



Empowering success by adopting new LC instruments within an existing network

Transforming the way pharmaceuticals are made

Patheon 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 (CDMO). With an exceptional history of innovation that began in the mid 1970's, Patheon's latest evolutionary step occurred in 2017 when it became part of Thermo Fisher Scientific. The newly combined organization delivers an end-to-end solution from initial drug formulation to clinical trials support, through to commercial production.

Enhancing the laboratory infrastructure

After many years of experience with Agilent® and Waters® LC systems, the new relationship between Patheon and Thermo Fisher Scientific prompted the evaluation of new analytical technologies. The aim was to enhance their current capabilities to attract additional customers while fitting within their current informatics deployment.

Having previously standardized on Waters Empower® 3 Chromatography Data Software, it was required that any analytical equipment Patheon adopted could be operated under this environment. This would ensure that the new technologies would fit directly into their current network deployment and minimize disruption to daily operation over the course of the evaluation.

Deployment of the Vanquish UHPLC system at Patheon sites across the globe has enabled improvements in assays such as released glycan analysis, peptide mapping and monitoring, as well as purity and ratio analysis. In comparison with other vendors' HPLC systems, the Vanquish UHPLC system demonstrated superior retention time reproducibility (leading to more consistent ratio determinations) as well as enhanced peak area reproducibility, simplifying the quantitation of low-level impurities present in disparate amounts (Figure 1 and Figure 2).

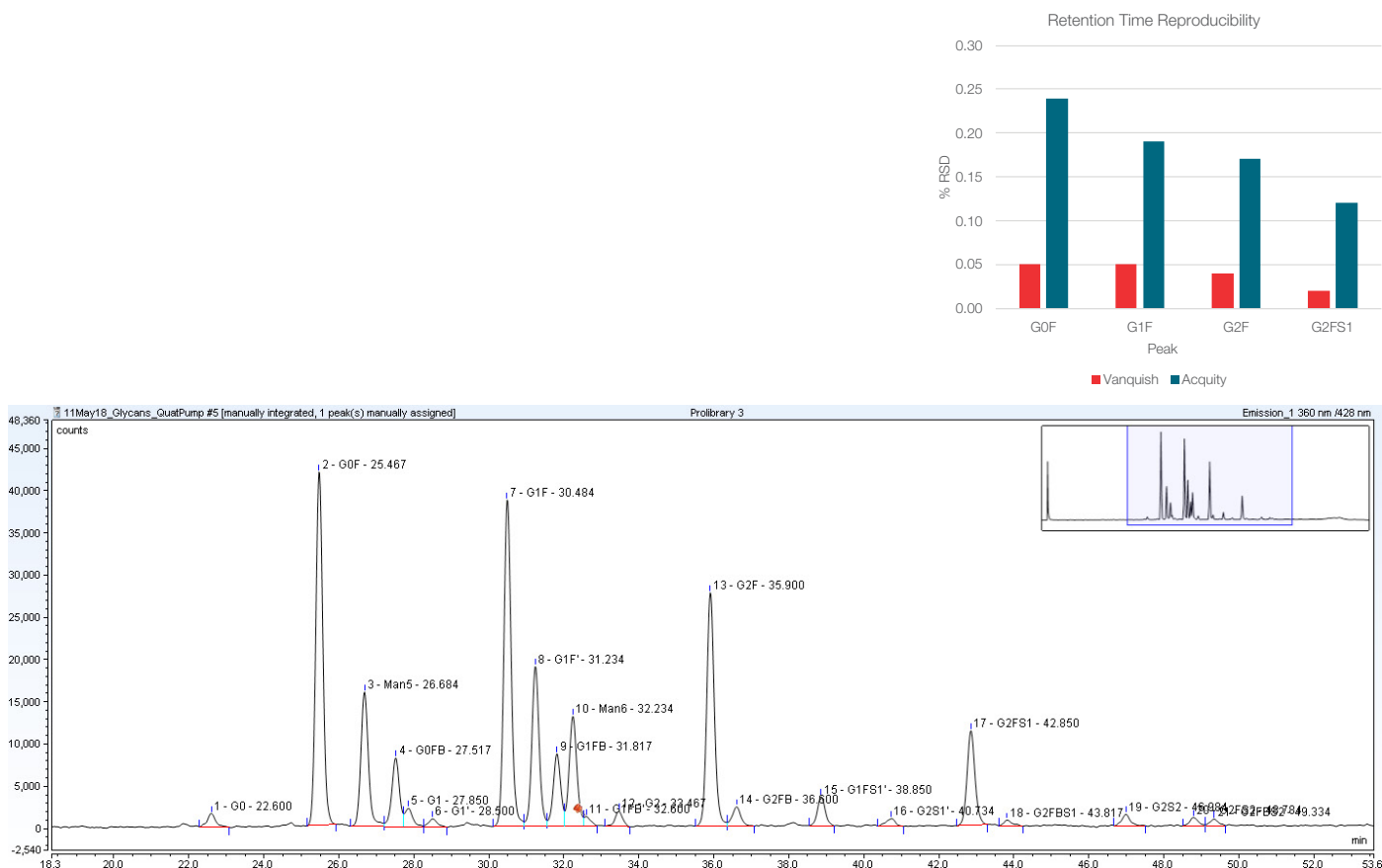


Figure 1: Monitoring of glycoprofiles (top) plays a large role in the determination of safety, efficacy and potency of biopharmaceuticals. In conjunction with the demonstrated resolution, the extreme retention time stability of the Vanquish Flex (bottom) improves structural characterization and quantification. Note that a shallow gradient profile of 0.32% ACN/minute is used.

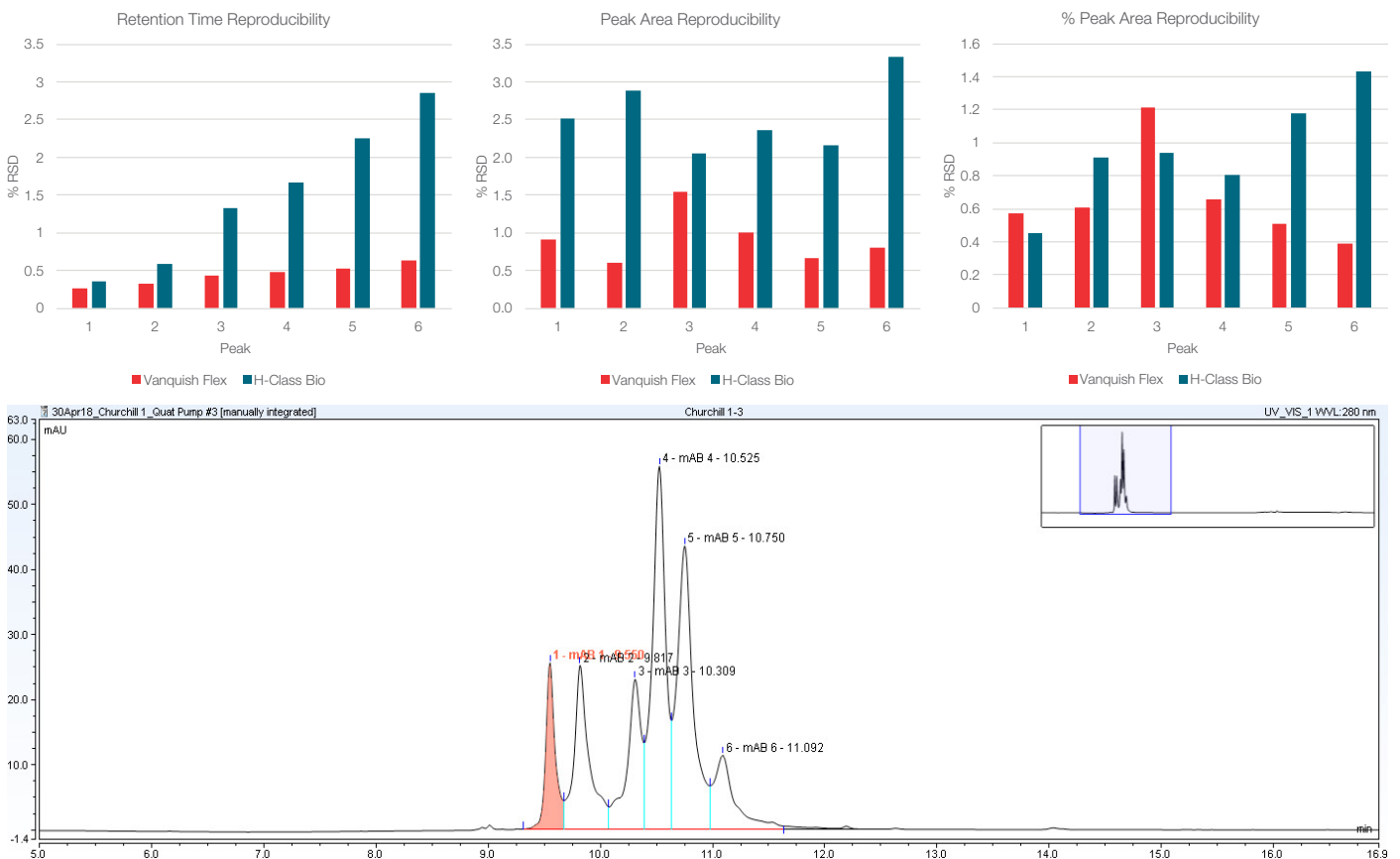


Figure 2: Direct injection and separation of 6 antibodies under a shallow gradient profile of 0.05% ACN/minute to determine the phase ratio. Vanquish Flex demonstrates superior retention time reproducibility leading to more consistent determination.



Ease of analytical method transfer

Diversity in analytical capability is an essential trait for any contract organization to meet the large range of needs and requirements of various sponsor companies. However, this diversity can lead to complexities in transitioning methods from one site to another or between different vendors' analytical equipment.

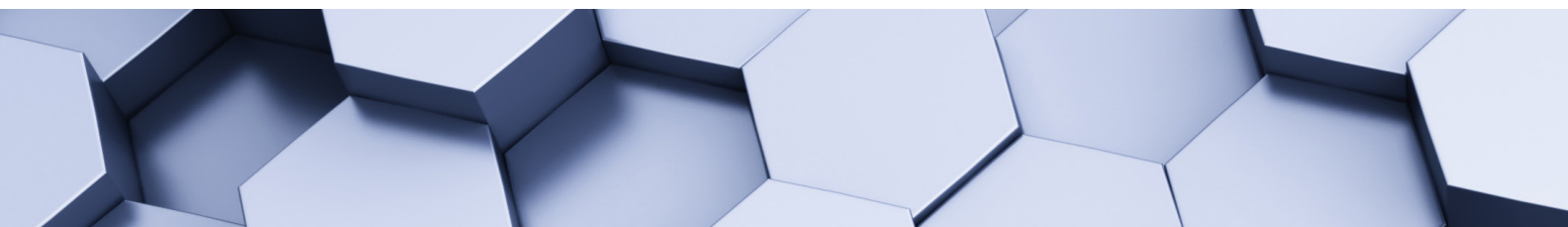
The Vanquish UHPLC platform architecture incorporates several intelligent features to significantly simplify the analytical method transfer process between different vendors' LC systems.

Table 1: Method Transfer capabilities of the Vanquish UHPLC platform

Feature	Benefit
Multiple column heating modes	Ability to emulate the thermal environment of any vendors' LC system, matching how the heat is dissipated from the column.
Active solvent pre-heating	Enhanced thermal consistency from unit-to-unit. Can also be used as a fine-tuning parameter that can be set independently from the column oven temperature.
Standard column heater accommodating columns up to 30 cm in length	Flexibility to have a single oven that supports both legacy HPLC methods and more efficient and rapid UHPLC methods.
Error-free fluidic connections (Viper fittings)	Simple, standardized, zero-dead volume, tool-free fluidic connections to any vendors' separation column.
Built-in adjustable Gradient Delay Volume (GDV)	Allows adjustments in the gradient delay volume without altering the gradient table. In addition, the injection can be decoupled from the start of the gradient to account for system volume differences. If larger differences exist between the origin and target systems, a suite of mixers are available to compensate for any differences between different vendors' HPLC systems.

Table 2: System suitability comparison for three UHPLC systems

Parameter	Criteria	Vanquish Flex	ACQUITY UPLC H-Class	Agilent 1260
No significant interference at RT of active and impurities in blank injection	NMT 0.1% of active area in 1st standard injection	No interference	No interference	No interference
USP s/n of sensitivity	NLT 10.0	17.0	15.0	12.0
Tailing factor (n=5)	NMT 2.0	1.0	1.0	1.1
%RSD of active peak area (n=5)	NMT 2.0%	0.0	0.2	0.1
%RSD of active peak area (n=all)	NMT 2.0%	0.1	0.2	0.3
%RSD of active RT (n=5)	NMT 2.0%	0.0	0.0	0.0
%RSD of active RT (n=all)	NMT 2.0%	0.0	0.0	0.0
Check standard (% Recovery)	98.0–102.0%	100.1	100.0	100.0
Resolution between impurity A and impurity B	NLT 1.0	2.1	2.2	2.1



Component	Relative Retention Time (min)		
	Vanquish Flex	Waters ACQUITY H-Class	Agilent 1260
Component 1	0.78	0.76	0.78
Component 2	0.80	0.79	0.80
Component 3	0.94	0.98	0.95
Active	1.0	1.0	1.0

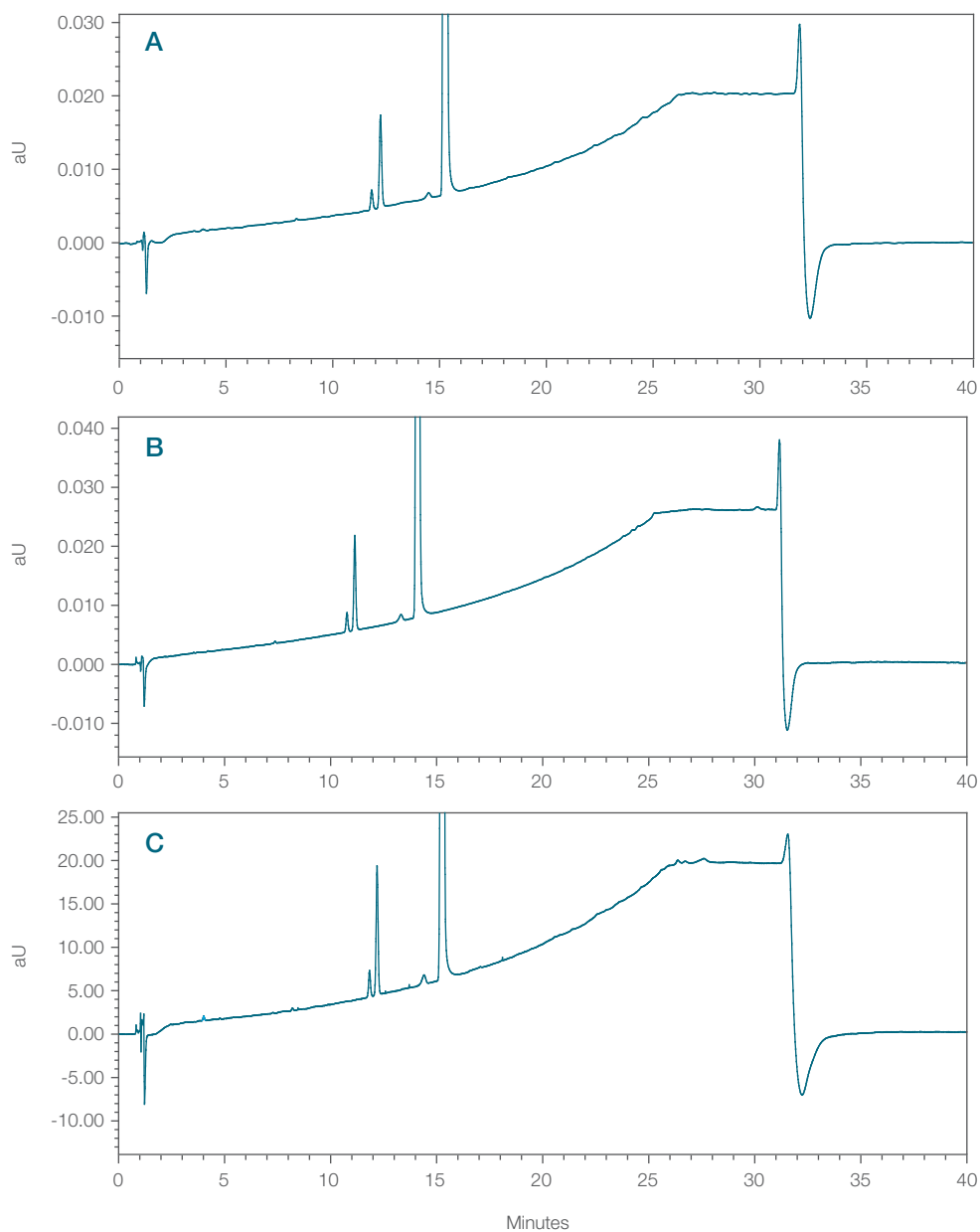


Figure 3: Separation of impurity profile on (A) Agilent 1260 (B) ACQUITY UPLC H-Class and (C) Vanquish Flex. Water / ACN gradient containing 0.05% TFA over 40.0 mins at 1.0 mL/min. 3.9 × 150 mm, 5 µm C18 column set to 35 °C; UV @ 224 nm





“Within our Analytical and Quality Control Laboratories, we have a very successful initiative called “Lean Labs.” This initiative optimizes all elements of laboratory testing, but especially significant productivity gains are achieved with the physical arrangement of the laboratory and the work flow of samples. By streamlining the movement of both analysts and samples, we have made substantial gains in productivity. The Vanquish Duo systems are an integral part of this initiative, achieved by increasing the chromatographic testing capacity with half the laboratory footprint. The Vanquish Duo’s are a quantum step in laboratory productivity.”

—William E. Weiser, Ph.D.,
Senior Director, Global Quality, Patheon

Maximizing laboratory productivity

As with any growing organization, being able to keep up with the increasing number of samples to analyze can cause an exceptional challenge. The investment in additional capital equipment, or hiring incremental staff to increase capacity, is not always a feasible option. The creation of additional lab space is an even less likely option.

When the Thermo Scientific™ Vanquish™ Duo UHPLC System was discussed with the Patheon team, new possibilities to increase the capacity of samples that could be handled within their current infrastructure were noted. Despite maintaining the footprint of a single HPLC

system, the Vanquish Duo offers the capacity and productivity of two HPLC systems in one. Two separate and independent fluidic paths are supported through:

- The Vanquish Duo Pump which houses two, ternary gradient pumps in a single module
- The Vanquish Dual Split Sampler which contains two independent injection units within a single module

This enables the analyst to run either the same method on both channels simultaneously, or two complementary methods on each fluidic path to maximize selectivity.

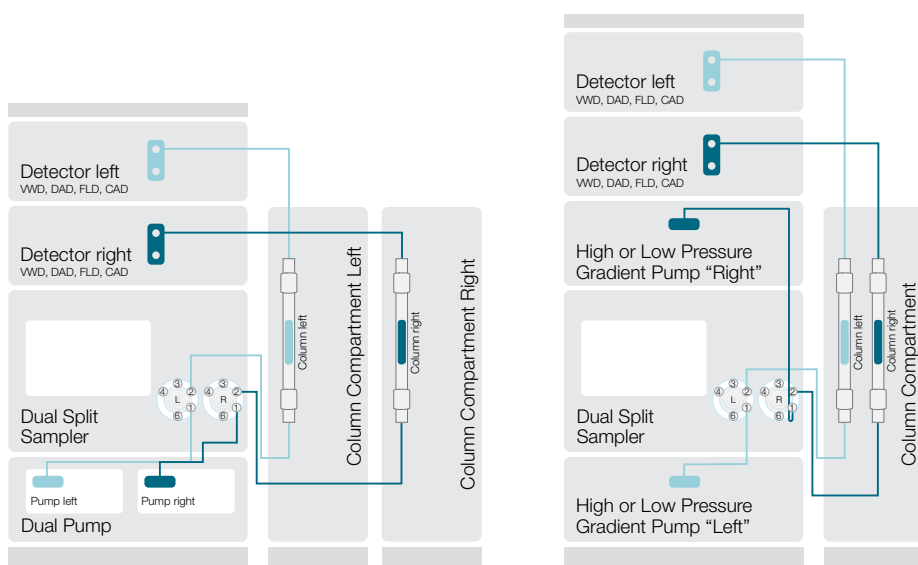


Figure 4: Vanquish Duo for Dual LC. In conjunction with the Vanquish Dual Split Sampler, the Vanquish Duo can be configured with the novel Dual Gradient Pump or utilize two separate pumps. Either configuration provides two completely independent fluidic paths for maximum throughput per unit of bench space.



The importance of informatics selection to enhance laboratory workflows

Patheon previously operated Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS) at several of their laboratories but a decision was taken to use Waters Empower 3 Software as the sole chromatography data system (CDS) for their laboratories. At the time of this decision, Patheon were unaware of alternative software that could equally address their compliance and data integrity requirements, as well as ensuring productivity within the lab and handling of the diverse range of chromatography instrumentation installed.

It was straightforward to control and acquire data from the Vanquish UHPLC platforms with the Thermo Scientific™ SII for Empower plug-in, ensuring Patheon could take advantage of the Vanquish UHPLC capabilities while, eager to learn more about the capabilities of the alternative CDS platform they now had at their disposal, Patheon embarked on an evaluation of the Chromeleon 7 CDS. Comparative results of feature sets are captured in Table 3.

Table 3: Comparative feature set of CDS

Feature	Empower 3	Chromeleon CDS
Instrument Control		
Native	Waters LC; MS - SQD, Legacy TDQ	Thermo Scientific LC/GC/IC; MS - Single/Triple Quad, HRAM
Third party	>300 instruments (as of FR3)	>525 instruments (as of 7.2.10)
Data Capture/Processing/Reporting		
User interface	QuickStart, Pro, Open Access	Standard, XPS Open Access
Wizards	Instr., Seq., Integr.	Instr., Seq., Integr.
System suitability	Add-on, basic IRC	SST, IRC
Data processing	Batch processing	Dynamic data processing
Custom calculations	Complex setup	Easy spreadsheet-type formulas
Custom reports	✓	Easy spreadsheet Report Designer
Data trending	✓	✓
Compliance		
21 CFR Part 11 controls	✓	✓
User roles/privileges	✓	✓
Audit trails	✓	✓
Data and audit trail rev.	Multiple locations	One location
Object versioning	✓	✓
Electronic signatures	✓	✓
Object unique identifier	Methods, sequences, samples, injections, results	Samples
Performance qual	Waters must execute	User cart execute
IT		
Scalability	Separate workstation, workgroup, Enterprise versions	Scalable workstation to Enterprise in same version
Licensing	Per named user	Concurrent user
Cloud capable	✓	✓
LIMS connectivity	No first-party LIMS solution, third party with customization	Direct to Thermo Scientific™ SampleManager™ LIMS and Watson™ LIMS, third party with customization
Network failure protection	Finished Queued Seq. only	Finished Queued Seq., Start New Seq., Process Data



Comparison of CDS Solutions

Chromeleon 7 CDS was extensively evaluated and found to meet all of Patheon's Compliance and Data Integrity Assessment criteria. Furthermore, it was shown that overall Chromeleon CDS required one third fewer mouse clicks and windows to perform the same tasks as Empower 3. Naturally this would translate to an increase in data system productivity within the labs enabling Patheon to further support their "Lean Labs" initiative.

Conclusion

Patheon has seen the potential for exceptional gains in efficiency by leveraging multiple elements of the Thermo Fisher portfolio and is undergoing widespread deployment. Through this, they are able to enjoy efficient method transfer, harness the benefits of high productivity instrumentation and utilize intelligent data systems to streamline their laboratory workflows.

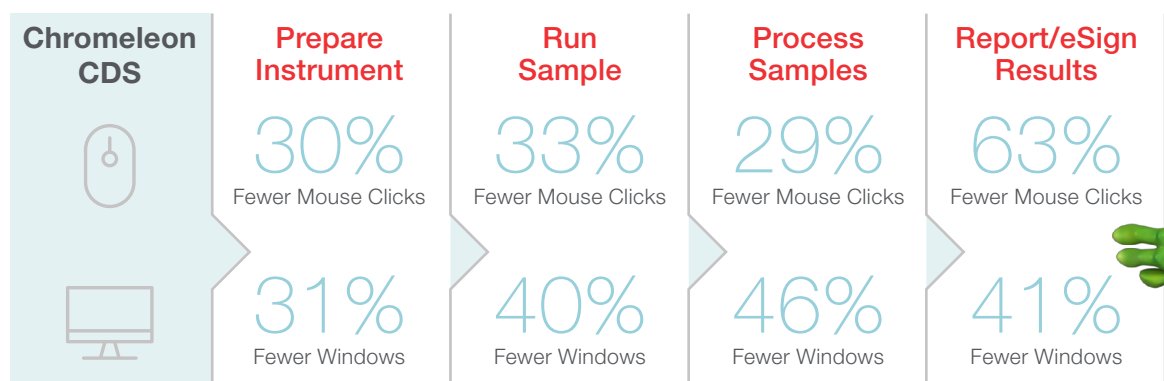


Figure 4: Chromeleon 7 CDS vs. Empower 3 common workflows comparison



What we offer:

- Risk free on-site LC evaluation with your samples enabling you to try before you buy
- High productivity HPLC systems and workflows
- Industry-leading productivity per meter of bench space
- Automated end-to-end workflow solutions including robotics
- Onsite support with qualification in Thermo Scientific Chromeleon and Waters Empower 3 CDS
- Method transfer and optimization services
- Alternative financing and leasing options
- Tailored solutions to guarantee low cost of operation.
- Flexible compliant Chromatography Enterprise Data system with multi-vendor and MS support
- Fast service response and access to our global Customer Solution Centers and Experts

Find out more at thermofisher.com/Vanquish