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Digital Transformation of Monoclonal Antibody Characterization Analytical Workflows

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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.

The Agilent software portfolio is designed in a way that allows different software to integrate and collaborate. This high degree of integration largely prevents or minimizes disruption to existing operations.

In this study, a small-scale analytical laboratory was configured to emulate a biopharmaceutical quality control (QC) lab for monoclonal antibody (mAb) release tests, aggregation and charge variants analysis. Aggregates and charge variants are critical quality attributes (CQAs) and must be closely monitored and tested as per regulatory requirements[2].

To digitalize the two analytical workflows, a network infrastructure was established as depicted in Figure 1.

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

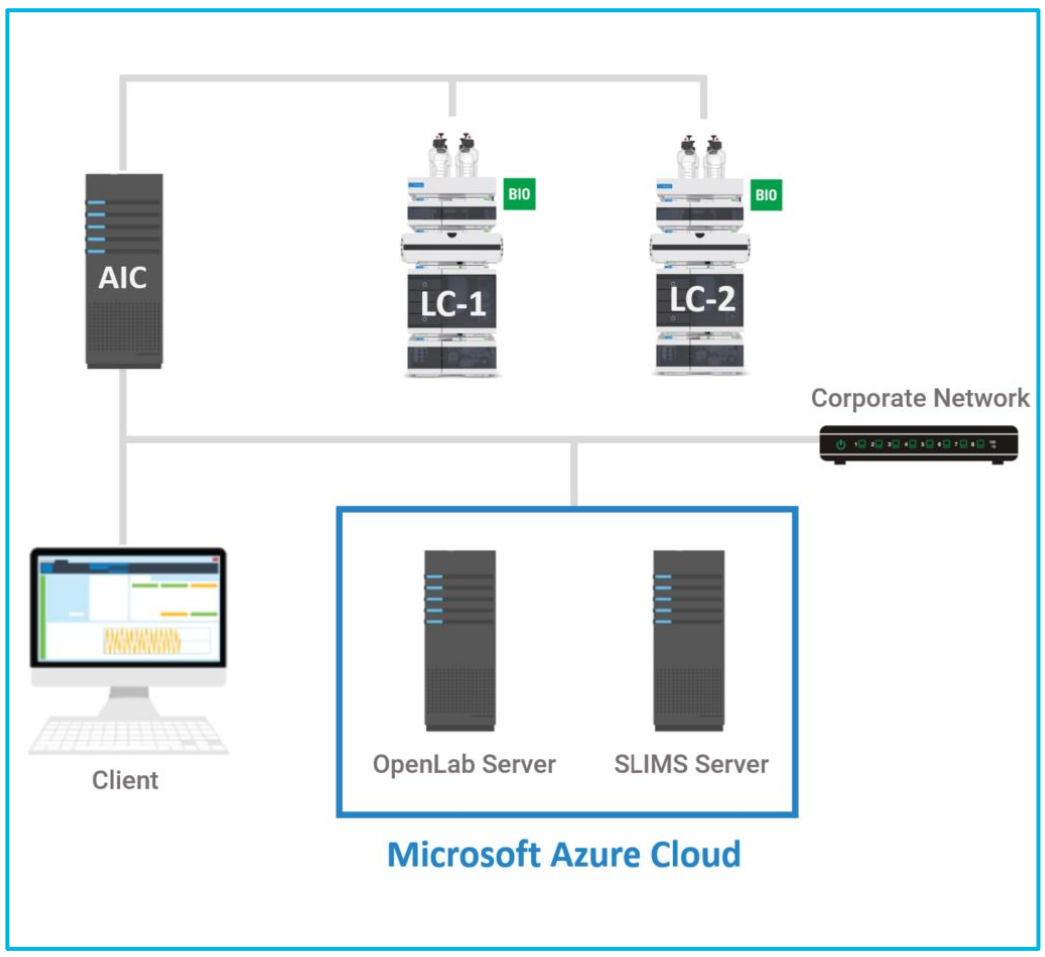

Figure 1. Cloud and network infrastructure of the Agilent OpenLab client/server and SLIMS environment.

Experimental

Instrumentation and cloud infrastructure

LC-1 configuration for aggregation analysis

- 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 for charge variant analysis

- 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

Results and Discussion

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 2).

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.

Resource management

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.

Mobile phase preparation

Both the aggregation and charge variant analysis in this study used phosphate buffer-based mobile phase (MP)[3]. The MP preparation protocols, involving various steps. In the SLIMS software, these intricate paper-based protocols were transformed into a visualized workflow (Figure 3). This enhances the usability and reduces the risk of human error.

Upon the execution of a protocol, the corresponding amount of chemicals consumed is automatically deducted from the respective chemical inventory. The visualized, step-by-step MP preparation protocols guarantee a smooth and foolproof operation.

Analysis

The aggregation and charge variant analysis were integrated into the mAb QC workflow (Figure 4) in a manner similar to the MP preparation workflow. Whenever an mAb QC order is created, it undergoes both aggregation and charge variant analysis to achieve a complete assessment of the mAb sample.

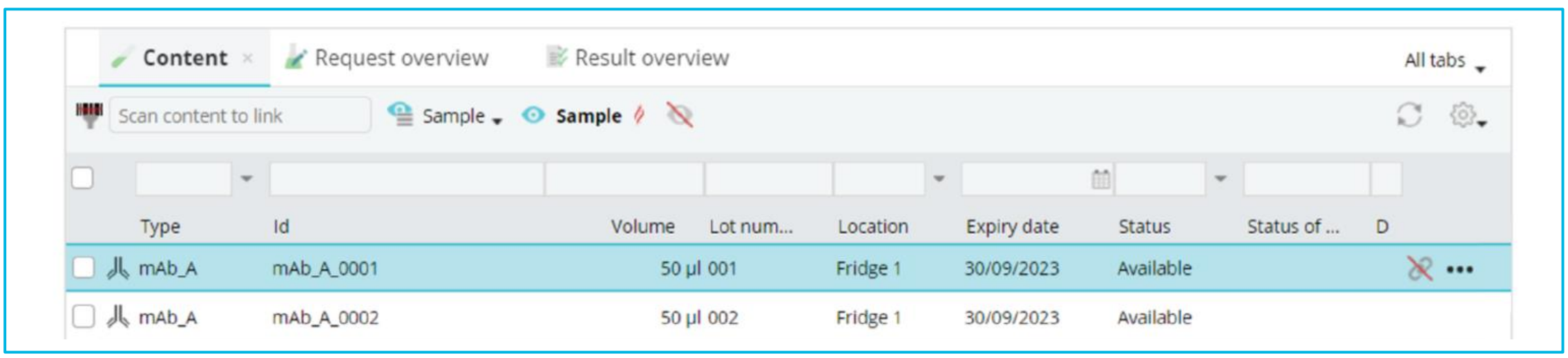

Figure 2. The analytical request overview in the SLIMS Order window.

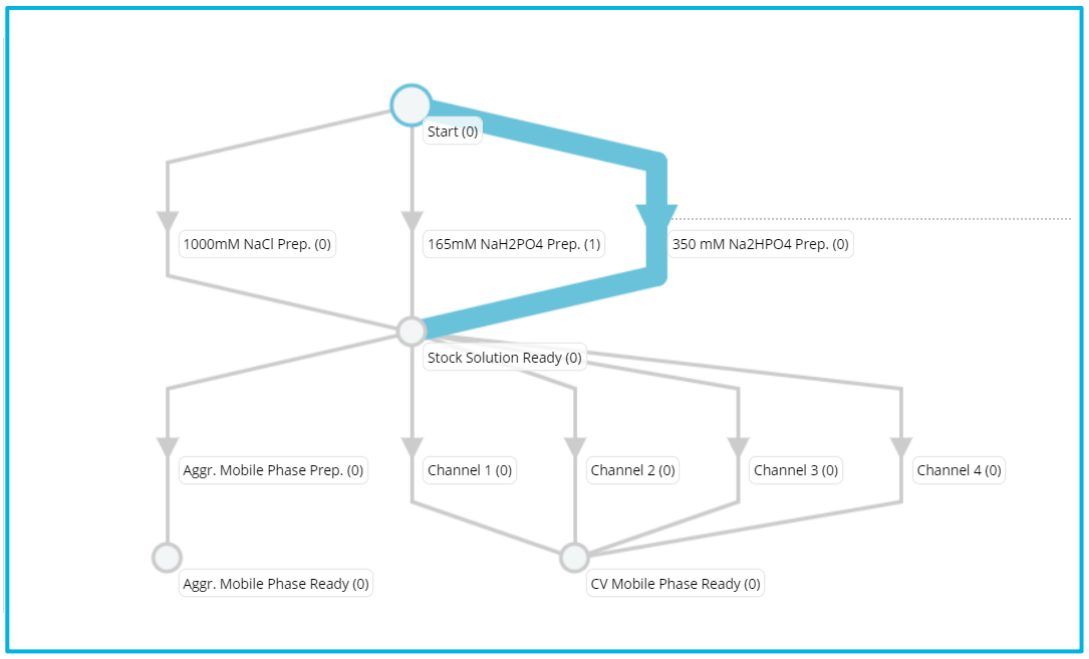

Figure 3. The mobile phase preparation workflow includes multiple sub-protocols for stock and working solution preparation.

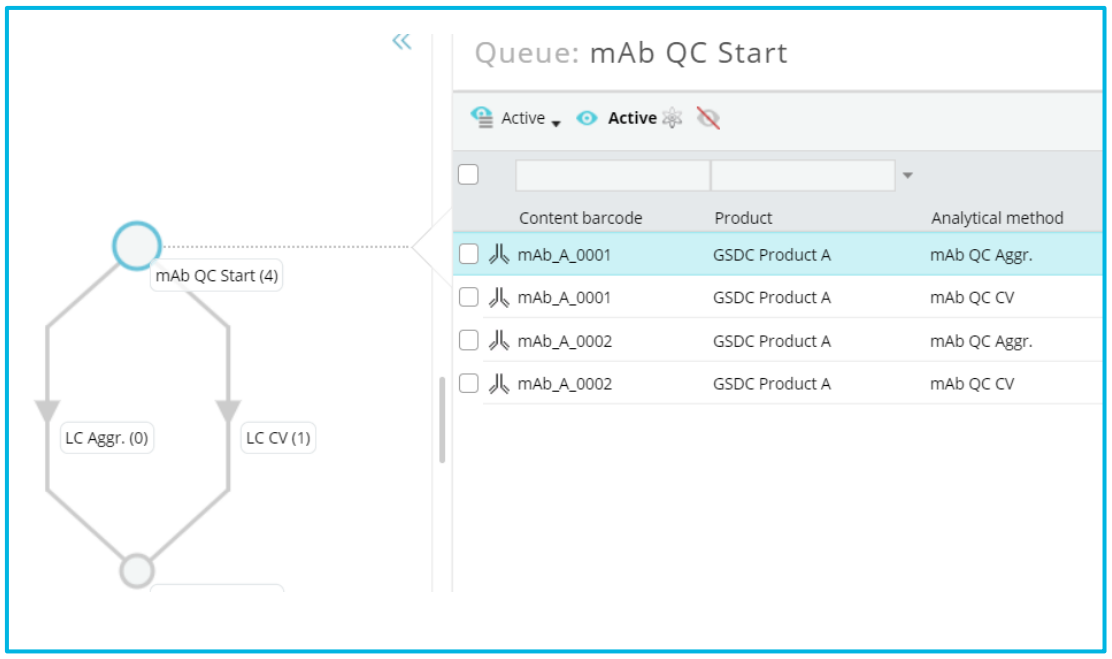

Figure 4. The mAb QC workflow consisting of aggregation and charge variant analysis.

Results and Discussion

The integration between SLIMS and OpenLab CDS allows the relevant information to be seamlessly routed to the respective instruments. As a result, data acquisition can be operated directly from SLIMS without the need to launch 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 5.

Result Evaluation

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.

Figure 6 shows an overview of the charge variant results. The specification for acidic variant is between 15 to 25% and basic variant between 10% to 15%. Warnings were given to one sample which was out of specification.

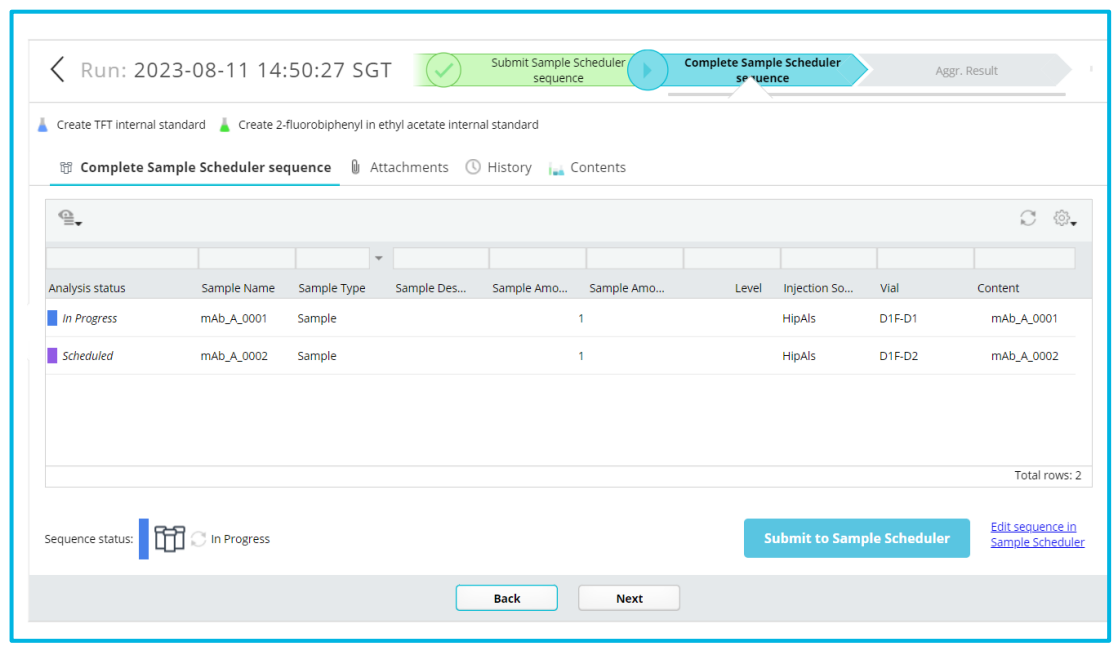

Figure 5. The seamless integration between SLIMS and OpenLab CDS.

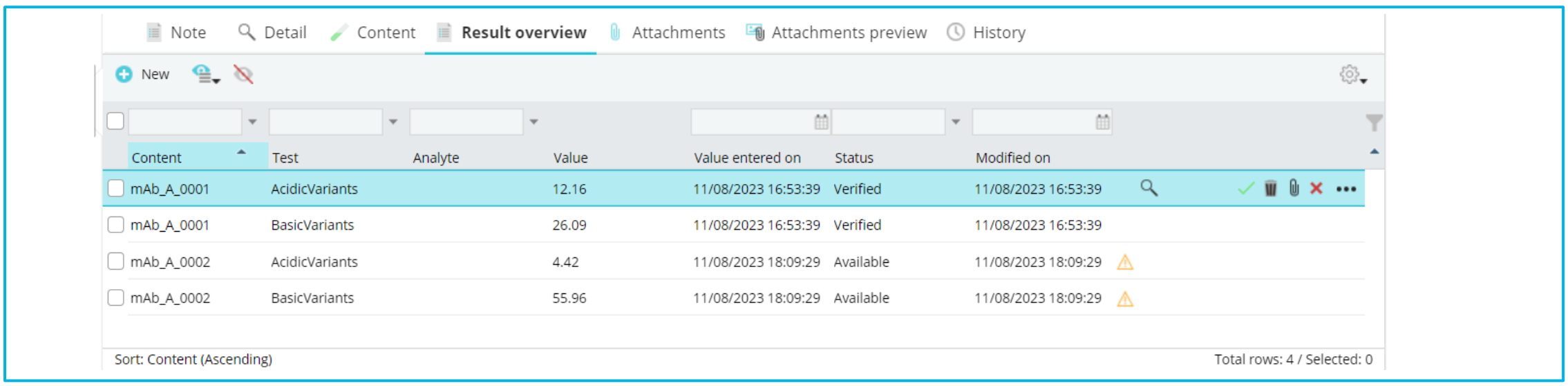

Figure 6. Sample results overview and warnings of out of specification results.

Conclusions

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 Agilent SLIMS, Agilent OpenLab Sample Scheduler, and Agilent OpenLab Client/Server software platforms.

References

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2. ICH Harmonized Tripartite Guideline Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products Q6B.
3. Bian, Y. Charge Variant and Aggregation Analysis of Innovator and Biosimilars of Rituximab. Agilent Technologies application note, publication number 5994 1496EN, 2019.

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