Automating LC-MS/MS analysis for streamlined clinical testing workflows

Liquid chromatography-tandem mass spectrometry (LC-MS/MS) technology has emerged as an important tool for a wide range of analytical applications. However, the manual, multi-step processes involved in LC-MS/MS workflows have limited its adoption in clinical laboratories. In this article, we look at how the latest automated LC-MS/MS technology designed specifically for the clinical laboratory is simplifying these workflows, allowing laboratory scientists to harness the full potential of this approach.

LC-MS/MS methods have been widely adopted by a broad range of research laboratories, due in large part to their ability to accurately measure multiple analytes in various matrices with high specificity and resolution.

Within clinical laboratories, however, LC-MS/MS methods are used across a relatively limited number of disciplines, most notably endocrinology, immunosuppressant and therapeutic drug monitoring, toxicology, new born screening, microbiology, as well as small molecule, peptide and protein marker analysis. This powerful technique brings many advantages to clinical workflows, enabling laboratory scientists to analyse multiple analytes with greater specificity and sensitivity than alternative methods, such as some immunoassays.

Despite its numerous benefits for patient care, LC-MS/MS technology has not been adopted across the wider clinical setting. One of the biggest barriers preventing its broader use has been the lack of commercially available automated systems that address the specific needs of the clinical laboratory.

The importance of fast turnaround times

Conventional LC-MS/MS workflows typically involve a large number of manual and time-consuming processes. Indeed, while advances in the performance of LC separation and MS analysis techniques mean that measurement acquisition steps now take a matter of minutes to complete, batching of samples, sample preparation, data analysis and equipment maintenance can significantly extend the length of time that must be invested in each sample run. Moreover, the burden associated with manual data entry can significantly lengthen timelines. To ensure quality, further data validation steps are required before final reporting, resulting in significant amount of time devoted to processes that do not add real value to operations.

Traditional LC-MS/MS methods also require users to ensure careful batching and multiple runs need scheduling at appropriate times, which may prove challenging when faced with shift patterns or a weekend testing service. Overall, the labor intensive LC-MS/MS workflows limit sample throughput, while requiring a high level of human input and incurring a significant operating expense. As such, these methods do not fit well with the working practices of the clinical laboratory.

The need for accurate analysis

Manual methods also leave measurements vulnerable to human error. Even when analyses are performed by the most experienced laboratory scientists, these multi-step workflows are susceptible to mistakes, omissions or even small variations in the way protocols are conducted. If errors are identified, repeat experiments are required to correct them. This can significantly add to the time taken to obtain clinically useful insights, prevent timely patient treatment decisions and even undermine confidence in the accuracy of findings.

Given the complexity of conventional LC-MS/MS workflows, and to reduce the potential of human error, the operation of these systems has traditionally been assigned to highly skilled scientists with specialist knowhow. High levels of expertise are also essential for sample preparation and data analysis. As a consequence, many clinical laboratories have been facing the need to train their personnel, which can place an additional burden on budgets and bandwidth.

Automated LC-MS/MS driving process optimization

Analytical methods within the clinical lab must be automated, reliable and provide walk-away capabilities to meet clinicians' need for rapid turnaround of accurate results. By eliminating many of the error-prone and time-consuming manual steps

Cascadion SM Clinical Analyser

involved in traditional workflows, fully automated, random access LC-MS/MS systems are well placed to simplify and accelerate the collection of high quality data. This ability to assess samples quickly, while maintaining a high level of accuracy, would be especially beneficial to those assays that involve more complex processes, since they could be streamlined and automated to simplify workflow.

Undoubtedly, the future of clinical analysis is trending towards the broader adoption of fully automated systems. Automation will greatly benefit LC-MS/MS workflows, making this powerful technique accessible for a wide range of clinical applications, without the need to create a new team of highly trained experts. Laboratories that are already performing clinical LC-MS/MS testing will also be able to better manage their highly trained experts and apply their talents to the development and early implementation of newer, more esoteric, high value analytes – expanding the laboratory's overall service capabilities as a result. Furthermore, while the capital cost of currently available LC-MS/MS systems is relatively high, operational costs related to materials are actually low. If the volume of samples is high enough, then the economy of scale will make cost of ownership comparable to alternative clinical testing methods.

Labs already performing laboratory developed tests (LDTs) using LC-MS/MS may be more resistant to automation. The development and validation of MS assays takes a significant amount of time and expertise, so there may be concern over the impact that automation will have on their existing LDT protocols. However, automation will not be a limiting factor in a laboratory's ability to develop and implement LDTs. Automation has the potential to reduce the need for highly trained staff to apply themselves to the repetitive tasks, allowing them to focus on the development of emerging, clinically needed LDTs.

Meeting the needs of clinical LC-MS/MS analysis

The need for an automated LC-MS/MS system that addresses the unique requirements of the clinical laboratory has led to the development of the new Thermo Scientific™ Cascadion™ SM Clinical Analyser*. Designed to eliminate, automate and simplify many of the manual processes involved in traditional LC-MS/MS workflows, the system gives users all of the power of this important technology in an easy to implement tool.

Owing to its random access capability, the Cascadion SM Clinical Analyser removes the need for long periods of batch loading, and instead facilitates continuous, uninterrupted operation for rapid turnaround of results. This is particularly important for the out-of-hours service and processing of STAT samples. Moreover, by minimizing the potential for human error, the technology is enabling the collection of accurate measurements, the first time around. When implemented in the clinical setting, this level of dependability is helping to accelerate clinical outcomes and deliver real value for clinical laboratories.

Furthermore, because the system can be operated by non-LC-MS/MS experts, experienced scientists have more time to work in other capacities. With more time back in their daily routine, this gives clinical researchers, for example, the opportunity to develop new tests to meet an urgent unmet need or to support better patient care. This level of ease-of-use and simplicity not only relates to run-to-run performance, it also extends to system maintenance too. A recent study from Argent Global Services has found that monthly maintenance takes approximately 18 minutes, meaning that significant amounts of time can be saved and put to better use.

Conclusion

LC-MS/MS systems offer clear benefits for clinical applications. However, the lack of automated systems has posed a barrier to their broader uptake in the clinical setting. Requiring expert operation and the investment of significant time and resources to ensure compatibility with sample preparation processes and data review and reporting systems, traditional technologies have, until now, not adequately addressed the needs of clinical laboratories.

Fully automated, random access LC-MS/MS technology, designed specifically for clinical use, is alleviating these pain points and enabling clinicians to benefit from quality results at high throughputs, while reducing the need to perform repetitive manual tasks. The impact of these systems is benefitting clinical laboratories, helping to improve operational efficiencies and ensure clinicians receive the results they need to make informed treatment decisions in a timely fashion.

**This product is IVD/CE-marked. Product is not 510(k) cleared and not yet available for sale in the U.S.*

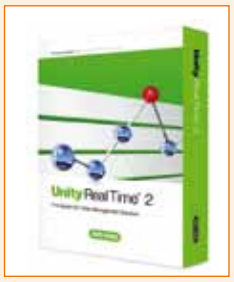
Reference

Zhang V & Rockwood A. "Impact of Automation on Mass Spectrometry". Clinica Chimica Acta 450 (2015): 298-303.

www.thermofisher.com

FRONT COVER PRODUCT

Measurement Uncertainty Report in Unity Real Time 2



Bio-Rad Laboratories recently announced the availability of a new Measurement Uncertainty Report in their Quality Control Data Management Software Unity Real Time 2 Service Pack 5 upgrade. Under ISO 15189, Measurement Uncertainty is a mandatory requirement and allows labs to calculate their analytical test dispersion. This new report allows laboratories to calculate their Measurement Uncertainty according to one of three different calculations. The three different calculations include the standard expanded Uncertainty based on the lab's imprecision (consistent with RCPA and NABL), and two combined expanded uncertainty calculations which contain either the bias or the calibrator uncertainty (consistent with the SH GTA 14 Guideline from France).

Unity Real Time 2 is Bio-Rad's expert QC Data Management solution for desktop users which facilitates compliance under CLIA and ISO 15189. It provides run validation with real-time bench and supervisor QC data review with comprehensive audit trails. It allows labs to participate in Bio-Rad's Unity Interlaboratory Program with over 50,000 participating instruments. All QC data can be uploaded from any LIS, middleware or instrument via the Unity Connect software. Users can also reduce non-essential retests with Analytical Goal options and implement the best QC rules with the Westgard Advisor or use Bio-Rad's latest QC design tool Mission: Control which provides a risk based approach to Quality Control.

http://www.qcnet.com/datamanagement/

BIO-RAD

i www.clinlabint.com & search 27730