

# Sigma-Aldrich CMO helps customers comply with 21 CFR Part 11 using Chromeleon CDS software

SAFC Madison is one of Sigma-Aldrich's many contract manufacturing organizations (CMOs) facilities catering to pharmaceutical and biopharmaceutical organizations in need of development and scale-up manufacturing of an active pharmaceutical ingredient (API). The Madison facility specializes in highly-potent APIs (HPAPIs and HPAIs). Michael oversees the transition of the analytical technologies from the customer to the SAFC Madison site. His analytical lab performs method transfer, development, and qualification of assays designed to measure the purity of final product and intermediates, mostly by liquid chromatography (LC) and gas chromatography (GC). Supporting synthetic development and scale-up requires not only analysis at the isolated compound stage but also during the chemical transformations. The lab is charged with not only performing these analysis at the various stages of synthesis but also with scrutiny of the analysis techniques which may include

System Suitability Testing (SST), linearity, and specificity testing to assure the methods used are appropriate for the product. The Analytical Group works closely with the Process Development team to create a complete information package that can then be transitioned to GMP production and quality control.

Two years ago, SAFC Madison installed Thermo Scientific™ Chromeleon™ 7.1 Chromatography Data System (CDS) software as a building-wide solution for approximately 45 LC and GC systems divided roughly in half between their Analytical/Process Development groups and their Manufacturing/Quality Control groups.

**Michael Faley is Analytical Supervisor at SAFC® Madison, one of Sigma-Aldrich's many contract manufacturing organizations (CMOs). He received an MS in analytical chemistry and has worked in analytical process groups in the pharmaceutical, inorganic, and paper industries.** Michael started with Sigma-Aldrich performing raw materials and product testing before being promoted to Analytical Supervisor. He is a 16-year veteran of the company.

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Michael Faley  
Analytical Supervisor  
SAFC, Inc. (a wholly owned  
subsidiary of Sigma-Aldrich®)  
Madison, Wisconsin, USA

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## A closer look before Chromeleon CDS

Before installing Chromeleon CDS, every two instruments from a variety of manufacturers had their own computer and software. The fact that their systems were not networked created several problems and significant losses in efficiency:

- The biggest problem was lack of sufficient flexibility for multiple analysts logging in and using the two instruments controlled by one computer.

*“The computer would lock after a certain amount of non-use to accommodate company regulations, requiring another log-in by the same individual. If the chromatographic run spanned two shifts, or the instrument was needed after the run was complete, there was only one person who could access the system. No one else had access to the data generated or either of the instruments controlled by the one computer.”*

- Every time a new method was developed, they had to manually enter it into each chromatography system, which was both time consuming and had a higher potential for error.
- Because data was stored on individual chromatography systems without central access, gathering data and generating reports was time consuming. With their previous software, they entered data manually into a Microsoft Excel® spreadsheet, and then calculated system suitability results and assay values, which again is prone to transcription errors.

*“All of the manual data entry that was being used required a significant amount of time not only for analysis but also for review to ensure data accuracy.”*

- Having multiple data systems dependent on the instrument manufacturer also caused a huge barrier in training. It became complex and time consuming to train users on a multitude of operating, chromatography, and reporting software systems.

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**“We needed CDS software to assist in compliance with 21 CFR Part 11, which applies to data integrity of analytical instrumentation. Among other issues with our historical data systems, the lack of a full data audit trail was a big concern. We needed to be able to trace who did what, where, and when to chromatographic data. That meant having a networked solution with centralized data storage.”**

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## Criteria for selecting a CDS software

Although the major driver for purchasing a CDS software was for compliance and validation, one of the main reasons SAFC Madison selected Chromeleon CDS was because it was very intuitive and has an easy-to-use interface. This is a testament to the principles of Operational Simplicity™ followed in the development of the software.

*“After a brief familiarization it felt like you could just walk up to the system and accomplish what needed be done without jumping through an excessive number of hoops. You can tell that the software was built for the user’s ease. It has a familiar layout with the list of chromatography instruments on the left side. The first thing we noticed was how easy it was to put report templates together, to search for data, to set up a sequence, and to designate between samples and standards within your sequence allowing for the generation of a standard curve.”*

## Audit trail — mission accomplished

Many of their analytical challenges were solved by the networking capability of Chromeleon CDS software, which controls different types of chromatography systems (e.g., LC, GC, IC) from multiple manufacturers. The analysts report that one of the most convenient advantages is being able to use the software at their desk. From any location, employees with appropriate predefined access privileges can control instruments, review data, generate reports, and move information from one instrument to the next and from one lab to another.

For Michael, however, solving the audit trail problem was more important.

*“Now everyone can log on as individuals, and we know who generated the data and when. Chromeleon tracks every change.”*

The audit trail is not only helpful for regulatory compliance.

*“We find it really useful for troubleshooting the method or instrument. If one of the instruments does not function as expected, it’s a lot easier to troubleshoot with the audit trails that Chromeleon provides.”*

## Efficiencies gained!

The network data system is an upgrade in itself.

*“Compared to our previous standalone data systems, Chromeleon is so much more efficient. Rather than manually generating methods for each system computer, we can develop a method once and copy it along with other files to whatever system we need. This significantly reduces the opportunity for error and gives big savings in time. Now we don’t have to reinvent the wheel.”*

Chromeleon CDSs Report Designer feature also increases efficiency. This powerful spreadsheet-based reporting feature employs formulas and charts and other capabilities to define how data is displayed, printed, or exported. It includes modern report templates with the ability to create your own customized reports.

*“We always want to do things quicker, and the Chromeleon reports save us a lot of time. For example, previously for a residual solvent analysis of seven to eight solvents, we would transfer all the SST, calibration, and concentration data into controlled Excel spreadsheets for calculations. This could take up to an hour per sequence. Now, Chromeleon pulls the information directly into the report and all we have to do is review and print it. By avoiding the process of taking the data and putting it into Excel we are saving mountains of time and reducing opportunities for errors. All data is reviewable in Chromeleon, there is more reassurance of the data in the report, and it frees the analysts to spend more time doing other, more valuable work.”*

Because it’s so easy, Michael is continually looking to refine report templates to update, change, and improve data reporting. As a result, SAFC Madison uses Chromeleon CDS for instrument verification reporting which includes linearity, specificity, and reproducibility, and they have created reports to calculate the results. Chromeleon CDS also includes the Extension Pack, which comes with designed templates for verification and validation reports that could further simplify the process.

The reporting is also a major benefit to SAFC Madison customers. All of the data reported is standardized from instrument to instrument, even from LC to GC.

*“This is a benefit for not only SAFC but for our customers as well who want to see consistent reporting each time. It makes it easy to review when you know exactly where the data you’re looking for is reported. We have generated a generic report template that covers the majority of our assays, and the user simply changes the sequence requirements in their injection [sequence] table to pull all the required data into the report.”*

## Training significantly simplified

With only Chromeleon CDS to learn, training is now a lot simpler. All of their users took the Chromeleon CDS Level 1 and 2 Trainings onsite – about 10 in the Analytical/ Process Development groups, and about 15 to 20 in the Quality Control group.

*“The North American Centre of Excellence support team who performed the training was wonderful. The after sales support was excellent and we spent quite some time talking to them as we refined the Chromeleon setup.”*

## Next Steps —

### Electronic signatures, eWorkflows, and Chromeleon CDS with mass spectrometry control

Now with the Chromeleon CDS in place and validated, SAFC Madison will be implementing electronic signatures soon.

*“We are currently testing that they are working and functioning as expected. The goal is to ultimately have everyone from the analyst to the QA reviewer sign the data before a hard copy — which is filed with the master batch record — is generated. Electronic signatures are really going to save us a lot of time. They will replace and streamline the process of printing the data and handing it to the next person to review.”*

After electronic signatures, eWorkflows™ are the next feature SAFC Madison plans to implement. eWorkflows capture and automatically implement chromatographic details—such as the instrument conditions, injection sequence requirements, and results calculations. Thus automated eWorkflows can increase efficiency and reduce errors.

*“With Chromeleon on every instrument in the building and all data residing on one server, and with the data for each lab segregated using privileges and access control, I envision being able to transfer methods into the QA/QC lab using eWorkflows. Report Designer will be part of that, simplifying steps from data entry to final report creation, making the process even quicker and including actions based on SST results. The eWorkflows will be another check to ensure each method is run exactly as it should be.”*

The release of Chromeleon 7.2 CDS, is the first CDS that combines separation (GC/LC/IC) and Mass Spectrometry (MS) in an enterprise (client/server) environment. Chromeleon 7.2 CDS is the first CDS fully integrating MS into routine and quantitative workflows.

*“Currently MS is the detection method of choice for identification and measurement of low-level impurities. That is something we will be doing a lot more of as the need for ppm and ppb level analysis increases and a path that we will be moving toward. Having the data in the same CDS will maintain our compliance, improve our ease-of-use, and increase training and reporting advantages.”*

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**“Our customers actively requested a 21 CFR Part 11 compliant systems for purity analysis. Now that the system is in place they feel more secure knowing their data is safe and that we have full audit trails with user actions recorded for each chromatogram. It’s also very helpful for them when compiling data packets for regulatory filing.”**

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## Unexpected Advantage of Networked systems – 30% savings in lab bench space

Before Chromeleon CDS was installed, every other instrument had a computer, monitor, keyboard and mouse. Seven of the lab benches were full of instruments and computer systems.

After Chromeleon CDS was installed, the computers systems were removed and only one user interface was needed per lab bench, which freed two lab benches for other uses. That’s a 30% space saving.

## Reference

1. Compliance Guide: Using the Thermo Scientific Dionex Chromeleon 7 Chromatography Data System (CDS) to Comply with 21 CFR Part 11. <http://apps.thermoscientific.com/media/cmd/Teamsite/Chromeleon/Compliance-Guide-21-CFR-Part-11.pdf>

Chromeleon CDS follows these simple principles of Operational Simplicity™:

- Minimize the number of steps needed to perform any task
- Make all the steps easy to understand and use
- Minimize time needed to perform any task



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