TECHNICAL NOTE 73237

Chromeleon CDS workflow for bioanalysis

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Introduction

Bioanalytical studies are a fundamental part of the drug development process. They involve the quantitative measurement of compounds of interest and/or their associated metabolites in biological samples. Tandem quadrupole mass spectrometry coupled with high-performance liquid chromatography (HPLC-MS/MS) is primarily used for compound detection.

Developing sensitive and selective assays remains a significant challenge for today's scientists, as the industry strives to keep pace with increasing demands for a robust methodology that will ensure proper dosage, efficacy and safety of any therapeutic product. Alongside this are the ever-evolving regulatory guidelines and intensified demands on data integrity in this market space, which means that the modern-day Chromatography Data System is coming under close scrutiny throughout every stage of the bioanalysis workflow where traceability, accuracy, and integrity of the data is vital. Thermo Scientific™ Chromeleon™ 7 Chromatography Data System (CDS) can address these needs by providing an end-to-end solution from samples to results, interfaced to a Laboratory Information Management System (LIMS) that is designed for bioanalysis.

One software package

Analysis often involves multiple software platforms for Chromatography and Mass Spectrometry, but Chromeleon CDS provides a single software solution that is scalable, from a local standalone workstation to a multi-site enterprise system, with built-in features to help users meet compliance requirements. Chromeleon software provides robust and reliable control of the HPLC and MS with integrated MS/MS functionality for data acquisition and processing. This technical note highlights the key features of the Chromeleon CDS workflow for bioanalysis.

Compliance

Ensuring that a potential therapeutic product is safe for use means adhering to regulations outlined by regulatory bodies such as the U.S. Food and Drug Administration (FDA) and the Medicines and Healthcare products Regulatory Agency (MHRA). With Chromeleon CDS, you can satisfy regulatory requirements without sacrificing efficiency by using the integrated security system, audit trails, and version management tools.

Data integrity

Data integrity applies equally to paper and electronic data. However, electronic data is deemed more secure since it reduces human oversight, is more difficult to manipulate or change, with such changes being easier to detect.

There is a definite drive, even in society in general, to use technology to automate and mitigate many of these issues. Chromeleon CDS can help you overcome the challenges faced when implementing technical controls in the laboratory, as it is a robust system that provides an outstanding set of access controls and security features that complement mass spectrometry and bioanalysis.

The Chromeleon Administration Console provides a comprehensive yet simple interface (Figure 1) with complete system configuration (Figure 2), flexible user management (Figure 3) and secure access control (Figure 4), which incorporates electronic signatures (Figure 5) for compliance with 21 CFR Part 11 requirements to aid the implementation of a paperless environment.

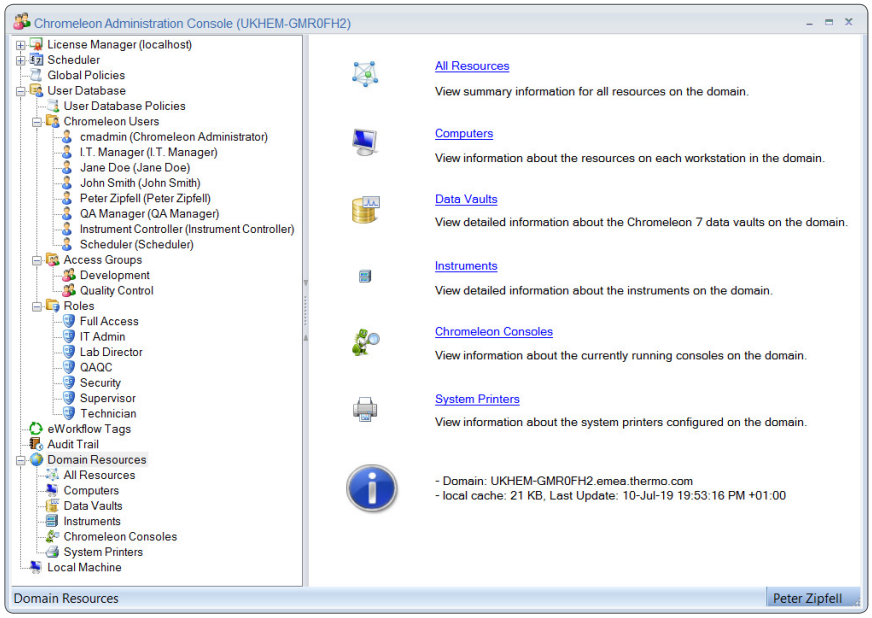


Figure 1. The Central Administration Console allows easy implementation and management of technical controls.

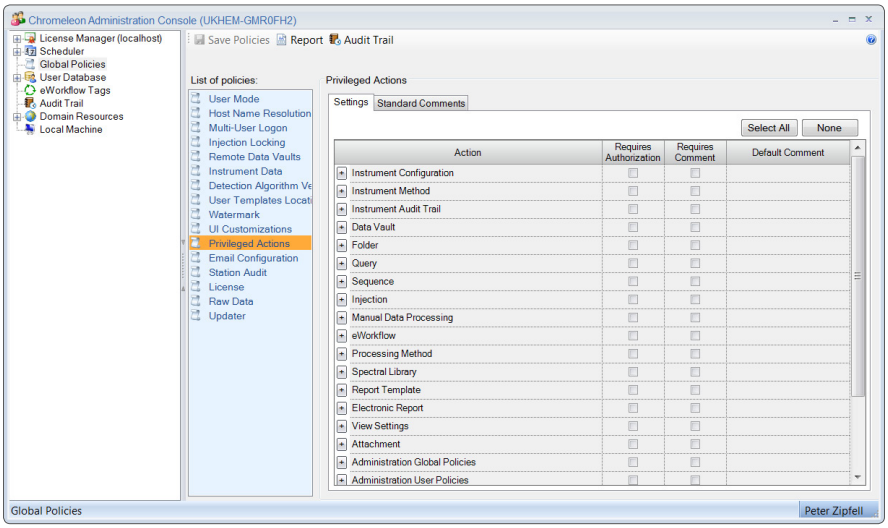


Figure 2. System configuration with Global Policies. Privileged Actions can enforce when, and how, passwords and comments must be applied when users make changes.

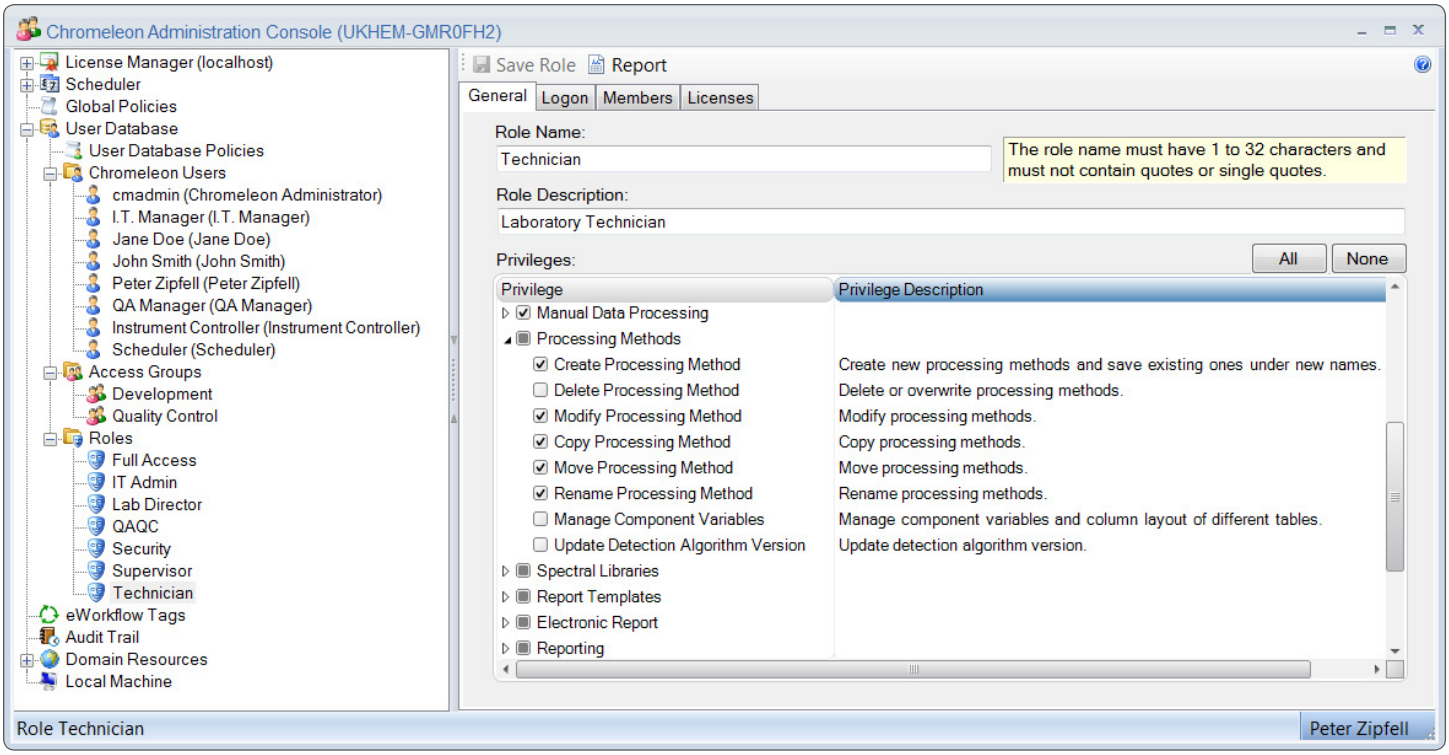


Figure 3. User Management in Chromeleon CDS: Privileges define what users can and cannot do.

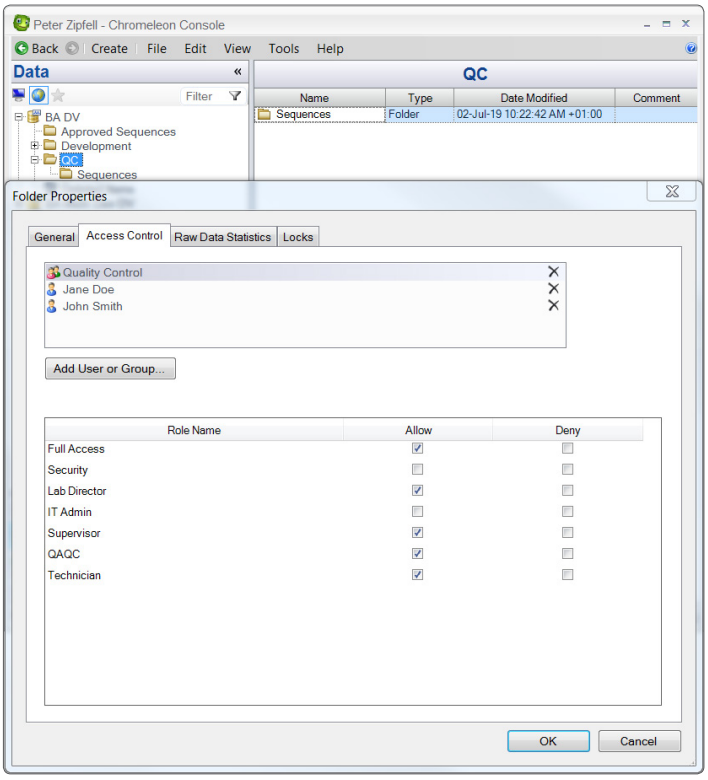


Figure 4. Access Groups can be used to control access to specific Data Vaults, folders within Data Vaults, and instruments.

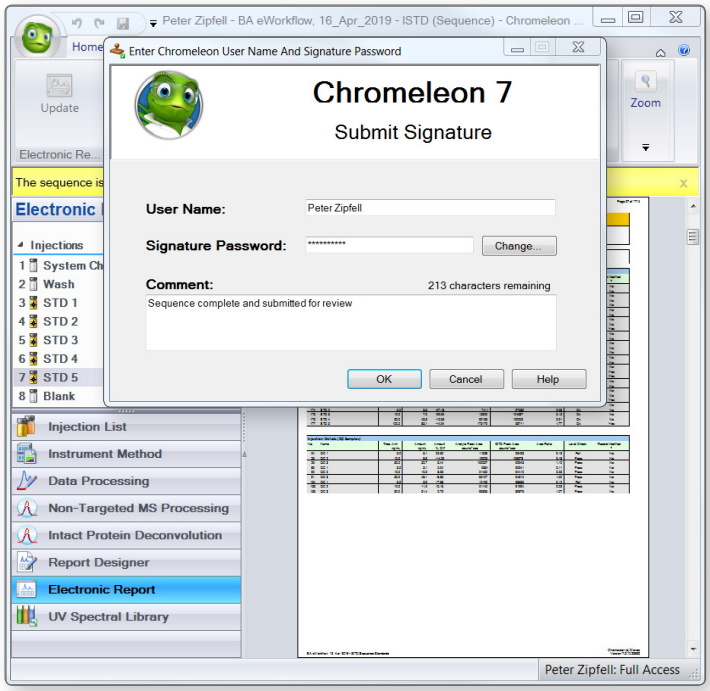


Figure 5. Showing electronic signatures. Once signed further modifications are not permitted and the sequence can only be reviewed by a user with the associated privilege.

Audit trail review

With a comprehensive set of audit trails covering data, instruments, user management and system administration, Chromeleon CDS provides traceability, records historical changes for data reconstruction, while making audit trail review simple and less onerous.

The software records versions for data objects (Processing Method, Instrument Method, Report Template etc.), while the “Show Changes” feature provides a quick and easy comparison of object versions with a simple side-by-side display featuring icons that clearly flag insertions, deletions, and changes (Figure 6). At any point, a current version may be restored to a previous version as long as versioning has been enabled.

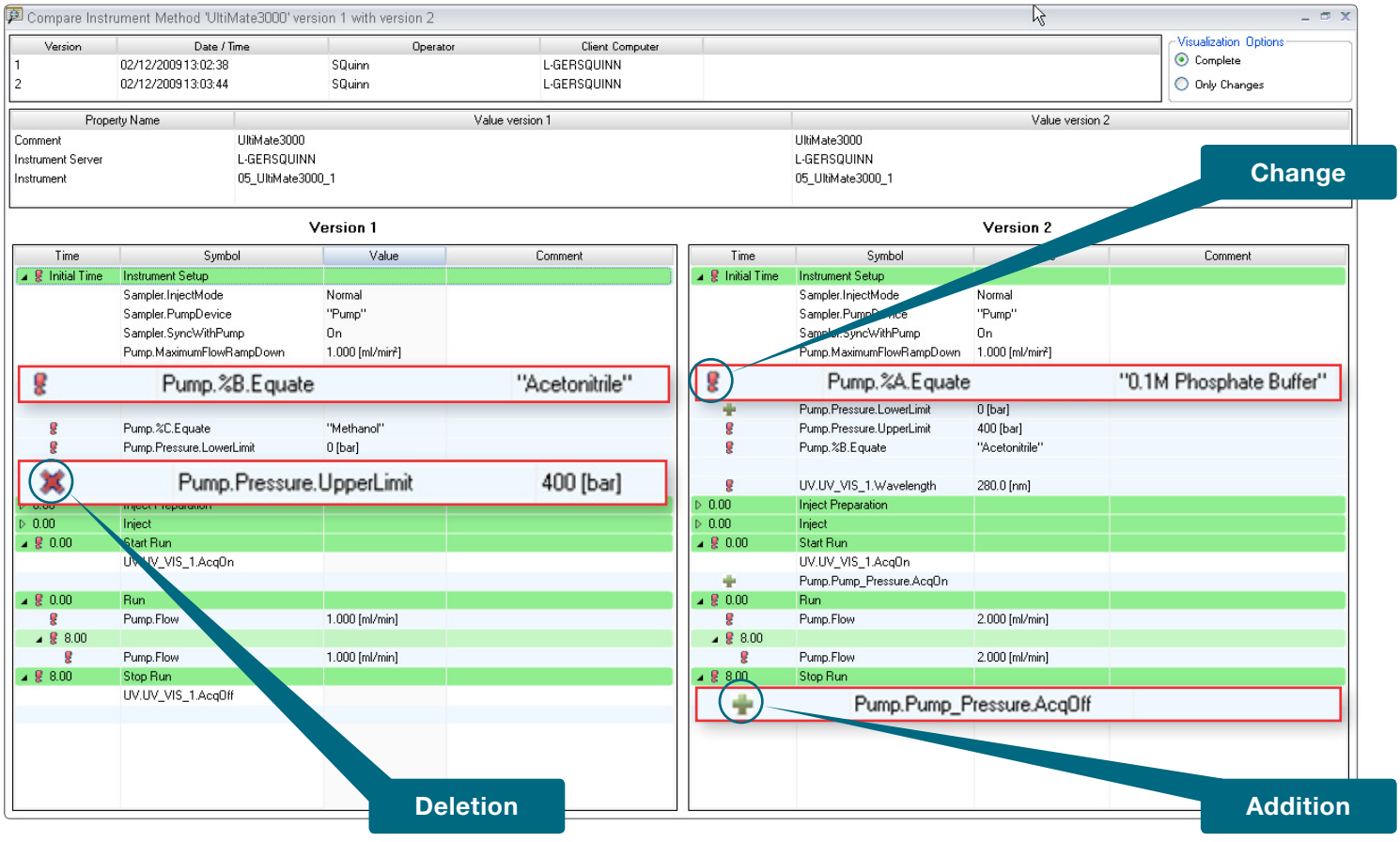


Figure 6. Illustrating the “Show Changes” feature within Chromeleon CDS.

Going one step further Chromeleon CDS provides a visual comparison by opening selected items from the data audit trail in a corresponding Chromeleon Studio window (Figure 7), thus any changes made can be clearly verified during the review process. To maintain the integrity of the data, all objects remain read-only except for the View Settings. It's also possible to open up several Chromeleon Studio windows with different versions (Figure 8).

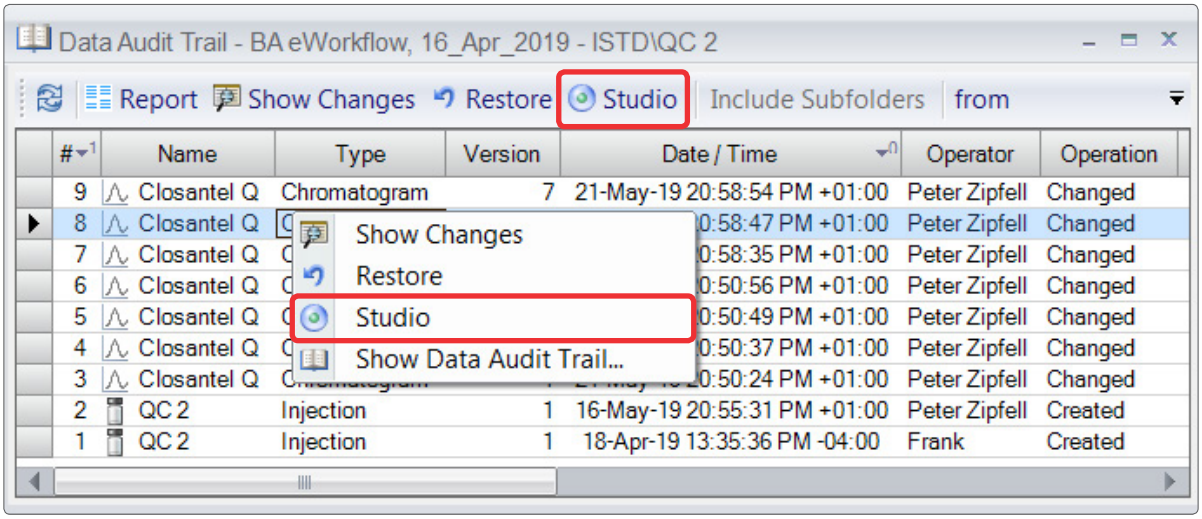


Figure 7. Illustrating the first stage of a visual audit trail review.

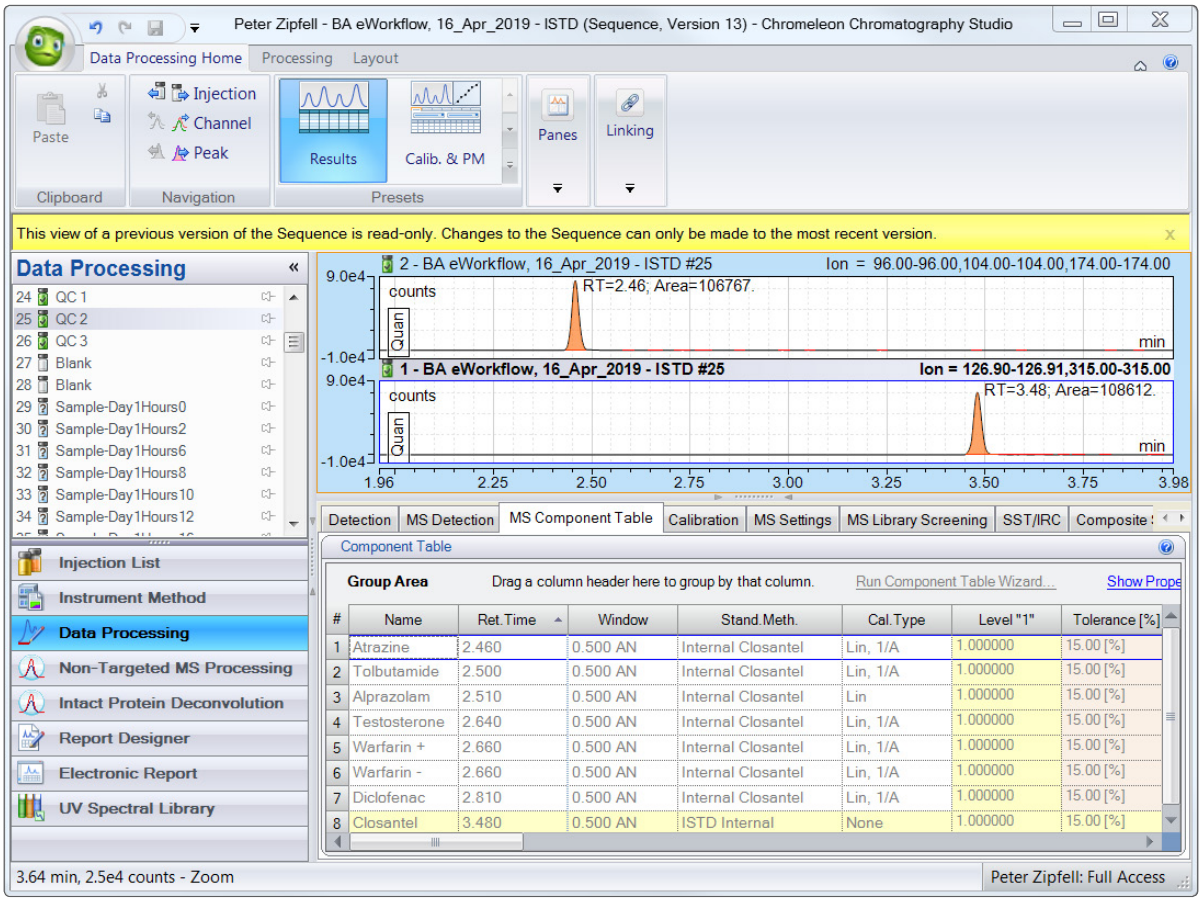


Figure 8. Showing a visual comparison when reviewing audit trails. Note how changes to the sequence are not permitted—shown by the highlighted yellow bar.

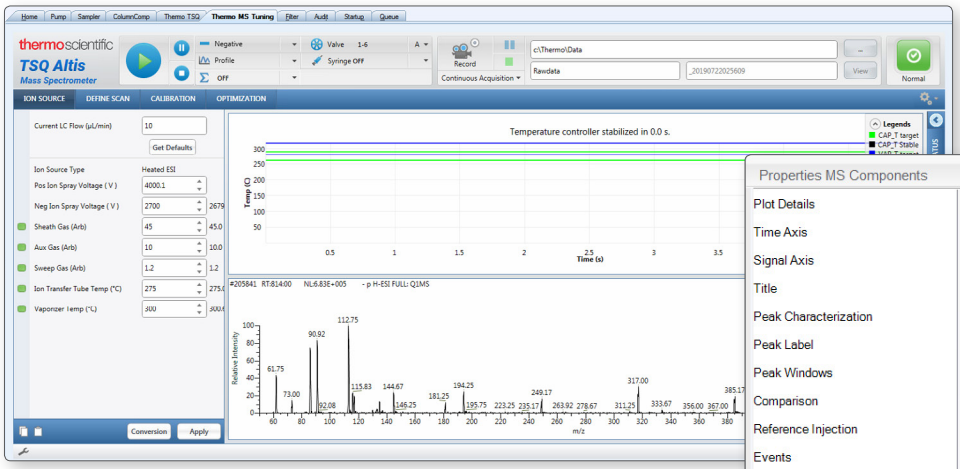
Compliant mass spectrometry tuning

Typically the tune application resides as a separate component from the software that's in place for instrument control and data acquisition. Compliance requirements in bioanalysis demand that all points of access are controlled, and that even the tune files are safely stored and audited accordingly. That's why such files are securely stored within Chromeleon CDS.

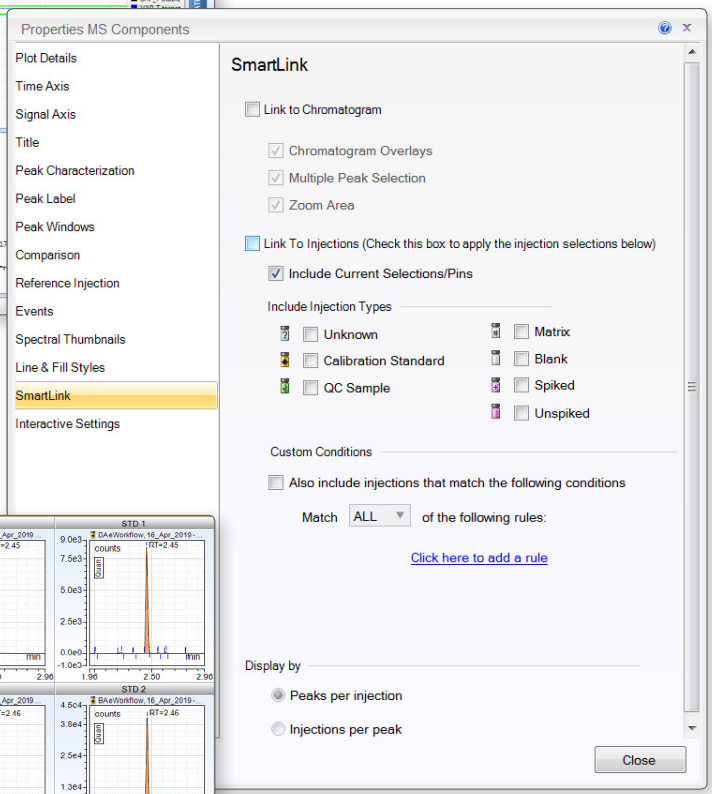
The ability to perform MS manual tune or calibration solely from an ePanel (Figure 9) within Chromeleon software can also be privilege controlled (Execute On-Demand MS Manual Tune/Calibration). This ensures that control is exercised on a permission basis, with all activities being recorded in the audit trails. It is then not possible for a user to open up the tune application outside of Chromeleon CDS, preventing inappropriate access.

Working with your data

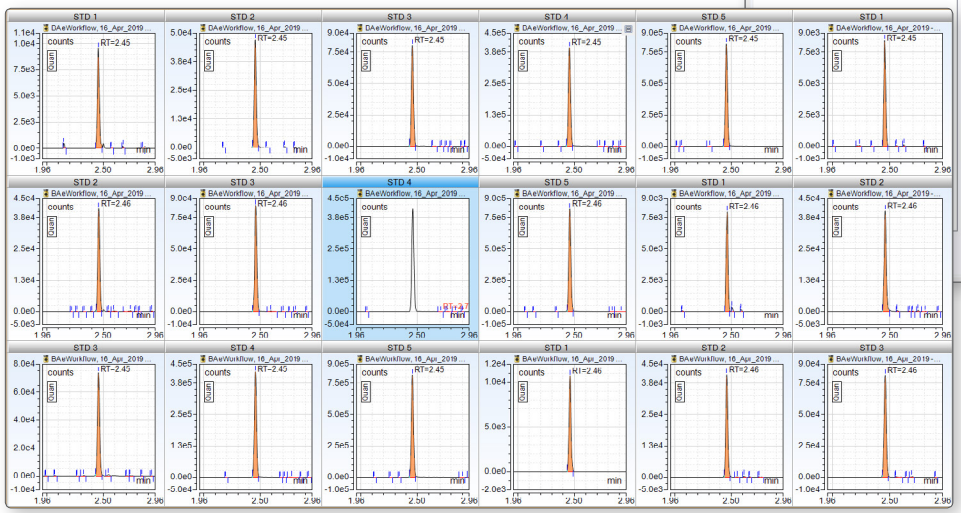
It's important that a CDS can handle large datasets without compromising on productivity, whether processing or simply reviewing the data. With Chromeleon CDS, there are a number of tools and features that complement the bioanalysis workflow, with simplicity and efficiency at the heart of its design. SmartLink provides users with pre-defined component-centric templates that enable users to choose which injections to include (Figure 10) and the associated orientation of the plot layout. This allows for an easy comparison of the data, identifying trends straight forward and recognizing data discrepancies, such as missing peaks uncomplicated (Figure 11).



▲ Figure 9. Compliant tuning via a Chromeleon Instrument ePanel



▲ Figure 10. SmartLink options for the associated Chromeleon View Settings.



▲ Figure 11. Calibration Standard Quantitation Ions across a sequence for a specific component per injection. Notice the un-integrated peak.

In addition, there may also be instances where a user needs to make injection specific changes to the detection settings, possibly due to chromatographic interferences or a poor injection. Using this approach, it can be possible to reduce the need for manual integration. Accessing the MS detection tab (Figure 12) found in the Chromeleon Processing Method allows a user to apply changes to a specific injection or all injections.

QC terminology

Quality Control Samples play a vital role to ensure consistency, validity, and reliability of results. They should be analyzed in every single assay to demonstrate robustness and acceptability. It's important that they are easy to define (Figure 13) and that clear indicators of pass or fail are available (Figure 14). Chromeleon CDS provides a comprehensive collection of features for both Calibration and Quality Control Samples that enable users to review the results quickly and effortlessly.

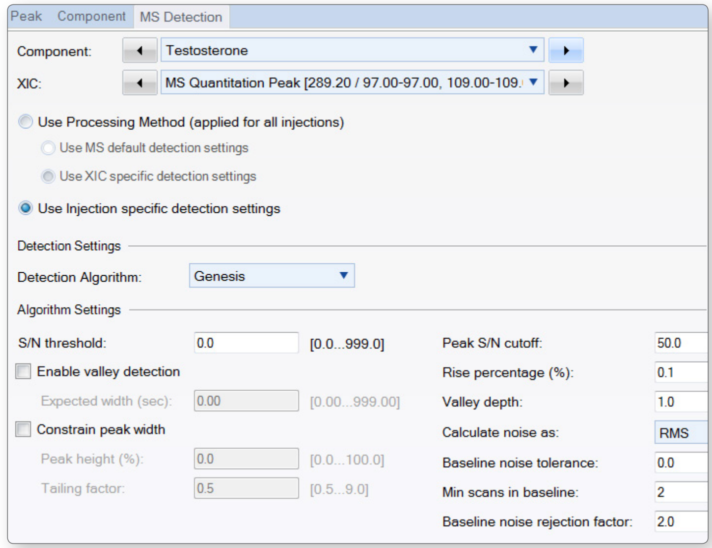


Figure 12. MS Detection settings can be applied to a whole sequence or specific injection.

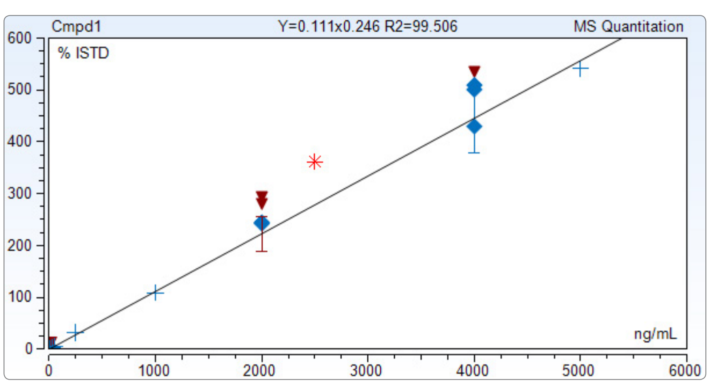
Level "QC1"	Tolerance [%]	Level "QC2"	Tolerance [%]	Level "QC3"	Tolerance [%]
5.000000	15.00 [%]	10.000000	15.00 [%]	50.000000	15.00 [%]
5.000000	15.00 [%]	10.000000	15.00 [%]	50.000000	15.00 [%]
5.000000	15.00 [%]	10.000000	15.00 [%]	50.000000	15.00 [%]
5.000000	15.00 [%]	10.000000	15.00 [%]	50.000000	15.00 [%]
5.000000	15.00 [%]	10.000000	15.00 [%]	50.000000	15.00 [%]
5.000000	15.00 [%]	10.000000	15.00 [%]	50.000000	15.00 [%]
5.000000	15.00 [%				
5.000000	15.00 [%]				

Figure 13. Easy to apply tolerance levels.

Figure 14. Clear pass/fail results with calibration plot indicators.

Injection Details (QC Samples)

No.	Name	Theo. Amt ng/mL	Amount ng/mL	Amount % Diff	Analyte Peak Area counts*min	ISTD Peak Area counts*min	Area Ratio	Level Check	Record Modified ?
24	QC 1	5.0	4.8	-4.24	926	1558	0.59	Pass	No
25	QC 2	10.0	8.1	-19.10	1779	1773	1.00	Fail	No
26	QC 3	50.0	48.4	-3.17	9104	1516	6.01	Pass	No
89	QC 1	5.0	5.3	5.74	994	1516	0.66	Pass	No
90	QC 2	10.0	10.1	0.66	1965	1573	1.25	Pass	No
91	QC 3	50.0	46.2	-7.62	9055	1580	5.73	Pass	No
154	QC 1	5.0	5.1	2.69	1047	1644	0.64	Pass	No
155	QC 2	10.0	9.8	-2.42	1856	1533	1.21	Pass	No
156	QC 3	50.0	52.0	4.04	9667	1498	6.45	Pass	No



Plot indicators

- ◆ Check standard/QC sample point within its tolerance limits.
- ◆ Check standard/QC sample point within its tolerance limits (when it is the selected injection).
- Level tolerance line with check standard/QC sample point within its tolerance limits.
- ▼ Check standard/QC sample point outside its tolerance limits (outlier).
- Level tolerance line when check standard/QC sample point is outside its tolerance limits.

Pre-defined report template for bioanalysis

Of course, data processing inevitably ends with a report output of some sort and for that the software has a built-in report template (Figure 15). With a spreadsheet-based approach, the template is highly customizable with predefined calculations that are common for bioanalysis.

Scalable infrastructure for mass spectrometry

Mass spectrometry data acquisition and control has often been standalone, and data is often stored locally or on a file share with access only from the instrument computer. With a networked, or enterprise CDS, it is possible to extend the capabilities for bioanalysis and provide the security and reliability that's needed when it matters most.

Delivering these capabilities across a network brings a unique set of challenges. The sheer volume of data may pose a problem, however Chromeleon CDS has been designed and optimized to overcome these challenges and brings the following benefits to the bioanalysis workflow:

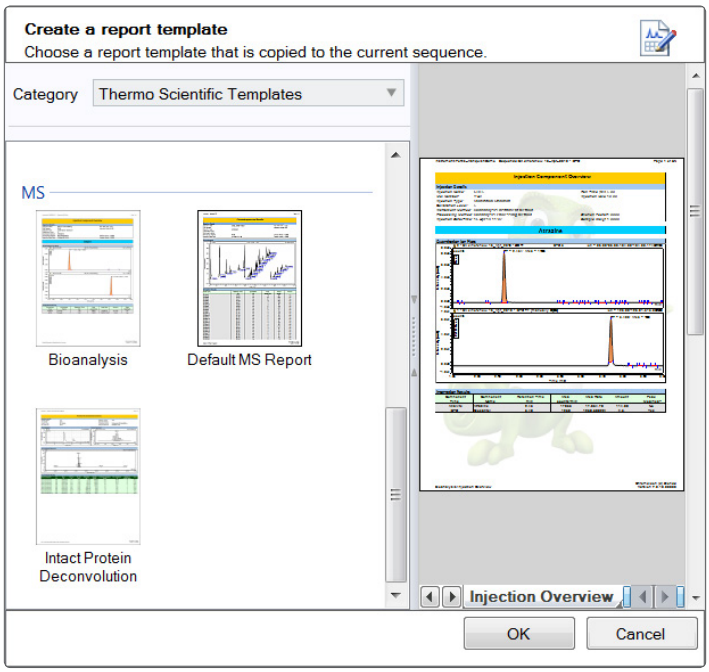


Figure 15. Built-in Report Template for bioanalysis.

- Scalable architecture from local standalone to multi-site enterprise provides a seamless solution that can grow alongside any business expansion
- Remote Instrument and data access means there is no need to be in the lab to view data or even to control the mass spectrometer
- Centralized data storage with a relational database at the heart of the application provides security and peace of mind
- Tools for network failure protection ensure that data is not lost in the event of a network outage
- Built-in archiving capabilities provide flexibility and easy management of the data
- Data consistency checks to ensure data are tamper-protected

Bringing it all together—eWorkflow procedures for MS

Streamlining workflows in any bioanalysis laboratory is never an easy task, however with sequences often tied to a Standard Operating Procedure (SOP) they follow a repetitive trend for analysis and structure that remains the same. eWorkflow™ procedures provides an ideal solution, where the process of sequence creation can be automated, guiding the operator through a minimal number of choices needed to create a complete, correct sequence with predefined files and a well-defined structure (Figure 16). Using an eWorkflow simplifies sequence creation and minimizes the amount of training required, allowing users with little training to run routine MS analyses without error, saving valuable time and resources.

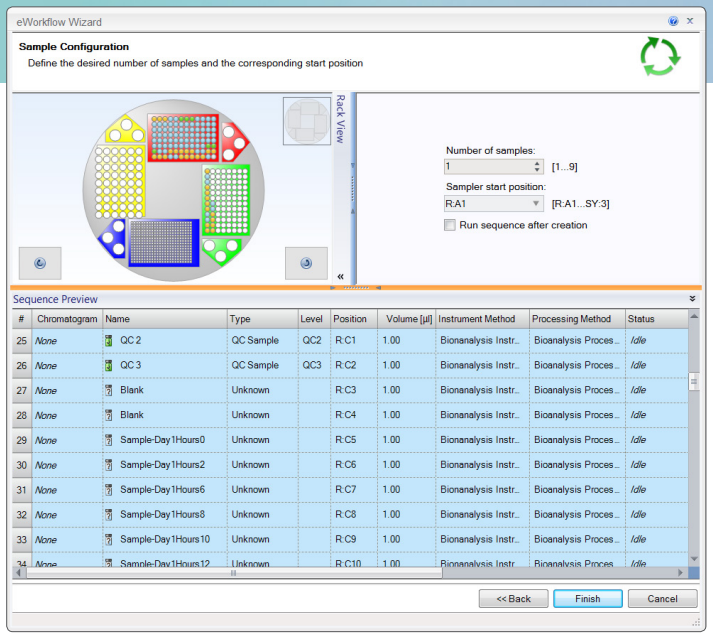


Figure 16. Starting an eWorkflow—select how many samples you want to analyze and the sequence is populated from predefined rules and templates.

A leading combination from an industry accepted data management system together with a gold standard CDS platform

The need to ensure accuracy and consistency throughout the data life-cycle has never been more important for bioanalytical studies. Thermo Scientific™ Watson™ LIMS software is built for bioanalysis with its extensive options to manage compliance throughout an entire workflow. From study management and design, samples can be tracked, analyzed, and reported using pharmacokinetic and toxicokinetic calculations available in Watson LIMS software.

Harmonizing and automating the complete bioanalysis workflow is achieved thanks to the out-of-the-box Chromeleon CDS and Watson LIMS Gateway (Figure 17). Utilizing eWorkflow procedures, data from an analytical run can be sent from Watson LIMS to create a sequence in Chromeleon CDS with the resulting data from the processed sequence being imported back into a Watson study.

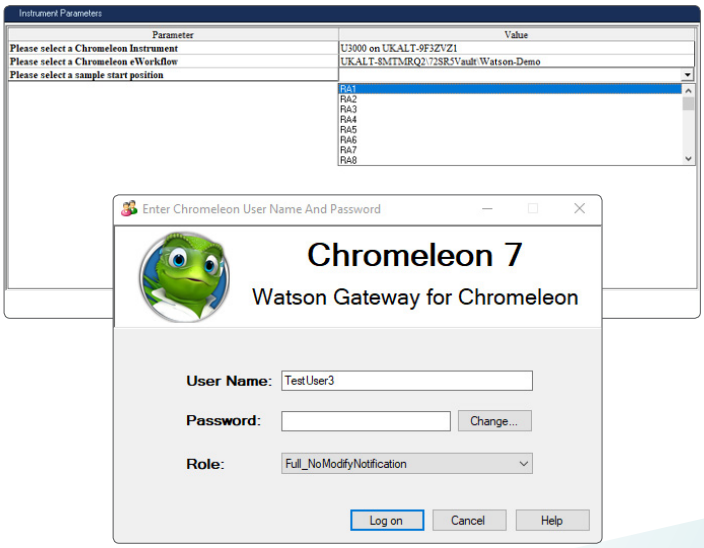


Figure 17. Watson Gateway for Chromeleon CDS—easy sequence creation.

One software package for LC and MS control and data acquisition
Simplifies training and provides familiarity – only one software to learn

Compliance built-in from the ground up
Designed to meet current and future regulatory requirements

Fully integrated MS and MS/MS functionality
Data processing features for bioanalysis that extends functionality for MS users

Remote access to data and instruments
Control across a network reduces the need to be in the laboratory, providing flexibility

Central data storage
A relational database at the heart of the application provides security and a structure than can handle complex queries

Smart tools like eWorkflow procedures and SmartLink
Streamlines workflows, minimizes error and increases productivity

Integration to Watson LIMS
A bi-directional interface to Chromeleon CDS with bioanalytical specific functionality – study design, sample tracking and pharmacokinetic/toxicokinetic calculations – improve efficiency with compliance

Scalable deployment
Seamless user experience from local standalone to multi-site Enterprise

Find out more at **thermofisher.com/chromeleon**

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