LIMS-Driven Acquisition, Processing, Reporting and Storage of Data from Multiple LC/MS/MS Workstations

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Overview

Purpose: To development a Laboratory Information Management System (LIMS) driven data acquisition and processing software for triple stage quadrupole series instruments.

Methods: A LIMS system that acts as a centralized control point to multiple LC/MS/MS systems in the laboratory has been developed. The LIMS acquires the data and stores it in a database where it can be processed and reported from remote locations through a web interface, without requiring local installation of LIMS software. User access and security permissions to analytical studies and which LC/MS/MS instruments can acquire data for the study are controlled by the LIMS. The LIMS system is a networked storage location for study information, data, results and audit trails, placing all analytical study records in a single database, simplifying archival.

Results: A LIMS-driven application has been developed to simultaneously handle system security, acquisition, processing, reporting and storage of data from multiple remote triple stage quadrupole series instruments.

Introduction

Historical approaches to interfacing bioanalytical LC/MS/MS instruments with LIMS have usually involved the use of two disparate data systems. This has often resulted in the required maintenance of two archival record sets in order to fully document the analytical studies per 21 CFR Part 11 guidelines. This has increased the level of effort required in software validation and direct data analysis, and requires persistent documentation to support other users of the results, such as internal quality assurance offices and external regulatory bodies.

This poster describes a new, integrated approach that results in increased efficiency through the reduction of validation efforts while providing a single archival record set.

Methods

Thermo Scientific Watson LIMS version 7.4 together with the TSQ Module™ was used as a centralized control point for multiple Thermo Scientific TSQ Series mass spectrometers, including the TSQ Vantage™ LC/MS/MS system. The Thermo Scientific TSQ Module was used to submit analytical runs directly from Watson LIMS to any configured LC/MS/MS system on the network. Using the TSQ Module, the LC/MS/MS data was acquired directly into the Watson LIMS database. Watson LIMS was used within web browsers from remote locations via the Thermo Scientific Web Access Suite to create analytical runs, review and process data, and generate reports. Access to analytical studies, and the TSQ Module, was controlled by permissions configured within the Watson LIMS. Also the TSQ Module was used to send previously submitted analytical LC/MS/MS runs back to Watson LIMS so the analytical run could be sent to another configured TSQ Series instrument.

Results

An application has been developed that controls user access to multiple analytical projects, remote LC/MS/MS instrument workstations, and software functionality. The multiple remote LC/MS/MS systems were added to the LIMS database as separate instrument stacks that could be assigned analytical run sequences. The application allowed analytical run sequences created within the LIMS to be sent to the remote LC/MS/MS systems. The analytical run sequence was assigned and submitted to a particular LC/MS/MS instrument within the LIMS. The analytical run sequences on the remote LC/MS/MS systems were only available to the specific users that were granted access to the analytical run from within the LIMS. These users were then able to submit the analytical run sequence to the particular LC/MS/MS system instrument queue.

FIGURE 1. Configuration of multiple acquisition workstations. Extensible architecture allows multiple workstations to be configured with multiple sample inlets.

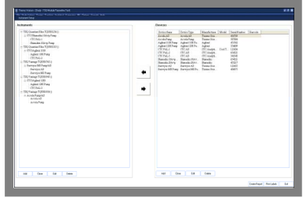


FIGURE 2. Analytical method importation into the database.

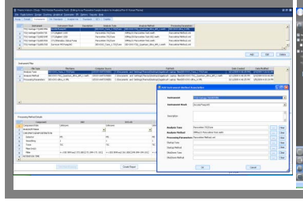


FIGURE 3. Real time display of the currently acquiring sample.

Multiple analytical runs have been successfully submitted to an LC/MS/MS instrument queue and acquired in succession without additional user input. No additional user input is required because each analytical run in the queue begins acquiring data to the LIMS once the preceding analytical run completes its last sample and the raw data is written to the LIMS database.

Analytical run raw data was sent from the remote LC/MS/MS instrument workstations to the LIMS where it was stored, viewed, integrated and then regressed. Viewing and processing of the data was performed from remote workstations through a web interface. This data was archived and then restored to the database from which the archive was created, as well as other separate installations of the LIMS application.

Successful multiple concurrent data acquisitions from many acquisition workstations, with users reviewing and processing the acquired data in near real time from multiple concurrent remote locations have been performed. Only those acquisition workstations added to the LIMS database can receive analytical runs and acquire data (Figure 1). Access to both the acquisition workstation module and the remote LIMS application software functionality are managed by the same set of permissions resulting in greater efficiency.
Analytical methods used to acquire and process data are developed at an acquisition workstation and then imported into the database (Figure 2). The imported analytical method is associated with a particular instrument at this point, resulting in the correct instrument receiving the analytical run once it is submitted to an acquisition workstation module.

The system provides users with access to both the currently acquiring sample as well as those that have already been acquired. The real time data display of the currently acquiring sample is viewed from the acquisition workstation module at the acquisition workstation (Figure 3), while already acquired samples can be viewed from the remote LIMS application (Figure 4).

FIGURE 4. Review of acquired data and selection of data for reinjection. Samples 6 through 9 are selected for reinjection.

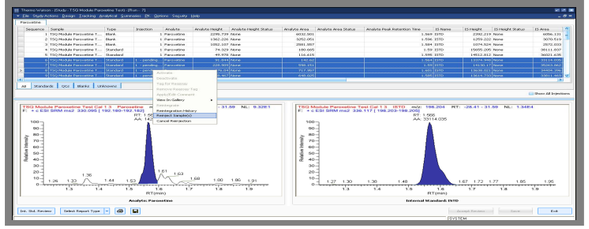
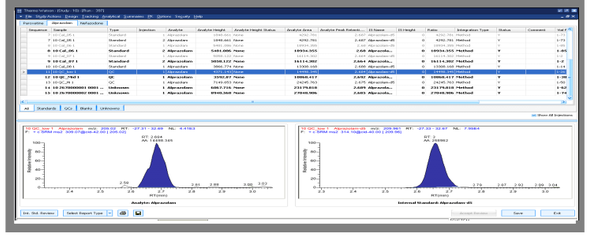


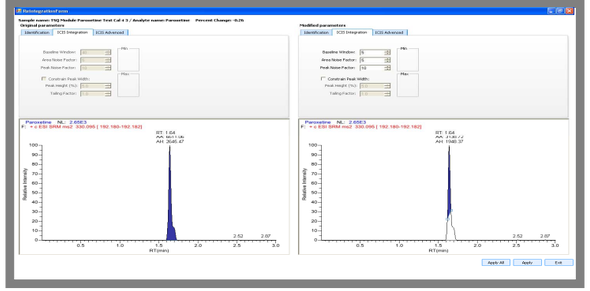
FIGURE 5. Data review of reinjected samples. Original injections are displayed in gray, while the injection used in regression calculations are shown in black.



It was important that a sample could be reinjected if required, and then regressed with the other samples in the analytical run without overwriting the original injection. This system is capable of sample reinjection, from both the module at the acquisition workstation if the analytical run in still in progress, or from the remote LIMS processing application once the analytical run is complete. The original injection data is not overwritten and remains in the database where it can be viewed, but cannot be used in the analytical run regression. Multiple reinjections of a sample may be performed, but only the last injection is used in the data regression (Figure 5).

The LIMS application is also capable of reintegrating samples when required. The system allows users to change integration parameters and then apply the new parameters to a single sample or the entire sequence of samples. It is also possible to perform manual integrations, but a manual integration may only be applied to the current sample. The original integration parameters and chromatogram are displayed as a reference in the same window as the modified integration parameters and chromatogram (Figure 6). Integration changes can be displayed and printed in a historical report showing how each integration change affected the chromatogram.

FIGURE 6. Reintegration of acquired data. Original integration parameters and associated chromatogram are displayed on the left of the screen, and the modifications to the chromatogram for the changed integration parameters are displayed on the right side of the screen. Manual integrations are also performed on the right side of the screen, by selecting one of the squares and dragging it to the desired position.

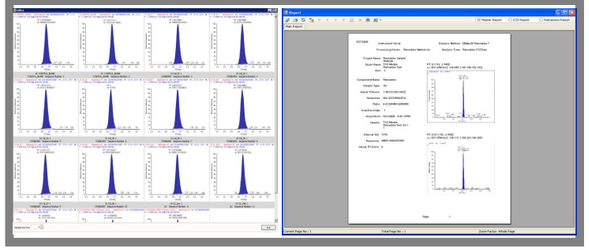


The LIMS application stores the analytical run chromatograms and chromatogram reports within the database. These chromatograms can be viewed using a gallery view function and in reports that contain the chromatograms and analytical conditions (Figure 7).

The LIMS application is capable of creating an archive for data retention outside the database. These archives contain all the information regarding the analytical runs, the receiving of samples, raw and processed data, reports, and the individuals that performed each action.

This LIMS-driven application performs functions that have historically been performed by multiple software packages. Separate software packages have been used for sample handling, data collection, storage, and processing of analytical results. Each application and interface between applications used in the process required its own validation and maintenance. Previously, a change to one application required additional efforts to confirm that the associated existing application interfaces were still functional or resulted in a cascade of changes through multiple applications. This LIMS-driven application approach reduces the number of applications that a laboratory administrator needs to validate and administrate, resulting in greater efficiency.

FIGURE 7. Review of chromatograms and creation of chromatogram reports.



Conclusions

A LIMS-driven application has been successfully developed to simultaneously handle system security, acquisition, processing, reporting and storage of data from multiple remote LC/MS/MS systems. Future work on the this project will include the ability to perform analytical method development within the LIMS-driven workflow.