Application Note

Biopharma/Pharma

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Digital Transformation of a Biopharma Quality Control Lab

Using a cloud-based infrastructure of chromatography data system and lab information management system to boost analytical lab efficiency.

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Introduction

Over the last 20 years, pharmaceutical laboratories have faced persistent regulatory pressure to adopt paperless operations (1). This push towards digitalization aligns with the industry's business needs and objectives to elevate overall lab efficiency. A highly efficient laboratory is characterized by its ability to achieve the shortest possible turnaround time while maintaining uncompromising quality in analytical results. Also, it operates as a cost-effective business, optimizing resource utilization, and productivity.

During this digitalization journey, it is crucial to ensure minimal disruption to current lab operations and prioritize an optimal user experience. This emphasis on a smooth transition is critical in pharmaceutical laboratories, which are known for their high degree of standardization.

The Agilent software portfolio is designed in a way that allows different software to integrate and collaborate, ensuring comprehensive coverage of the entire analytical workflow as shown in Figure 1. This high degree of integration largely prevents or minimizes disruption to existing operations.

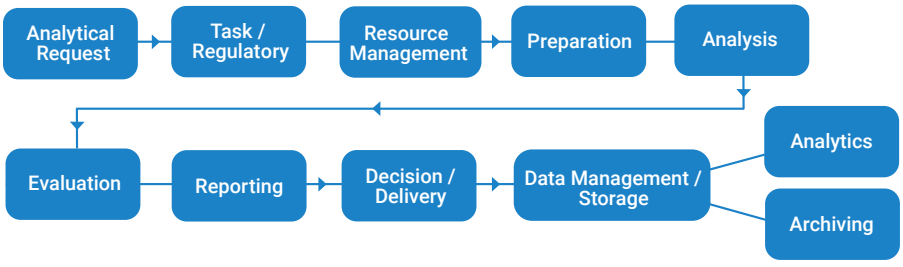

Figure 1. Agilent software ecosystem covering the entire laboratory analytical workflow.

In this study, a small-scale analytical laboratory was configured to emulate a biopharmaceutical quality control (QC) lab for monoclonal antibody (mAb) release tests. Each LC system was dedicated for one type of test. LC-1 was for aggregation analysis while LC-2 was for charge variants analysis. Aggregates and charge variants are product-related impurities that arise during the manufacturing process or storage. Their presence in the end product negatively impacts stability, activity, and efficacy. Therefore, they are considered critical quality attributes (CQAs), and must be closely monitored and tested throughout the manufacturing process and before batch release as per regulatory requirements (2).

To digitalize the two analytical workflows, a network infrastructure was established as depicted in Figure 2. Both an Agilent OpenLab client/server system and SLIMS were installed on cloud servers. Local control of both LCs was achieved via an Agilent instrument controller (AIC). Communication between servers and the AIC was through the corporate network.

The primary aim of this study is to showcase a streamlined mAb QC analytical workflow from sample submission to final answers in the OpenLab CDS and SLIMS ecosystem. Furthermore, the study emphasizes the significance of digitalization in elevating the operational efficiency of analytical laboratories.

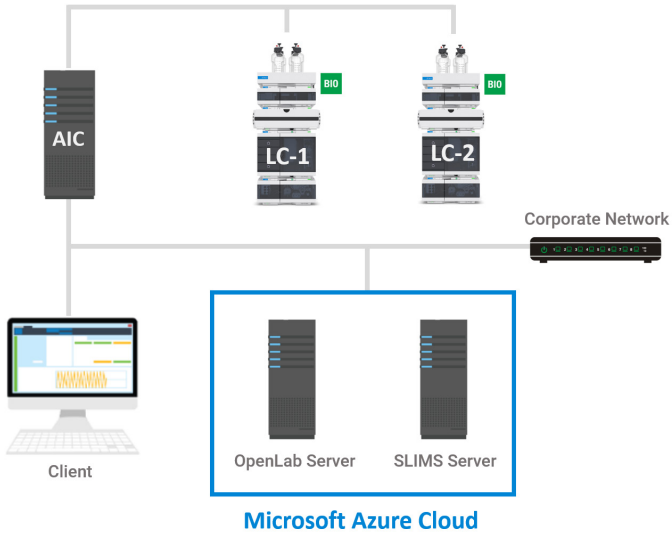

Figure 2. Cloud and network infrastructure of the Agilent OpenLab client/server system and Agilent SLIMS environment.

Experimental

Instrumentation and cloud infrastructure

LC-1 configuration

- Agilent 1290 Infinity II bio high-speed pump (G7132A)
- Agilent 1290 Infinity II bio multisampler (G7137A) with Agilent Infinity II sample cooler option #100)
- Agilent 1290 Infinity II multicolumn thermostat with bio heat exchanger (G7116B)
- Agilent 1290 Infinity II diode array detector (G7117B)

LC-2 configuration

- Agilent 1290 Infinity II bio flexible pump (G7131A)
- Agilent 1290 Infinity II bio multisampler (G7137A) with Agilent Infinity II sample cooler (option #100)
- Agilent 1290 Infinity II multicolumn thermostat with bio heat exchanger (G7116B)
- Agilent 1290 Infinity II diode array detector (G7117B)

Software

- SLIMS 6.9
- OpenLab CDS client/server 2.7
- Sample Scheduler for OpenLab version 2.7

Cloud server

- Two Microsoft Azure cloud servers for OpenLab CDS and SLIMS respectively

Analytical request and task assignment

In this study, two mAb samples originating from distinct batches were tested to assess their aggregate, acidic, and basic variants content. To initiate the sample tests, a new QC order was created in SLIMS, and the two samples were registered under this order. Sample details like volume, storage location, and lot number can be stored as sample details (Figure 3). In addition, the tests associated with the two samples immediately appeared in the Request Overview panel (Figure 4).

An order in SLIMS serves as a centralized sample context, housing essential sample information, test requests, associated workflows, and final results. It ensures proper documentation and organization of sample-related information throughout the analytical process.

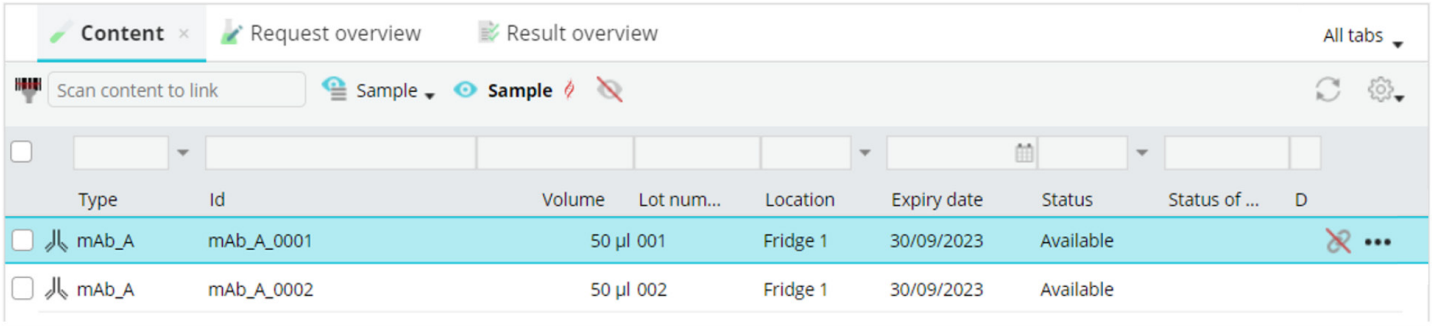

Figure 3. The QC order overview in the SLIMS Order window includes a Content view.

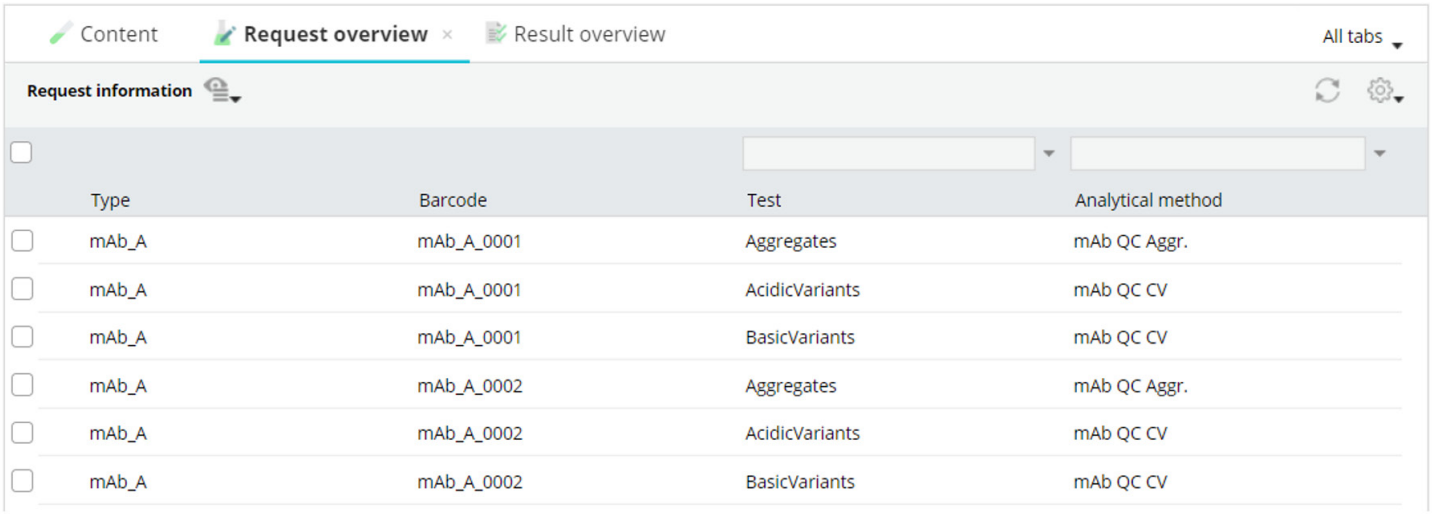

Figure 4. The QC order overview also includes a Request Overview.

Resource management

After sample test submission, consumables and chemicals need to be located for test preparation such as mobile phase (MP) preparation and column selection. LC columns and chemicals were defined in SLIMS and their consumption and expiration were monitored and tracked. This resource management function ensures that these essential resources are readily available and still valid before initiating any analysis.

Also, users have the flexibility to create custom views, tailored to their preference or current lab practice, facilitating the efficient management of laboratory resources. Figure 5 shows the four custom views created during this study, based on samples, solid chemicals (Figure 5), liquid chemicals, and LC columns (Figure 6).

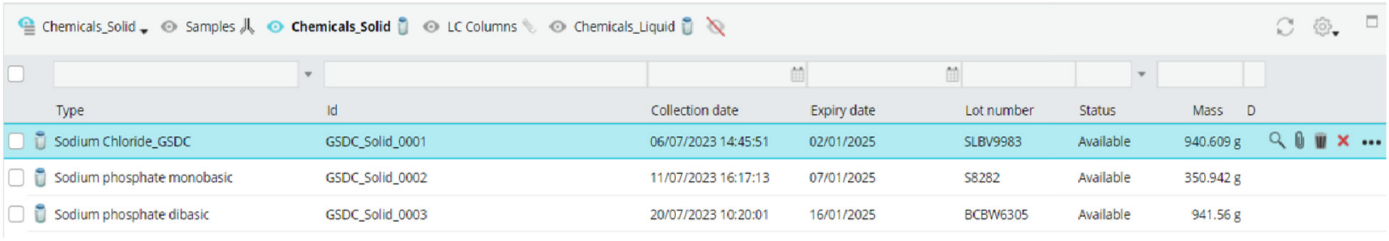

Figure 5. Samples, chemicals, and consumables tracking in the SLIMS Consumables view, for the Solid Chemical inventory.

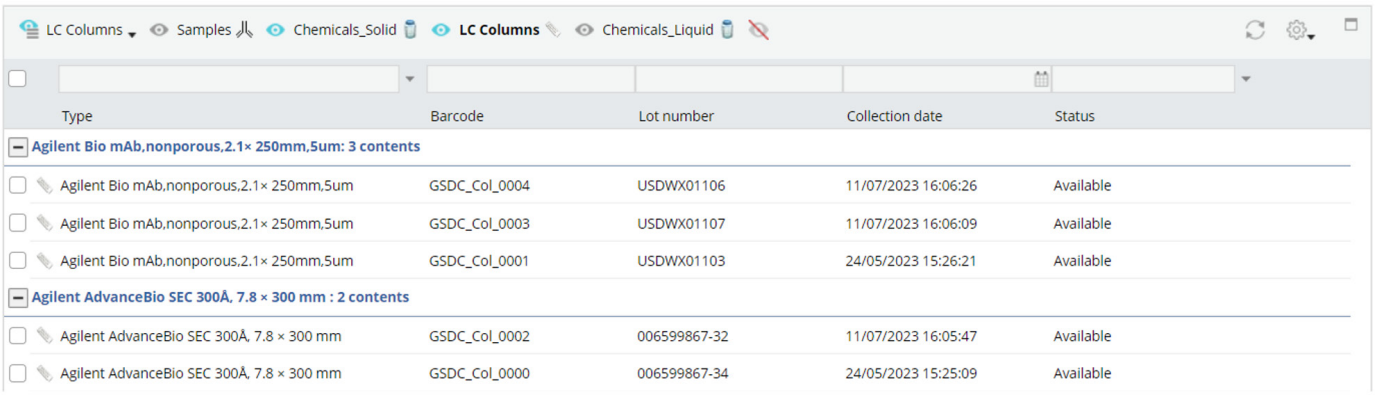

Figure 6. SLIMS Consumables view shows the LC Columns inventory.

Furthermore, the Dashboard view offers an at-a-glance look of expiring chemicals and instrument calibration/preventative maintenance (PM) schedules (see Figure 7). These resource management tools ensure that the analysis strictly adheres to quality guidelines and regulatory standards using only qualified chemicals and instruments.

During this study, the availability and expiry dates of LC columns, sodium chloride, sodium phosphate monobasic, and sodium phosphate dibasic were carried out before proceeding with the subsequent experimental procedures.

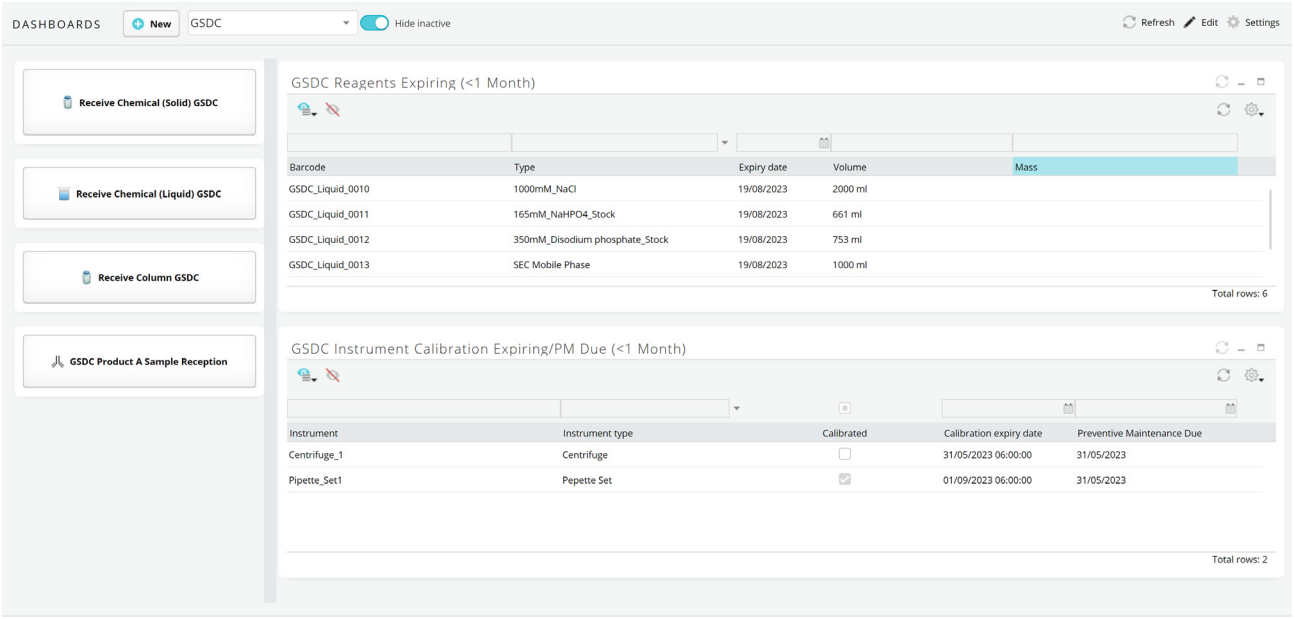

Figure 7. Dashboard view of expiring reagents and instrument calibration/PM.

Preparation workflow

Both the aggregation and charge variant analysis in this study used phosphate buffer-based methods (3). The MP preparation protocols, involving various steps such as weighing, dissolution, dilution, and mixing, can be found in Table 1. In the SLIMS software, these intricate text-based protocols were transformed into a visualized workflow (Figure 8) to enhance its usability and reduce the risk of human error.

Table 1. MP preparation protocol for aggregation and charge variant analysis.

Stock Solution			
Name	Chemical	Amount (g)	Remarks
A : 1,000 mM NaCl	NaCl	19.797 g	Dissolve in water and make up to 1 L
B : 165 mM NaH2PO4	NaH2PO4	49.686 g	Dissolve in water and make up to 1 L
C : 350 mM Na2HPO4	Na2HPO4	58.44 g	Dissolve in water and make up to 1 L
Aggregation MP (100 mM sodium phosphate buffer + 150 mM NaCl, pH 7.0)			
Stock Solution	Volume (mL)		Remarks
A : 1,000 mM NaCl	150		
B : 165 mM NaH2PO4	189		
C : 350 mM Na2HPO4	197		
HPLC water	Make up with HPLC to 1 L		Confirm working solution pH at 7.0
Charge variant MP			
MP Channel	Volume (mL)		Remarks
A : HPLC water	500		
B : 1000 mM NaCl	500		Pour 500 mL from Stock A (1,000 mM NaCl)
C : 55 mM Na2HPO4	450		Pour 150 mL from Stock B and dilute with water to 450 mL (three-times dilution)
D : 50 mM Na2HPO4	350		Pour 50 mM Stock C and dilute with water to 350 mL (seven-times dilution)

In Figure 8, each arrow represents a specific protocol. The steps and necessary quantities of chemicals are indicated within each protocol as displayed in Figure 9. Upon the execution of a protocol, the corresponding amount is automatically deducted from the respective chemical inventory. The visualized, step-by-step MP preparation protocols guarantee a smooth and foolproof operation.

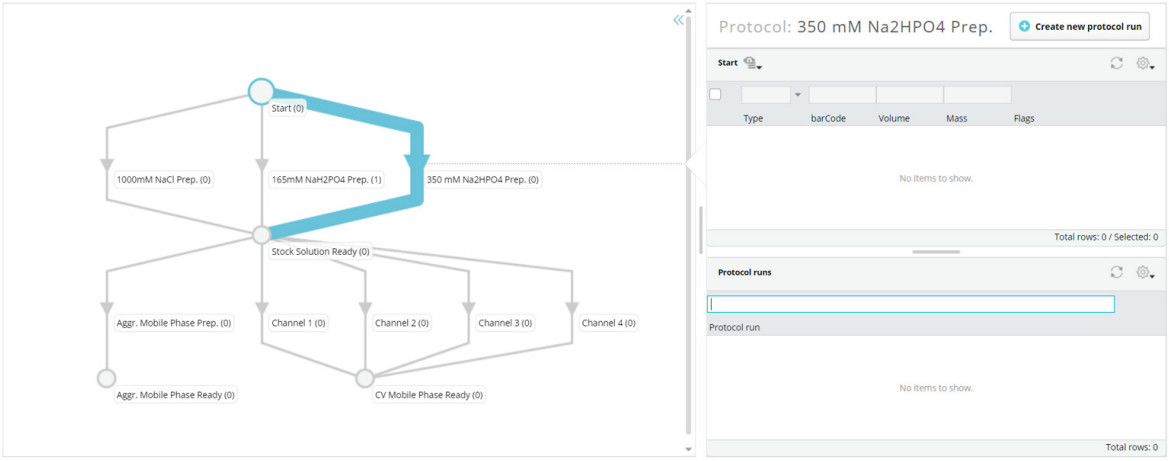

Figure 8. The MP preparation workflow includes multiple sub-protocols for stock and working solution preparation.

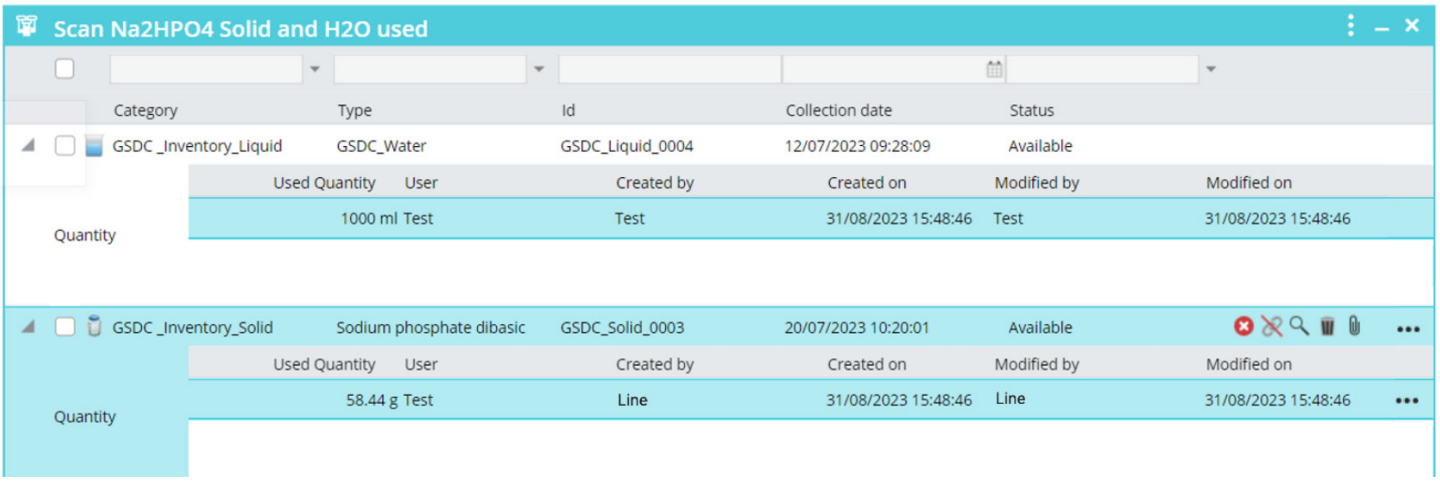

Figure 9. Each protocol requires a chemical type and a quantity.

Results and discussion

Analysis

The aggregation and charge variant analysis were integrated into the mAb QC workflow (Figure 10) in a manner similar to the MP preparation workflow. Whenever an mAb QC order is created, it undergoes both aggregation and charge variant analysis within the workflow to achieve a complete assessment of the mAb sample.

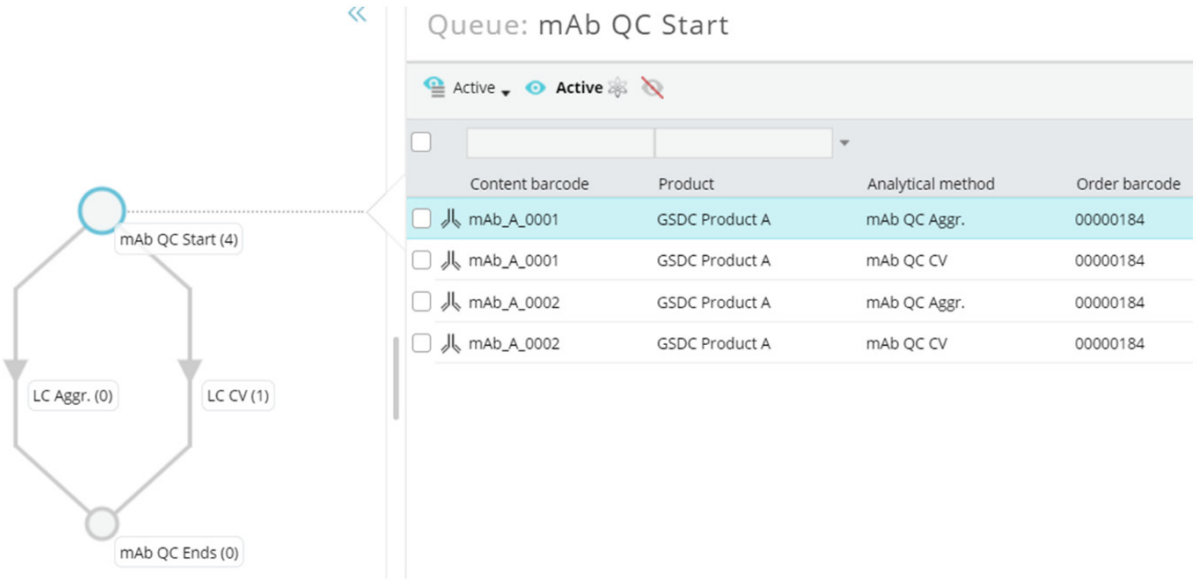

Figure 10. The mAb QC workflow consisting of aggregation and charge variant analysis.

To submit samples from SLIMS directly to OpenLab CDS, specific instruments, project folders, acquisition, and processing methods are preconfigured and linked to their corresponding protocols. The integration between SLIMS and OpenLab CDS allows the relevant information to be seamlessly routed to the respective instruments. As a result, instruments can be operated directly from SLIMS without the need to launch OpenLab CDS separately. In fact, all the OpenLab user roles, privileges, and groups are in sync with SLIMS user credentials.

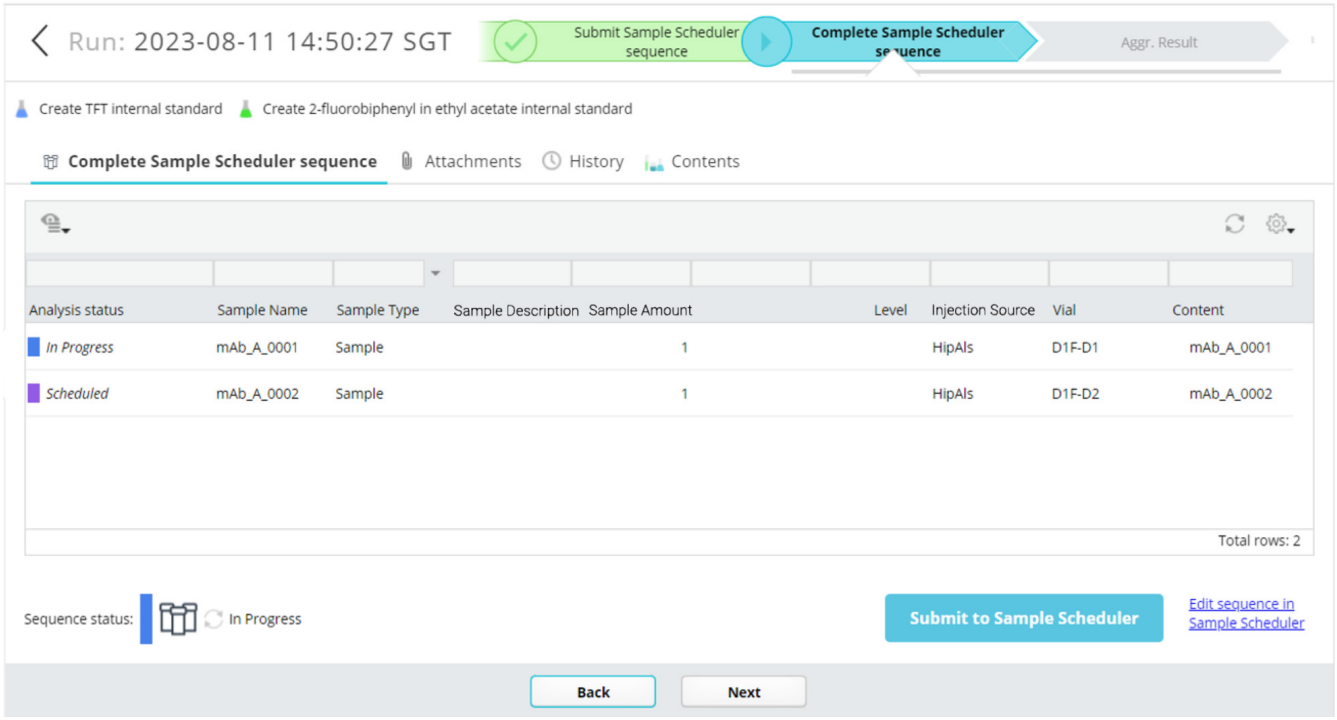

Figure 11. The seamless integration between SLIMS and OpenLab CDS.

Step-by-step recording of experimental procedures is preconfigured in the protocol run. It includes sample information, column and mobile phase used, sample sequence, and results as displayed in the colored top panel in Figure 11. This digitalized standard operating procedure (SOP) guarantees optimal operational consistency, which in turn enhances the quality of the results obtained.

The two batches of mAb samples went through the mAb QC workflow. Each sample underwent duplication injection, and the results were then averaged. The results of aggregation and charge variant tests are displayed in the Result Overview panel in Figure 12.

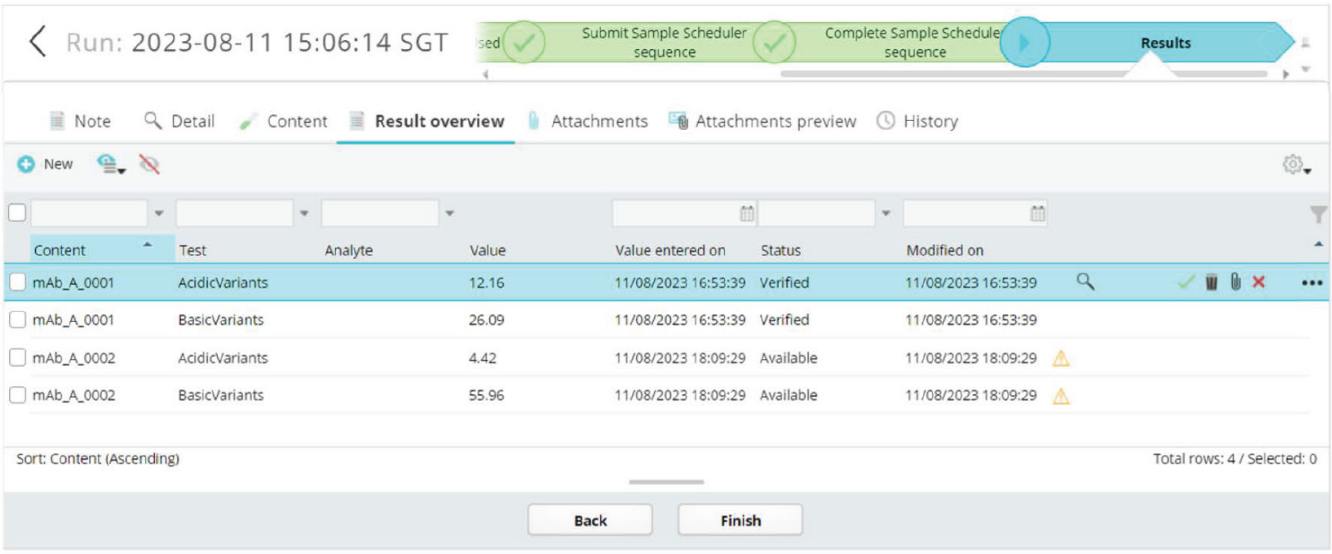

Figure 12. Sample results of charge variant analysis of the two batches of samples. The A02 sample result was out of specification and a warning sign was displayed next to the result.

Evaluation, reporting, and decision

In SLIMS, similar to OpenLab reporting, product specifications can be established as result evaluation rules. These rules allow for automated monitoring of data, and warnings are generated whenever a value falls outside the specified limits. In the case of the mAb sample analyzed, the following product specifications were set: (1) aggregate area percentage (%Area) no more than (NMT) 1%; (2) acidic variant between 15 to 25%; and (3) basic variant between 10% to 15%.

Figure 12 presents an overview of the results for both the A01 and A02 samples. It is evident that the A01 sample met all the product specifications, while the A02 sample's acidic and basic variants percentages were out of specification (OOS). Consequently, a warning sign promptly appeared on the result line.

In such situations, the lab manager or chemist must adhere to their lab's SOPs and make informed decisions. In this case, the A01 sample was verified, whereas the A02 sample was rejected and scheduled for a rerun. Within SLIMS, result evaluation is a straightforward process, and decisions regarding OOS results are well recorded, fulfilling data traceability requirements listed in regulatory guidelines.

Data management and archiving

The chromatography data obtained from the two LCs in this study were automatically saved in the OpenLab Server, along with methods, sequence, and report templates. The OpenLab Server offers a compliant environment not only for storing chromatography data but also for managing SLIMS data. The integration between OpenLab CDS Server and SLIMS is seamless, enabling reports generated from SLIMS to be automatically uploaded to the OpenLab Server.

This centralized storage system for all laboratory information allows easy access to data whenever necessary. Besides, it ensures that the data are securely stored and versioned for the required data retention period, meeting regulatory requirements for traceability and integrity during auditing reviews.

Conclusion

This study provides an example of how an entire mAb QC workflow was successfully digitalized, covering everything from the initial sample request to final data archiving. This transformation was made possible through seamless integration of the SLIMS, Sample Scheduler for OpenLab, and OpenLab Client/Server software platforms.

The implementation is smooth and instantaneous, causing no disruptions to the ongoing operations. With the digitalized workflow, lab technicians can effortlessly follow the SOPs integrated into SLIMS to prepare solutions and conduct sample runs. Lab chemists and scientists can now have complete peace of mind, knowing that their methods will remain intact by access control. In addition, it is assured that each step has a thorough track record for retrospective investigation if necessary. Furthermore, the lab manager gains a comprehensive understanding of sample status, instrument utilization, and laboratory inventory, thanks to the centralized digital platform. Above all, all essential data is automatically archived on the server with versioning, facilitating future audit reviews.

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