Case study

Applying LIMS to streamline lab operations at Patheon Pharma Services

The deployment of a new Laboratory Information Management System (LIMS) software solution across a world-leading global Contract Development and Manufacturing Organization faced much of the configuration and implementation process during the unforeseen challenges and unavoidable operational detritus brought by the global pandemic. The immediate and game-changing impact on the efficiency, management and output of the laboratory function and resources provided unquestionable business benefits.

Overview of Patheon pharma services

Patheon pharma services provides integrated, end-to-end capabilities across all phases of development, including the manufacture of active pharmaceutical ingredients (APIs), biologics, formulation, clinical trial solutions, logistics services and commercial manufacturing.

Their site in Cork, Ireland, has championed science to serve patients globally since its inception in 1975. The object of the site endures to this day: as a pharmaceutical manufacturing plant making complex ingredients for medicines that treat diseases such as Cancer, Parkinson's, Depression, HIV and Diabetes.

The plant was procured and incorporated into Thermo Fisher Scientific in 2019, strengthened by its rich legacy of serving pharmaceutical science and underpinned by an incredibly dedicated workforce. It contains 270 cubic meters of reactor capacity, 10 production buildings, an R&D pilot plant and lab infrastructure to support process development, and the scale-up and physical characterization of APIs.

With over 400 skilled personnel, many of whom have worked at the location for over three decades, the Cork site continues to grow its capacity to manufacture APIs for medicines. This work shapes its collective and unerring drive to serve cutting-edge medicine, but also to support STEM education, partnerships and apprenticeships with local school colleges and universities around Cork.

Business challenges

The site's capacity was previously underutilized, and a drive by Thermo Fisher to increase investment globally into manufacturing operations has allowed the Cork team to ramp-up its capacity to meet growing customer demand for complex APIs. The site will develop production capacity for a range of global pharmaceutical organizations.

The change of ownership and incorporation into Thermo Fisher also provided the plant with the ideal opportunity to change its existing LIMS software. The maturity and specific configuration of the existing LIMS created inherent challenges and limitations for the team, such as being unable to check certifications, or easily extract data from both the LIMS and certificates of analysis. Manual processes were subsequently introduced, as the existing LIMS was lost through the transition.

Solution

The team, led by the Laboratory Applications Lead of Patheon pharma services, planned to implement Thermo Scientific™ SampleManager™ LIMS software, to replace their existing LIMS. The new system would be hosted on Amazon Web Services (AWS) Cloud.

The installation comprised a roll out across sites globally, where the business wanted to have a unified enterprise-level LIMS solution, across the breadth of the organization, to help share best practices and push the business towards a digital Pharma 4.0 operating model. The Cork site has led the global deployment and is paving the way for the other global sites to come on board. While each of these sites are at different stages of deployment, the Cork team can now advise the others, and share best practices on subjects such as instrument integrations, Lab Execution System (LES) method development, and static data share.

As a modern software solution, SampleManager LIMS was deemed to meet not only the validation and compliance, testing and analytical reporting needs of the business, but was also expected to accelerate the group's ability to move quickly on innovative products, adhere to manufacturing process, and ensure the quality, validity and compliance of analytical results.
The investment in a global solution would help the business scale up and position for the future, with a high degree of automation, and paperless digital processes, through an interconnected, easily accessible enterprise platform. The system would enable senior management easy access to amalgamate the data, and create actionable insights on the pharmaceutical products, based on the facts.

Installation

The upgrade and renewal of the LIMS was inevitable for the site, (and while the team worked on the project planning in advance), the impact of the pandemic and subsequent lockdown meant the team had to adjust to working from home during the initial implementation.

The project was initiated 12 March 2020 during the COVID-19 pandemic and lockdown. Shortly after the project was underway, with only mandatory site-based operations going ahead, analysts had to rely on a combination of online training, and training on the job. The implementation team also ensured regular interactions, guidance and training support calls from the central Thermo Fisher support team.

To ease the transition from previous LIMS, the team complied a spreadsheet of their existing data and specifications, prioritizing the capabilities they would initially need, and with the plan that others would be added as required. This approach meant minimal reliance on IT, to avoid unnecessary delays.

> "You can tell the Thermo Fisher support team have worked as LIMS System Managers themselves. They understand our issues and know how best to fix them. They know how we need things to work."
>
> —LIMS Specialist
> Patheon pharma services

The restrictions had an obvious impact on the installation plan, as well as the subsequent planned enhancements in the configured software; however, the team were able to roll out further capabilities in April 2020. This included the addition of several features: multi-level parameters (MLP) for materials specification; sample lifecycle; product workflow; interface to their Waters® Empower™ Chromatography Data System (CDS); Certificates of Analysis; and specification reports.

Following the introduction of those features, an evaluation determined the most valuable capabilities to add. In July 2021, stability management was deployed, and in June 2022, the Laboratory Execution System (LES), consumables management and simple instrument interface were added.

The team continues to be supported – by Thermo Fisher Scientific's Global Laboratory Office (GLO) and support team, who are on hand to guide not only the design of the SampleManager software configuration, set up and installation of the system, but also to provide ongoing support and training.

Impact and benefits

The software has brought significant operational benefits to the site, and to the wider Patheon pharma services business, some more pronounced than others.

- **Multi-Level-Parameter (MLP) specifications**—SampleManager software has better equipped the team to manage MLPs, which was easy to set up and configure, and offers an equally simple approvals process. The team reported that MLP specification management is much easier than in their old system, simplifying parameter visualization on a single screen with tabs for different specifications.
- **Certificates of analysis**—The ability for the system to produce certificates of analysis is relished by the team. Certifications are now easily configured, in stark contrast to previously requiring considerably more time to manually generate, and for peer review. The team can now easily check certifications directly in the software before they are issued, markedly cutting down on time needed for this process.
- **Simple instrument interface**—The simple instrument interface capabilities strengthen data integrity and also add to the time saving benefits of SampleManager LIMS, by easing data recording and peer review.
- **Simplified regulatory compliance**—Ireland's Health Products Regulatory Authority (HPRA) are very impressed with the LES capabilities in SampleManager LIMS and the Cork team's ability to demonstrate its benefits. On seeing that the system was able to check live in the LIMS for staff training records and instrument calibrations, to ensure acceptability for use in the lab's workflow, the HPRA regulator was satisfied that processes were being executed in a compliant way.

  In the same vein, the Cork site also has to demonstrate compliance to the Food and Drug Administration (FDA), and host multiple customer audits. Across all audits, the fact that SampleManager software can highlight critical steps in an execution to draw an analyst's attention to important points and confirm actions, has also been commended. The software provides assurance that steps are being performed repeatably every time – previously analysts could interpret SOP steps differently, or perform actions inconsistently, causing variances in outcome – now with SampleManager software, they are driven to perform them each time in the same way, and in the same order.
- **Process compliance**—According to the team, the most significant benefit has been brought about through the configuration of the Laboratory Execution System (LES). The team describe this tool as a 'game changer' for the Cork lab.

  Through its ability to support instrument calibration, instrument usage, oversee calculations, method limits, and competency training, LES alone has transformed how the team now work.

  LES method data or results can be sent to samples, instruments or reagent stock batches. It can help to ensure:

  - the lab's instruments are calibrated prior to use
  - all reagents are within expiry date prior to use
  - that analysts are competent to perform analyses
  - that results are within an expected range and volume ratios are within limits for reagent preparation
  - that all weights from balances are automatically recorded
  - that data is recorded in real-time
  - that labels can be automatically printed
  - that all changes are captured in an audit trail – with a change reason sent for review

  Perhaps more pragmatically, it enables the team to remove the need for worksheets, logbooks and validated spreadsheets, bringing time saving advantages for the team's analysts—particularly around subsequent peer review activities—and by providing the team with the ability to automate tasks in the lab, such as automatically updating stock batches and printing labels.

  Before the configuration of the LES, up to eight laboratory staff were required for peer reviews. The team previously had fourteen validated spreadsheets for items such as reference standards, instrument usage, stability testing and calculations. Staff had to do a lot of arduous administrative work, just to keep these documents up to date, and therein a lot of paper was needed to document every single product release – approximately twelve sheets of paper including countersigned balance printouts per review. Not only was the manual element of paper processes a burden, but with all the paper records having to be held in an archive, this was an additional storage and archival cost to the business. Previously even PDF documents were created, in addition to the manual paper records, as a backup, in case print outs would fade over time. Now with the LES a single certification of analysis is created and stored electronically. The raw materials lab in Cork used to have at least fifteen logbooks in use at any one time – the lab is now entirely paper free.

The LES is set up so the team can automatically accept instrument readouts from integrated instruments such as balances, pH meters and density meters. Previously, manually transcribed data was error-prone and needed to be sent for review – taking additional time and involving another person.

LES executions make processes simpler and more efficient. For example, balance calibrations would take a member of the team over an hour and require an additional person to approve the calibrations. There are 15 balances in the Cork lab, each one requires one monthly calibration and one weekly calibration. This amounts to 960 calibrations every year. With SampleManager LIMS, one calibration takes an analyst approximately eight minutes to complete rather than more than an hour. In summary, this saves 832 hours each year of analyst time.

Alongside the time saving benefits on balance calibrations, the team are also reporting the same time savings across the board, through the application of LES in-lab processes. Another example is assay analysis. A complex assay calculation for multiple chromatography runs for a single product would have previously taken an experienced analyst approximately three to four hours (for five-to-six batches) to write out the calculations, check instrument calibrations for balances and HPLC instruments, method versions, print out weights and stick the results into log books, and therein undertake peer review. Using the LES in SampleManager software, this is reduced to just 10 minutes. This leaves Cork's Senior QC Analyst free to focus on other work, and not waste time on a dated review process. Also, the LES doesn't allow analysts to start a new execution if they have another already in progress, to ensure outstanding work is completed.

"Previously, assay analysis was very labor intensive and time consuming. The time reviewing was crazy – several hours just for one analysis. The LES is brilliant, I'm very impressed with it. Everything is in one place."

—Senior QC Analyst
Patheon pharma services

SampleManager software provides robust reagent management capabilities. To survey the stock and condition of reagents, the team used to have to set and manually type in a unique 21-character number. This process was prone to human error, and the team report inevitable duplicates because an incorrect number had been entered. Now, the team are able to simply scan reagents, and their expiry dates are automatically held in the software – this again brings an added level of comfort, as the ability to have a consolidated, centralized view of reagents, better supports regulatory compliance, since the system can check on reagents during executions, to be sure they are in date and safe to use. The team can also view reagent use per client, which enables them to bill specifically for reagents used for their projects.

As a direct result of using SampleManager software, the team have been able to clear a backlog of tests. The site was also able to significantly increase manufacturing capacity.

"Using SampleManager software has meant a reduction in testing backlog and cycle times, even with this increased capacity."

—LIMS Specialist
Patheon pharma services

- **Data visualization**—SampleManager LIMS enables the team to view data through dashboards, displaying key insights from the lab, including resource availability, stock information, location status, and lab performance in a clear interactive format. A connection to Microsoft Power BI delivers powerful knowledge from the data stored in SampleManager LIMS. Within Power BI, the lab has set up a dashboard of pending samples and other KPIs, which helps support shift planning. This dashboard automatically updates three times a day to show the current jobs in queue. This eliminates the constant maintenance of a physical wall planner in the lab.
- **Staff training**—All training records are now noted in SampleManager LIMS. This is has a positive impact on the management of the lab, as SampleManager software won't allow analysts to execute a process if they are not qualified in a process or instrument that is required. Previously, training used to have to be checked manually, again this procedure in itself was prone for error.

> "Workflows are really powerful to pull data from instruments into the LIMS. SampleManager LIMS is much more capable and more flexible than our previous system."
>
> —Laboratory Applications Lead
> Patheon pharma services

- **Capacity**—SampleManager software has again freed-up analysts, to allow them to work more effectively. They have been able to increase the number of clients and manage their API's with the same level of care. The team now have over 20 clients – meaning they have more specifications to manage than ever before, something they couldn't have done without SampleManager LIMS.

SampleManager LIMS is undoubtedly relieving the burden to ensure adequate and consistent data collection, allowing the entire team focus on science.

The software helps the team reduce, and even eliminate as much human error as possible. The team can now do their work in a very standard way, supported by the software. Innovation is fostered as the site's analysts are less encumbered by having to record the data, and instead can focus more on what the data and the results mean. SampleManager LIMS is a powerful tool to much more quickly analyze, interpret and report the complex data taken from various sources in the lab, and as a result speed the delivery and capacity of a quality API output – this ultimately builds critical trust in the capability of the site to produce excellent products.

The move to SampleManager software, also benefits customers through a more seamless experience as they work with the site. For example, certificates of analyses, stability protocols and reports generated, will now follow a unified common format worldwide. As a Patheon pharma services customer prepares regulatory submissions, being able to quickly consolidate stability data, will simplify product registration to achieve quicker and more efficient approvals. This ultimately means that patients can benefit from medicines and treatments being available for use, delivered using high quality processes.

Future roadmap

Patheon pharma services continually evaluate their solution to determine a path for further enhancements to the software. This will include an SAP interface to enable automatic product release – once sample data has been authorized then the approval is sent to SAP to release the batch.

The team will also deploy capabilities in the software to implement reduced testing protocols - these are currently managed on paper, which leads to errors - tests are done that are not required and vice versa. Managing this in SampleManager LIMS will help to make this far easier and more efficient.

Another planned addition is the Environmental Monitoring (EM) programs that are also currently managed on paper. The team must deliver quarterly water reports for their process and purified water to the Irish Environmental Protection Agency (EPA). Like many of their paper processes, this is also very arduous and time consuming. The team are currently unable to really identify any trends in the data – and look forward to being able to do this more easily once EM is managed in the LIMS.

Summary

The global installation of SampleManager LIMS at Patheon pharma services has been transformational, supporting an enhanced operation model, and enabling digitally connected laboratories, as the organization moves into the Pharma 4.0 future. The core of this is the robust IT foundation that the software brings, and the ability of the solution to evolve with the changing needs of the business, supporting informed product quality decisions.

SampleManager software connects manufacturing data, stability and release data, and pulls this together, integrating these once disparate systems, delivering holistic knowledge that is vital to delivering critical pharmaceutical products to global customers with speed and agility.

Learn more at **thermofisher.com/samplemanager**