

## Abstract

Modern mass spectrometry labs usually contain instruments from multiple vendors generating data for hundreds to thousands of samples per day. The challenge facing most labs today is not data generation. Rather, it is data interpretation. How do labs keep from being buried under all of the data they can generate? We have implemented a software suite (Analytical Studio) to automate the workflow process of interpreting the qualitative and quantitative LC/MS analysis of small molecules. Specific attention was paid to workflow management, data review, exception handling, multi-vendor support and interfacing with legacy systems.

## Background

Sample throughput in compound characterization, the process of qualitative and quantitative analysis of a **compound of interest (COI)**, is often limited by the data interpretation process. To scale up throughput in a spectrometry lab, the quality of interpretation is often compromised in order to get results out quickly. Furthermore, when a variety of instruments are employed in the lab, additional informatics tools must be built to overcome limitations and inconsistencies across various data formats, processing approaches and reporting tools.

To overcome these and other limitations, Virscidian has developed a general analytical data handling framework, Analytical Studio, based on a plug-in architecture to enable a combination of standard and customized plug-ins to be developed and deployed to a lab. The framework is designed to function across process or network boundaries allowing for greater scalability.

Analytical Studio is a robust and flexible platform offering clean integration with external systems, quality data processing, expert data interrogation, exception handling, manual override functionality and flexible reporting tools. This is accomplished with custom plug-ins aggregated with standard core viewer and processing plug-ins to meet decision workflow requirements.

The objective of the compound QC workflow is to determine if the compound of interest (COI) is present, and if so, determine the purity and quantity. Analytical Studio was deployed with the core components along with the Compound QC workflow plug-in as a full featured client application and as a "black box" hands free processing and reporting engine to automatically generate results on any supported instrument.

## User Configurable Processing Methods

Analytical Studio allows the user to define a variety of processing methods to customize all aspects of the processing logic including peak picking, baseline estimation, spectra processing, COI scoring, quantity and quality calculations. Methods can be configured individually for each sample or applied to a set of samples. The user can also take advantage of several innovative approaches for improving processing performance, reducing archive file and report sizes.

Highly tunable peak picking and filtering settings can be individually configured for each chromatogram. Shown below is before and after adjusting the peak filter settings to remove unwanted peaks and improve AUC calculation accuracy.

Before applying new peak filter settings.

After applying new peak filter settings.

Quantity and quality calculation parameters support various detector types and quantitative calibration methods.

Peak scoring parameters are used adjust the criteria for automatic determination of the presence of the COI

## Manual Override Results

All input and output results can be manually overridden.

Override the automatic COI found result with a single click.

Detailed peak scoring explains the automatic decision making and scoring algorithm.

Single click peak splitting

Single click peak or peak group deletion

Step 1. Right click the peak and select delete selected peak group menu item

Step 2. Confirm the request to delete all peaks in a peak group.

Step 3. Peaks are deleted and results are updated.

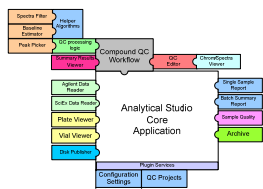
## Benefits

The use of Analytical Studio to solve workflow and processing challenges has resulted in significant benefits including:

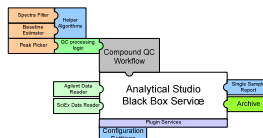
- Considerable cost savings for the QC workflow
- Vendor neutral solution allows us to choose the equipment that is best for the job
- Flexibility in scheduling the use of the lab instruments
- Higher quality results in a high-throughput operation with high efficiency
- Easy integration with client's internal systems (i.e. sample lists, data processing requirements, report formats)
- Facile efficient resolution of workflow exceptions preventing us from being bogged down with time consuming problems (i.e. sample list errors, instrumentation failures, specialty processing or reporting requests)
- Identify and remove bottlenecks
- Explain to customers precisely how the results were generated
- Automatic identification and commenting of processing points of interest (i.e. identifying non-COI masses of interest, COI present but no detection in purity or quantity detectors)
- Flexible reporting formats for a single sample or batches of samples
- Automated generation and report generation or complete client application with data review
- Complete manual override capabilities to correct exceptions in automatic processing (i.e. manual peak integration, peak deletion, purity override, quantity override, input override, COI found override)
- Automated tools for generating calibration curves for improved quality and constancy of quantity calculations
- Full interrogation tools for viewing raw data along side of processed data for improved decision making on the tough calls

## Analytical Studio Architecture

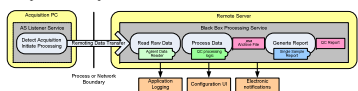
Analytical Studio Compound QC workflow deployed as a full featured client application with multiple plug-ins to support multiple raw vendor readers and multiple output report types. Plug-ins can be easily "wired up" and coordinated by a hosting application to automate most workflows.



Analytical Studio Compound QC workflow deployed as a stream-lined "black box" automatic processing service supporting multiple raw data formats and a single sample report output.



Virscidian has implemented a black box processing solution to remove bottlenecks inherent in automated high-throughput QC analysis to significantly reduce the time required to process a sample.



## Powerful Data Review Tools

Analytical Studio offers functionality such as the batch quality display, automated quant calibration, manual override of COI call, manual integration and easy peak deletion to accelerate the data interrogation and review process while delivering quality results.

Generating a calibration equation using a four component standard mix with the CLND is easy. COI peak areas from all processed standards for all COIs are automatically extracted and fitted to give a calibration curve anytime during or after the processing of a batch. Calibration curves can then be applied to individual samples in the event of instrument problems requiring a recalibration.

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Not all colored wells are the same! Applying Analytical Studio's innovative "query and tag" quality filter the user can quickly and clearly discern which samples to further inspect.

Build a query using a GUI and any supported sample attributes to group and display samples belonging to the group.

Plate view based on COI found color coding

Apply query

Toggle plate view to display wells based on query tags.

## Flexible Reporting

Unlimited reporting through custom plug-ins enables customers to receive their results in the format that meets their needs. By developing a custom report plug-in, a single sample report in PDF format is generated to the specification of the client. Each report plug-in supports settings to allow limited customization of the report output.

The single sample QC report outputs all the essential results associated the sample into PDF or MS Word format.

The QC summary report can be generated for any set of samples. The user can determine which properties are output to the Excel document. Customized versions of this plug-in allow for embedded logic to be applied resulting in custom fields being reported to their specifications.

The RPT report plug-in generates the same batch report into a Micromass browser compatible RPT file. Analytical Studio can embed additional information into an RPT file that can be used by RPT readers to deliver richer information using the RPT format.

## Conclusions

The purchase and operation of analytical instrumentation is often assumed to be the only cost of operating a high throughput analytical lab. However, there is significant cost associated with ensuring quality results are produced from the acquired data. This cost is directly related to quality of results and complexity of workflow.

Investing in building a general purpose analytical data handling framework helped Virscidian to operate a more efficient and flexible lab without compromising the quality of results returned to customers.

The compound QC workflow application is just one example of how Analytical Studio has been applied to a complex set of steps across a variety of instrumentation to save costs associated with processing analytical data.

## Acknowledgments

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## For Further Information

[www.virscidian.com](http://www.virscidian.com)

Contact Joseph Simpkins at [jsimpkins@virscidian.com](mailto:jsimpkins@virscidian.com)

Virscidian Inc. 128 East Hargett St, Suite 300  
Raleigh, NC 27601  
(919) 809-7651