

Pathfinder™ implements a 'Quality Information Management System' at AstraZeneca

On April 6 1999, the merger of **Astra AB** and **Zeneca Group PLC** created one of the world's top five ethical pharmaceutical companies. AstraZeneca has approximately 50,000 employees worldwide, is active in more than 100 countries and, in 1999, had healthcare sales of over \$15 billion, with an operating profit of \$3.5 billion.

Company:

AstraZeneca

Industry Sector:

Pharmaceutical

Environment:

Manufacturing

Software Used:

SampleManager™

Platform:

Windows NT®

As a result of the merger, AstraZeneca now enjoys a world-leading position in the areas of gastrointestinal medicines and anesthesia. Other therapeutic areas in which it specializes include cardiovascular, central nervous system, infection, oncology, pain control and respiratory disease. Pharmaceutical production at AstraZeneca employs over 12,000 people in plants in twenty countries. While Production at AstraZeneca fully recognizes all of its business responsibilities, product quality takes a very high priority.

QIMS (Quality Information Management System)

In 1994, prior to the merger, representatives from Astra Pharmaceuticals' three main production sites in Sweden began to address future requirements for LIMS (Laboratory Information Management Systems), primarily driven by Y2K compliance which was becoming a key

strategic issue at Astra. It was agreed at a very early stage that what was required was a QIMS (Quality Information Management System) rather than strictly a LIMS. Essentially, their vision was to create a system to ensure the consistency and quality of product throughout the whole manufacturing process.



Production in Sweden

The three Swedish locations were Astra Production Liquids (APL), specializing in injection and inhalation productions, Astra Production Tablets (APT) and Astra Production Chemicals (APC). The three sites were running an in-house developed LIMS which was over 10 years old and not Y2K compliant. System maintenance was proving expensive and the old technology required specialist skills to support it. Additionally, the system was character-cell based and the benefits of moving to software that resembled the Microsoft® Windows interface were recognised by the Astra project team. An intuitive and familiar menu-driven system, together with the associated rapid, steep learning curve for new users was a particular attraction of a Microsoft Windows® interface.



Key functional requirements

In terms of functionality, a fundamental requirement of a replacement QIMS was the ability to be able to track materials from delivery of main ingredients to the warehouse, through production, testing and quality assurance to packaging and removal from the site onwards to customers. In the past, information regarding a certain batch of product, its status and location was communicated via faxes and/or telephone.

Astra did not want warehouse staff using two systems - ie. a system for shipping and a LIMS to register deliveries. The project team realized that good communication between the systems was required. Therefore, an interface was required by which warehouse staff could register delivery of goods in the warehousing system, and automatically get a report of the sampling requirements and sample labels from the LIMS. The report and labels were needed to move samples to the laboratory. Additionally, as warehouse staff were drawing off samples themselves they needed easy access to additional information on the different methods of retrieving samples.

Also, Astra did not want Quality Assurance staff to be required to log into two systems. They also wanted to use the new solution as an interface to decide the status of materials through the manufacturing process. To this end, information from other systems needed to be able to be reviewed through the LIMS, and quality decisions made in the LIMS communicated throughout the organization.



The replacement project

From an initial feasibility study which began in the second half of 1994, Astra embarked on a 2-year specification process, conducting a comprehensive business analysis of their requirements for a QIMS. There was uniform agreement that all departments and all processes would be involved, from delivery to accounts. In 1996, it was realized that it would not be possible to develop the system in-house in time for the turn of the millennium, so the requirements were put to tender.

From a vendor shortlist of five companies, an intensive evaluation of Thermo LabSystems' SampleManager was conducted in Spring 1997. The evaluation went well and in the September, Astra Production Liquids (APL) awarded Thermo LabSystems the contract. Members of the APL project team placed much weight on Thermo LabSystems' track record of delivery in the pharmaceutical industry and its large customer base. Of equal importance was that APL was satisfied it could develop a strong business partnership with its vendor of choice.

SampleManager is a well established LIMS, designed to support laboratory operations and integrate those operations into the corporate enterprise. Even in the early stages of the project, the strength of SampleManager as an enterprise-centric solution appeared to be a good fit with Astra's requirement for a QIMS across its manufacturing operations. It features standard integration interfaces to solutions such as SAP R/3 enterprise resource planning system and AspenTech's InfoPlus.21 process information management system. Thermo LabSystems also supports its integration with leading laboratory instrumentation and desktop applications, using a number of accredited interfaces.

Thermo LabSystems operates a global services arm to its business. This worldwide team, Pathfinder, is responsible for services such as system implementation and validation, consultancy and business analysis, and project planning and management.

Over the last few months of 1997, a series of twelve workshops was facilitated by Thermo LabSystems Pathfinder and APL project teams. A maximum of twelve attendees underwent five days product training prior to each workshop. Workshops benefited from being composed of personnel from different departments.

The workshops were key to giving Thermo LabSystems Pathfinder a sound understanding of APL's workflow, the real requirements of its end users and deciding how best the SampleManager LIMS could be optimized to meet its requirements. The workshops were successful in bolstering the end-user 'buy-in' required and helped in user familiarization of the software and its capabilities. 'What is a sample?' may seem an elementary question, but in terms of APL's use of SampleManager, it was the type of point that needed resolving. During this period it was realized that all static data would require redefining.

Each workshop resulted in two protocols, one in English and the other in Swedish. These were compared and verified and issues were numbered and color-coded. Red signified an issue to be resolved, green indicated standard functionality in SampleManager and blue meant an issue that required either customization or configuration. The goal was to have no red issues at the end of the workshop process. The whole process resulted in a single functional specification and design specifications for fifteen new functions. In hindsight, APL now consider that insufficient time was given to the review of these documents, however due to constraint of delivery timeframes ahead of Y2K, spending any more time in reviewing was not deemed possible.

The new development commenced in early 1998 at Thermo LabSystems UK office. It involved both production and Pathfinder implementation specialists and, in order to meet the Y2K deadline, some prototyping ran alongside the design specifications phase.

A year into the implementation the project at APL was progressing to schedule, and the analysts had made considerable progress. By November 1998, APL had a well-documented system and the implementation project had been delivered on a number of critical build phases. On the strength of this progress at APL, Thermo LabSystems was invited to step in to investigate the possibility of integrating all three production sites on the SampleManager LIMS.

The Pathfinder team still had to analyze the APH and APT business requirements, so it was decided to run a series of nine combined workshops, the aim of which was to ascertain the specific requirements of the two other companies. In each case, Pathfinder encouraged the involvement of as many end users as possible. The workshops also served to introduce users to the replacement system and its capabilities.

Requirements and deliverables

Astra use ISO statistical methods to calculate sampling sizes for some components of their products. Determining the correct sample size involved manually searching complex tables for the correct values based on the batch size and various quality criteria. Thermo LabSystems automated this process by enhancing the standard product specification functionality to include the statistical quality information. This means that the statistically correct number of samples could be calculated automatically and sampled when the components are received, improving efficiency. The role of the technicians also became much simpler as the need for the complicated procedures and look-up tables was removed.

Astra also had a requirement for tracking details about samples, for example who should take samples, where and when. New functionality was required to help in the prediction of the laboratory's workload - previously the laboratory was only aware of work as it physically appeared for processing. This work-list and planning functionality would mean that the laboratory could plan its workload in advance, before samples were received, ensuring a smoother workflow. With the new module, samples are now received electronically as they arrive at the correct location, and marked as 'sampled' on the plant floor. This provides additional 'chain of custody' information throughout the plant and means that some of the sample retrieval and distribution could be done wholly in stores and on the plant, freeing up laboratory personnel and speeding up throughput of samples.

A new sample plan and test module now provides operators with automatically generated worksheets detailing the tests and samples that should be created, depending on the type of material being received and the supplier. Additionally, if Astra is buying supplies from a known, approved supplier then time can be saved by using rules-based testing, which provides reduced testing of product of a known quality, assessing the appearance and purity as quoted by the manufacturer.

Analytical worksheets was another feature that Astra wanted to enhance. Astra wanted to be able to track the location and progression of a sample through its life cycle and an efficient way of dividing the workload once in the laboratory. Each laboratory requires its own sample of a batch to allow analytical work to be performed in parallel. Once in the laboratory the testing to be performed needs to be easily allocated to the different analytical stations. The sample planning functionality allows the user to decide, for a batch, which tests should be performed in which laboratories. Enhancement of the worksheets functionality was also required to allow worksheets to be printed by analytical station.

A feature to manage batch disposition was a further requirement of Astra. In SampleManager, decisions on batch quality are made in the LIMS, so that a batch is assigned a quality status. This disposition information is sent to the other systems at Astra such as warehousing and MRP (Manufacturing Resource Planning) systems to allow the batch to be moved or processed further.

Astra also required Certificate of Analysis functionality, providing a summary of analytical results to compare against the requirements of the specification, stating how the analytical results conform to the specification. SampleManager now allows similar certificates to be generated for different products, customers and countries using an easy-to-use interface.

Arguably the most significant aspect of the new functionality is Article Management which drives a regime for users to maintain product and specification information. Each change requires users to follow a strict review, authorization/approval and confirmation process.

Integration



Systems were connected using an integration framework into the SampleManager LIMS as part of the implementation - the MRP system, the Manufacturing Execution system, the warehouse systems, the purchase ordering system and the customer ordering system. This enabled different departments to have a full picture of workload and status, speeding up the invoicing of customers and providing for some automation in the maintenance of stock levels.

Going live

Between December '98 and early '99, AstraZeneca (by the end of this period the merger had taken place) was busy completing validation of the new system. During this time, all static data was entered and there was a large-scale migration of article data (i.e. specifications). In May '99, the new SampleManager implementation went live in the company's Turbohaler production plant and by September '99 the system was in operational use at all three production sites, three months ahead of the Company's Y2K target.

Each location is currently running SampleManager version 3.2 on OpenVMS with Oracle 7.3.3.4 as its relational database management system on a server, with Windows NT 4.0 clients. Over the three sites, there are more than 1,300 users operating across the whole production process, including laboratory users, production, QA evaluation and warehousing and stock control. SampleManager handles almost 35,000 articles at the APL site alone (these include various specifications for geographic markets and specifications for in-progress, raw material and finished product). Articles for finished product add up to 10,000.

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Review process

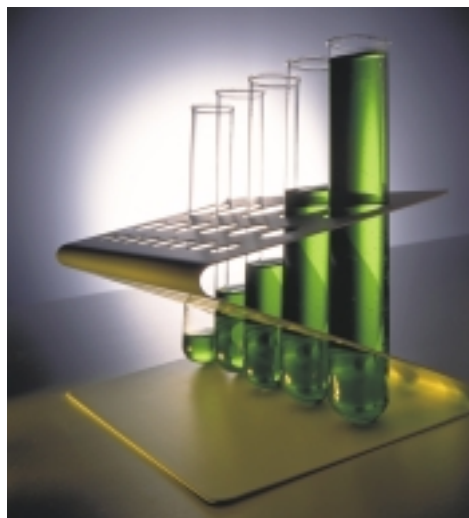
Nine months after going live, Thermo LabSystems Pathfinder undertook a system review at AstraZeneca to assess progress against plan and to revisit the original design specifications. It was found that there were a number of system enhancements specified by AstraZeneca that were being used either inefficiently or not at all. It was agreed to reconsider advanced training for some users to address this and to encourage common best practice in the system's use. Ideas for future enhancements were also discussed.



Future plans

There are a number of areas which AstraZeneca is looking to address in the coming months:

- By migrating to SampleManager 2000, AstraZeneca will be in a position to fully comply with the US FDA's rule 21 CFR Part 11 on electronic signatures. This is part of an AstraZeneca-wide compliance program.
- To utilize the SampleManager Reporter to create new report layouts with improved presentation templates.
- To extend and improve instrument integration to minimize time delays and further eliminate manual transcription errors.



Conclusion

AstraZeneca is satisfied that its original project objective has been met. Its three Swedish production sites are now using a common, integrated 'QIMS' solution, which was implemented and validated on time ahead of the Y2K deadline. Against the background of the merger, and the inevitable uncertainties and upheaval this brings, the success of this project was quite an achievement for the project team, the users and the Thermo LabSystems Development and Pathfinder teams.

Looking to the future, AstraZeneca is committed to an ongoing review process, undertaken in partnership with Pathfinder. This process allows both parties to monitor use of the system at the three plants and identify areas for system enhancement to ensure SampleManager LIMS keeps pace with changes in AstraZeneca's production process workflow.

Among the team at AstraZeneca, it is generally agreed that the laboratory analysts have been the real winners. Through the workshops, they were fully involved in specifying requirements and this has resulted in them using a system that supports the way they work.

Additionally, throughout the production process, the QA evaluators have much more of the right data to review and to query on, and are in a position to make more informed decisions.

From Thermo LabSystems Pathfinder's perspective, the Astra SampleManager project was a proving ground for the workshop approach. It has been a methodology recommended to many of its other clients since, with a great deal of success.

Author biography

Nick Arnold is the LIMS Product Manager for Thermo LabSystems. He has a PhD in Chemistry from Nottingham University in the UK. He has worked at Thermo LabSystems for two years during which he has carried out a number of LIMS implementations, particularly in the pharmaceutical industry including the AstraZeneca SampleManager project. Prior to joining Thermo LabSystems, Nick held various production, computing and quality roles for a large UK brewing company.

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