study determined the two platforms are comparable. Our next step would be gathering more data over a longer period with diverse methods to give a more complete picture of the instrument. We want to make sure we can perform any kind of project that comes to our door, just like we do now.”

The ACQUITY Arc HPLC has a software feature, Gradient SmartStart, that enables an analyst to easily factor in dwell volume differences between systems, thereby increasing the likelihood of success when translating methods between analytical systems with different specifications. Dr. Turk explains:

“I liked the fact that when transferring assays, the ACQUITY Arc HPLC’s Gradient SmartStart can adjust the injection relative to the gradient start to emulate other HPLC systems’ dwell volumes, without the need to alter the gradient table. That has a practical application to what we do, as it might eliminate some concerns from our customers. I’d also like to test it with ‘dirty’ assays to see how it performs if there’s a gradient with a lot of mixing or there’s reproducibility issues. We’d also like to see how the instrument performs under additional difficult assays.”

ACQUITY ARC HPLC SYSTEM

Ever-evolving regulations are impacting LC-based method approaches for product quality control and beyond.

Count on the ACQUITY Arc HPLC System for high-efficiency separations and quality data to help meet your analytical requirements with confidence.

ACQUITY Arc HPLC allows you to easily replicate and potentially improve the performance of existing LC methods and as part of an instrument replacement program, can help eliminate the burden of aging, less efficient LC systems.

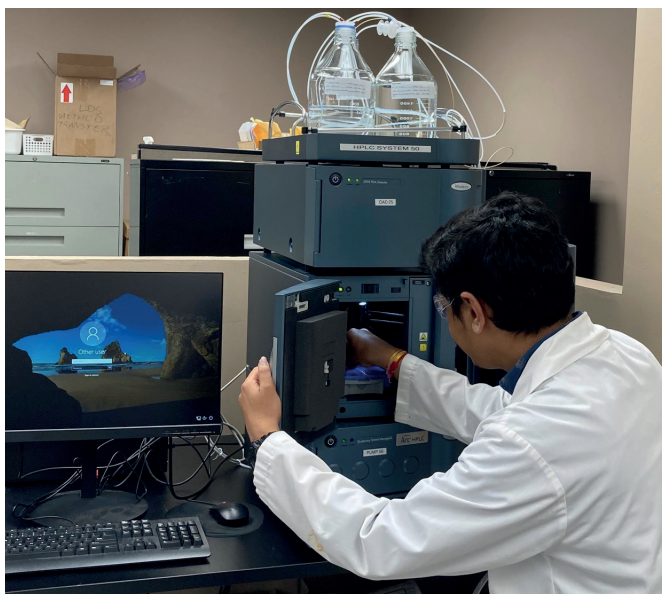
Rugged and reliable, the ACQUITY Arc HPLC delivers the ideal balance of performance and value for right-the-first-time analysis and trusted test results:

- Replicate existing methods on a modern HPLC platform
- Seamlessly receive methods translated from Alliance™ HPLC or other HPLC platforms
- Improve repeatability and consistency of results in comparison with aging HPLCs
- Take advantage of low analyte carryover, high injection precision, and high back pressure tolerance
- Benefit from expert training and method migration support provided by Waters professional analytical services team

EUROFINS BPT TORONTO PERSPECTIVE ON THE WATERS ACQUITY ARC HPLC SYSTEM

With the initial risk-based analysis showing equivalency between his existing LC systems and more modern platforms, Dr. Turk was keen to expand on the experience of having the system in the lab, and explain his impressions and hopes for the Waters ACQUITY Arc HPLC.

This collaboration between Eurofins BPT Toronto and Waters has shown the value of a strong partnership when embarking on such a project.



The project with Waters demonstrated to Eurofins BPT Toronto that methods can be migrated with confidence from aging assets to the ACQUITY Arc HPLC in a GMP environment.

With the support of Waters, Eurofins BPT Toronto will embark on further testing to help determine if the instrument upgrades will aid in the company's ability to maintain its role as a provider of the most comprehensive range of materials testing and certification services for the industry, as well as its reputation for exceptional customer service.

" We're always offering new services and that often gets a new client in the door. That's why we were interested in this risk-based analysis for method migration. We are always looking for opportunities to improve our business and this QbD approach for method migration to newer HPLC platforms is a very useful tool in our toolbox."

DR. DOUGLAS TURK

Business Unit Manager, Eurofins BPT Toronto

References

1. US Pharmacopeia General Chapter <621>.

Waters

THE SCIENCE OF WHAT'S POSSIBLE.™

Waters, The Science of What's Possible, Alliance, Arc, ACQUITY, UPLC and Empower are trademarks of Waters Corporation. All other trademarks are the property of their respective owners.

©2022 Waters Corporation. Produced in the U.S.A. March 2022 720007557EN PM-PDF

Waters Corporation
34 Maple Street
Milford, MA 01757 U.S.A.
T: 1 508 478 2000
F: 1 508 872 1990
waters.com