

## HPLC &amp; UHPLC

## Seamlessly integrating state-of-the-art (U)HPLC into an existing CDS framework

### Integrating cutting edge UHPLC technology in an existing regulated CDS framework

Thermo Fisher Scientific Pharma Services Group (PSG, also known as Patheon) provides industry leading Contract Development and Manufacturing Organization (CDMO) services with more than 55 locations around the world having the capability to support chemical and biopharmaceutical molecule drug substance manufacture, formulation, drug product manufacture, testing, packaging, and shipping. This pharma services team, streamlines the development and manufacturing of pharmaceutical and biopharmaceuticals through a comprehensive range of services that is unmatched by conventional contract development and manufacturing organizations.

#### Enabling connectivity

One of those pharma services sites in Greenville, North Carolina, has begun to replace older HPLC systems with the more advanced and robust Thermo Scientific™ Vanquish™ HPLC and UHPLC systems. The site historically has used Waters™ Empower™ 3 Chromatography Data Software (CDS) for control and operation of its chromatography systems and transitioning to a new platform can sometimes mean a change in CDS which can be a lengthy project. Fortunately, the Vanquish family of HPLC and UHPLC systems can be controlled in Empower 3 CDS using the Thermo Scientific™ Standard Instrument Integration (SII) for Empower 3, which works seamlessly with the Empower 3 CDS. When configuring the instruments into Empower 3 CDS the full functionality remains the same with the ability to prime, rinse, set-up, and equilibrate the system from a remote terminal, therefore retaining the familiar feeling for the user.

Analyses using the Thermo Scientific™ Vanquish™ Core HPLC, Flex UHPLC, and Horizon UHPLC systems are initialized the same way as with other instruments in Empower 3 CDS. When the instrument method editor is opened, the SII interface opens an easy-to-use instrument method wizard that walks analysts through settings of each instrument component with a review and correction step prior to saving (Figure 1).

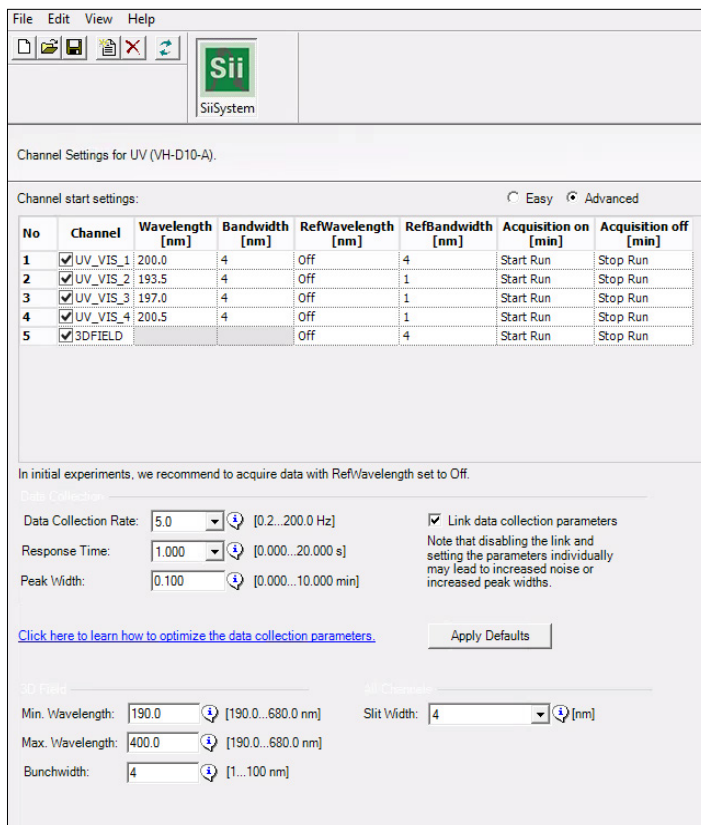


Figure 1: Simple method wizard to create methods easily

## Stable and simple to operate

SII is a very user-friendly environment. It integrates within the Waters Empower 3 CDS infrastructure and when setting methods or operating the Vanquish platform, has an embedded control panel with simple and visual display allowing an analyst to walk up and begin setting up methods with minimal training. The on-screen graphical display is intuitive and allows user to visualise and interpret chromatographic conditions easily.

PSG Greenville, NC location rely on their metrology group for operation and maintenance of their systems, and the group is key to the operational uptime of the department, along with robust systems and, critically, stable connections between instruments and servers, preventing expensive downtime.

“The SII interface is easy to control and requires no significant training on use beyond a short demonstration. The instrument works within the fully enabled audit trail in Empower and changes are tracked in the instrument audit log which is displayed at the bottom of the SII interface.”

—Nolan Dean, staff scientist

“From an administrator standpoint the software running on the local LAC/E servers actually is a lot better as far as the configuration of the system and it’s in the software compared to our other systems,” said a senior metrologist for Lab Services. “It’s a lot more detailed and there are options and functions that are a little bit more customizable than what we see with the standard Empower interface with other vendor liquid chromatography platform.”

Regarding instrumentation, “We have very harsh methods here and those methods which typically have caused a lot of downtime on some of our HPLC systems. We don’t see a lot of that havoc on the Vanquish LC systems. The overall operation of those systems far exceeds what I have seen as far with other LC systems,” said Nolan Dean.

## Working in GMP environments

The SII interface brings across a host of features developed for Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS) that deliver additional compliance capabilities.

“The SII interface contains a live audit trail that tracks instrument status in real time. This includes instrument settings, flushing/purging, and when compartments are opened or closed.” According to Nolan Dean, staff scientist in the Analytical Development department at the Greenville, NC location. “This audit trail data allows analysts to track system cleaning and equilibration for precise status updates and troubleshooting support.”

“As an additional protection to being tracked in the audit trail, if an analyst were to interrupt a run and make a system change after it had been started, that would be captured in the analyst individual error log that the run had been intercepted, and so we were able to continue using the Vanquish system by including copies of our error logs in our Vanquish run write ups. We back up all those error logs routinely and so we can get copies of those to check if we need to. Ultimately, we can see the history of each run which helps us from data integrity.”

## Technology improvements

Gradual upgrades from older HPLC systems to newer technologies has some great advantages like being able to modernize older methods and developing newer, faster, more sensitive methods to improve both throughput and quality of the data, ultimately providing more confidence that the drug manufacturing process is safe for the patient but also reducing operational costs. It is expected that the need to update instrumentations and methods will become key in the near future as indicated in the ICH Q2(R2) and ICH Q14<sup>1</sup> guidance on Analytical Procedure Development<sup>1</sup> (currently under review with the industry), which provides general recommendations for analytical procedure development and lifecycle management.

The analytical product lifecycle comprises several elements like the analytical procedure development, validation and change management which are interrelated. Part of change management is continual improvement of the analytical procedure, which can be achieved by modernizing instrumentations and transferring analytical methods to the latest technologies leading to improved specificity, enhanced precisions, accuracy, and overall lab efficiency gains. The Vanquish family contains intelligent features enabling all the advantages of a modern HPLC and UHPLC system but also features which allows legacy methods to be transferred with minimal issues.

Key features such as adjustable gradient delay volumes and a choice of column heating modes, along with passive or active mobile phase pre-heating options make moving methods from other vendors platforms a simple task. Thermo Scientific™ Viper™ fingertight, high-pressure fittings also allow for simple operation and changing of columns and compartments without having to worry about dead-volume in new connections, or constant tube cutting. During injections, the sample loop at atmospheric pressure is placed in line with the high-pressure flow path, typically resulting in a pressure drop. With regular UHPLC systems, this adversely affects retention time precision and column lifetime. SmartInject Technology automatically eliminates the pressure drop improving data confidence and reduced cost of ownership.

## About Nolan Dean



Nolan is a staff scientist in the Analytical Development department at the Greenville, NC site. His department is responsible for supporting the method development, validation, and transfer and analytical testing for pharmaceutical ingredients and drug products from the research and development phase through commercialization. Nolan has experience with Waters, Agilent™, Shimadzu™, and Thermo Fisher Scientific instruments and software.

## How to integrate Thermo Scientific LC systems into Waters Empower 3 Chromatography Data Systems in regulated environments

It is important that leading high-performance liquid chromatography (HPLC) systems, such as the Vanquish HPLC and UHPLC systems, can be seamlessly integrated into existing informatics deployments. In addition to Chromeleon CDS, Vanquish LC systems can also be connected to alternative CDS offerings including Empower 3 CDS software. Other instrumentation such as GC and IC can also be integrated within this network. For seamless connection to Empower enterprise deployments, Standard Instrument Integration (SII) for Waters Empower 3 software is required to enable instrument control. Data processing, reporting, and data storage for Vanquish HPLC and UHPLC systems will remain within Waters Empower software.<sup>2</sup>

### References

1. ICH Q14—Analytical Procedure Development, Draft Version, Endorsed on 24 March 2022, ICH 2022 [https://www.ema.europa.eu/en/documents/scientific-guideline/ich-guideline-q14-analytical-procedure-development-step-2b\\_en.pdf](https://www.ema.europa.eu/en/documents/scientific-guideline/ich-guideline-q14-analytical-procedure-development-step-2b_en.pdf)
2. Integrating Thermo Scientific LC systems into Waters Empower 3 Chromatography Data Systems in regulated environments <https://www.thermofisher.com/document-connect/document-connect.html?url=https://assets.thermofisher.com/TFS-Assets%2FCMD%2FTechnical-Notes%2Ftn-74067-ic-guidelines-regulated-environments-tn74067-en.pdf>

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