Is LC-MS/MS assay development restricting your clinical testing services?

Accelerate the implementation of LC-MS/MS technology in your laboratory using dedicated systems with complete pre-validated assay kits for specialty diagnostics

Advanced liquid chromatography-tandem mass spectrometry (LC-MS/MS) systems usher in a new era of rapid, effortless implementation of this powerful analysis tool for clinical laboratories. Featuring complete pre-validated assay kits as standard, the systems are poised to provide results for an expanding range of the most sought after clinical tests.

Clinical laboratory professional scanning solvents on the Thermo Scientific™ Cascadion™ SM Clinical Analyzer for specialty diagnostics

Setting the scene

Ongoing improvements in LC-MS/MS technology are expanding the possibilities in clinical analysis. The exceptional sensitivity, specificity and accuracy of the latest systems mean the technology now offers significant advantages over more established methods, such as immunoassays, across many applications.

Despite this exceptional performance, challenges around developing and implementing LC-MS/MS based laboratory developed tests (LDTs) means the technology has been largely limited to only the most specialist laboratories. A lack of standardized tests can also have a negative impact on the accuracy and consistency of patient results across different laboratories.

The latest technological advances have seen the introduction of LC-MS/MS systems that have been developed to effectively overcome these challenges, allowing any clinical laboratory to quickly implement this powerful analytical technology and start reaping the benefits.

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Limitations of immunoassays

A large proportion of clinical tests still rely on traditional immunoassays, the manufacture of which is very time consuming as it involves engineering highly selective antibodies to bind to the target analytes. However, antibodies may be very difficult, or even impossible, to generate for certain target molecules, while many antibodies cannot distinguish between small differences in antigens[1], meaning that many molecules are beyond the detection capability of immunoassays.

Additionally, some immunoassay reagents can be expensive to obtain and may also be subject to quality issues due to cross reactivity and interference (immunoassays tend to be susceptible to interference from other reactive molecules, resulting in lower specificity[2]).

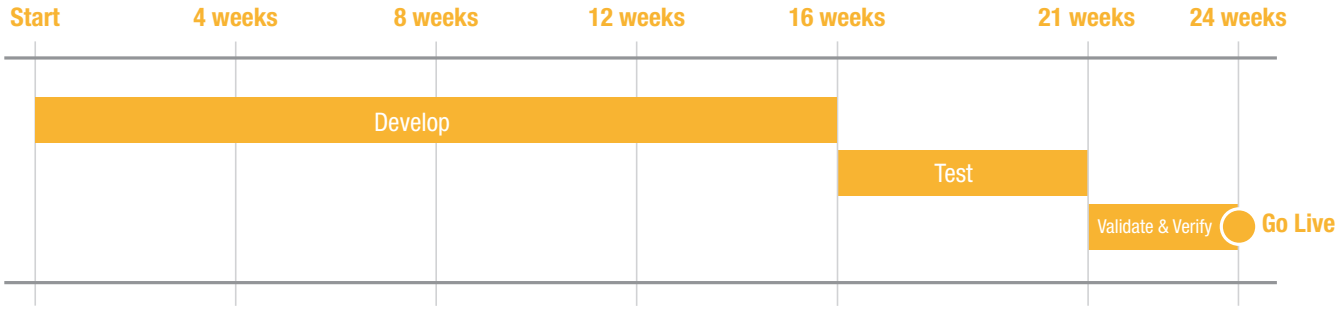
Limitations of open LC-MS/MS systems: Why these are only half of the solution

Conventional open LC-MS/MS systems entail developing, validating and implementing LDTs, which can be a very labor-intensive process, involving complex, manual workflows that require a high level of specialist technical knowledge.[3] This is also a very time-intensive process[4], with the total time from initial development through to clinical availability varying greatly based on the level of LC-MS/MS experience of laboratory professionals. Experts need approximately three months, those with average knowledge require around six months and novices may take eight months or more to complete the process. Given that most routine clinical laboratories lack the necessary specialization, developing, validating and implementing LDTs can prove very challenging.

Most commonly, LDTs are also being developed and implemented on a laboratory-specific basis, resulting in a large degree of inter-laboratory variability.[5] Furthermore, calibrators, controls, internal standards and other assay elements need to be individually sourced from multiple vendors[6], further amplifying the intra- and inter-laboratory method variability issue. Overall, the lack of standardization limits the consistency and reproducibility of results.[7]

These challenges highlight the need for an easy-to-use, turnkey solution to accelerate assay implementation and meet the need of clinical laboratories for ready-made, pre-validated assays. In response, Thermo Fisher Scientific has developed the Thermo Scientific™ Cascadion™ SM Clinical Analyzer for specialty diagnostics, a fully automated, fully integrated, easy-to-use and random access LC-MS/MS system designed specifically to allow a far greater number of non-specialist laboratories to access the power of LC-MS/MS technology for clinical testing in routine workflows.

Laboratory Developed Tests on Open LC-MS/MS Systems
Assay Implementation
Avg. cycle time (in weeks)*



*Implementation time varies for each lab based on:
1. Experience / expertise
2. Resources / funding
3. Complexity of molecule
4. Panel vs. single analyte

*Average time frames:
Expert: ~3 months
Moderate: ~6 months
Novice: ~8 months or more

Source: Voice of customer insight and interviews

The benefits of ready-to-use *in-vitro* diagnostic manufacturer-provided LC-MS/MS assay kits designed specifically for clinical laboratories

The Cascadion system offers four key advantages for clinical laboratories in terms of shorter assay implementation times, an expanding range of clinical tests, streamlined random access testing workflows and improved standardization. Jouni Sallinen, Director of Product Management, Clinical Mass Spectrometry at Thermo Fisher Scientific, explains these benefits in more detail.

Jouni Sallinen, Director of Product Management, Clinical Mass Spectrometry at Thermo Fisher Scientific

Rapid assay implementation

The implementation of LDTs using traditional open LC-MS/MS systems is often time- and resource-intensive, and involves lengthy assay development, testing and validation steps. This process can take anywhere from several weeks up to eight months or more to complete. For a typical clinical laboratory, the average time required to implement an LDT is approximately six months.

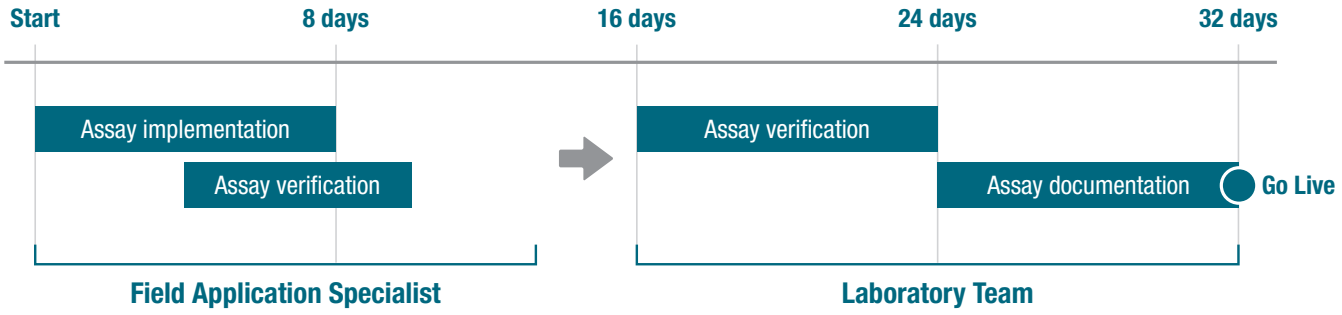
"One of the biggest advantages of the Cascadion system is the ease and speed with which assays can be made ready for routine use," explains Sallinen. "The system enables assay implementation and verification to be completed in just a few weeks."

> The Cascadion system enables a 70% reduction in the total time a laboratory needs to invest in implementing ready-made assays to routine clinical testing applications.

To support this capability, Dr. Yasmin Wissinger, Field Application Specialist at Thermo Fisher Scientific, recently implemented the Cascadion 25-Hydroxy Vitamin D assay in a clinical laboratory in the UK as part of a beta-trial evaluation.

"I couldn't imagine an easier or quicker implementation," says Dr. Wissinger. *"All I had to do was to upload a single file containing all assay parameters to the Cascadion system, which then calibrated the assay and performed a QC check to verify data validity, before proceeding with analyzing the patient samples. The entire implementation process took me just half a working day!*

Turnkey Assay Kits on the Cascadion SM Clinical Analyzer
Assay Implementation
Avg. cycle time (in days)



Source: Internal process standard, Thermo Fisher Scientific and average customer experience

"This rapid assay implementation means that clinical laboratories can have the Cascadion system up and running very quickly. With customer service and support at our core, we assign our own personnel to upload the assays and set the laboratory-specific parameters together with our customers. We also offer a Key Operator Training Program to ensure that even non LC-MS/MS experts will be able to operate the Cascadion system and run the assays with minimal effort."

Dr. Yasmin Wissinger, Field Application Specialist at Thermo Fisher Scientific

Expanding menu of assays

For any integrated clinical analysis platform to be of real value in the laboratory, it must offer an extensive panel of assays that meet real healthcare needs. Thermo Fisher is actively developing a range of assays that are specifically designed to meet the evolving needs of clinical laboratories, and is committed to expanding this menu of standardized clinical tests in the future.

"The Cascadion system currently offers an IVD/CE-marked 25-Hydroxy Vitamin D assay, with a range of specialty assays and a panel of immunosuppressant drugs in the development pipeline," says Sallinen. *"This offering is expected to further increase to cover several hundred analytes, with a particular focus on therapeutic drug monitoring, endocrinology and drugs of abuse applications.*

"Clinical laboratories increasingly recognize the potential to improve the services they offer using LC-MS/MS based assays. Investing in a fully automated, random access analyzer featuring a range of built-in assays of high medical value can offer a real competitive advantage in terms of output and service quality. As a leader in the manufacture of LC-MS/MS analyzers, reagents and other critical components, Thermo Fisher is ideally positioned to deliver on what clinical laboratories have very clearly asked for."

The IVD/CE-marked Cascadion 25-Hydroxy Vitamin D assay kit

Standardized, closed system

Standardization is an important requirement for clinical analysis applications, as tests must be able to deliver accurate and consistent results, regardless of the laboratory in which they are performed. LDTs are developed using multiple components, potentially from different manufacturers, which may require frequent adjustments over time.

"The very nature of LDT's means that even the most well-developed assay from a particular laboratory may be different to that from another laboratory also using LC-MS/MS technology," explains Sallinen.

To address this issue, the Cascadion system offers a closed system with built-in pre-validated assays designed to deliver highly reproducible results.

"As the system is IVD/CE marked for clinical testing use within the EU, all relevant regulatory requirements have been met in advance, simplifying and accelerating the implementation of assays in the laboratory," says Sallinen. "Additionally, the Cascadion 25-Hydroxy Vitamin D assay has been certified by the Centers for Disease Control and Prevention, and the included calibrators and controls are traceable to reference standards."

Overall, simplification of assay implementation facilitates greater standardization of clinical testing, which could make these reliable and reproducible assays available to a much broader range of laboratories, delivering enormous benefits to the healthcare system.

Integrated, all-in-one solution

One of the biggest challenges associated with applying research LC-MS/MS assays to clinical testing applications is the need for multiple connected components. In many ways, LDTs are like a recipe made up of many ingredients in a custom manner that takes lots of planning, preparation and experimentation to get just right.

The future lies with turnkey, plug-and-play LC-MS/MS assay kits, where the manufacturer holds the sole responsibility of bringing all necessary elements together on a standardized, easy-to-implement system to the benefit of laboratories.

"Let's be clear that there still is a need for immunoassays and LDT's - the Cascadion system will not replace them entirely," states Sallinen. "However, clinical laboratories now have a new solution available to them that allows for select assays to be better served on a system that is quicker and easier to implement, and designed to improve the quality of the generated results.

"The Cascadion system is fully integrated, allowing clinical laboratory scientists to run pre-validated tests using a single sample injection on one analytical instrument. Streamlining workflows in this way not only improves the reliability of data, it also offers the potential for shorter turnaround times, allowing clinical decisions to be made with greater confidence, more quickly."

Conclusion

LC-MS/MS technology is a powerful tool for clinical testing with the potential to improve the accuracy and speed of clinical decision-making. However, developing, validating and implementing LDTs by adapting existing LC-MS/MS technologies that were primarily developed for research use is both time- and resource-intensive, while also requiring significant technical expertise which is not always available. As such, clinical laboratories tend to rely on immunoassay methods that may suffer from poor specificity and may be unable to address all target analytes.

The Cascadion SM Clinical Analyzer for specialty diagnostics offers ready-to-use pre-validated assays, designed specifically for the clinical laboratory. This fully integrated, random access system allows clinical laboratories to take advantage of the unique analytical benefits of LC-MS/MS technology to quickly and easily run assays to generate consistent, reliable results with fast turnaround times. Supporting an expanding menu of assays, the Cascadion system allows laboratories to broaden their service offering to include therapeutic drug monitoring, endocrinology and drugs of abuse applications.

By simplifying and accelerating assay implementation, along with offering a growing test menu, the Cascadion system could make the 'gold-standard' of LC-MS/MS technology available to a wider range of clinical laboratories, ultimately benefiting physicians, patients and the wider healthcare system.

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