System Performance Check (SPC): The Essential Partner for Multi-Attribute Method (MAM)

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Background and Hypothesis

Traditional quality control (QC) methods in biopharmaceutical analysis are time-consuming, resource-intensive, and often lack real-time insights. To address these limitations, a next-generation platform currently in beta testing is being developed to enhance Multi-Attribute Method (MAM) workflows. This platform integrates advanced LC-MS-based MAM with automated system performance checks (SPC), intelligent anomaly detection, and real-time monitoring of targets and critical quality attributes (CQAs). By improving specificity, compliance, and workflow efficiency, it aims to set a new standard for analytical rigor in biopharmaceutical QC.

<u>We hypothesize</u> that the integration of SPC and anomaly detection within MAM workflows will improve data quality, instrument reliability, and decision-making efficiency, enabling more robust and compliant biopharmaceutical characterization.

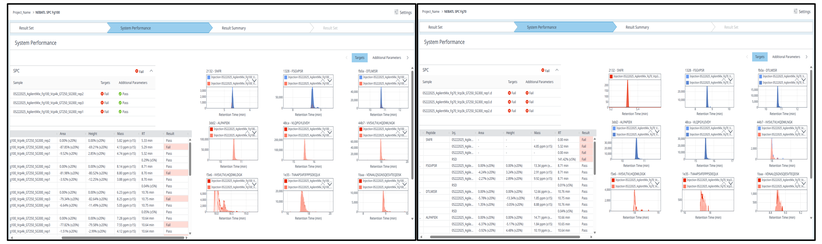
Objectives

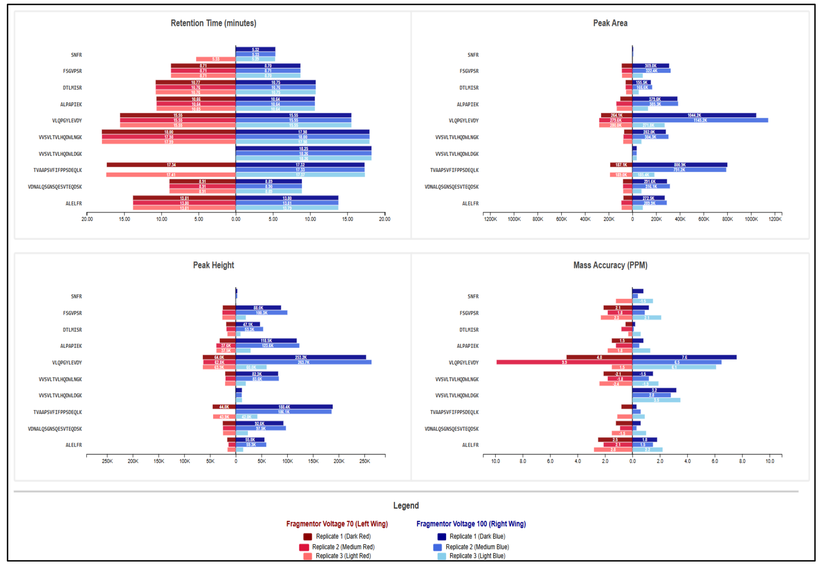
- **Identify limitations in conventional QC workflows.**
- **Demonstrate the role of SPC in ensuring reliable and reproducible MAM results.**
- **Evaluate the beta version of an automated platform with built-in SPC, intelligent analytics, and compliance-ready design.**

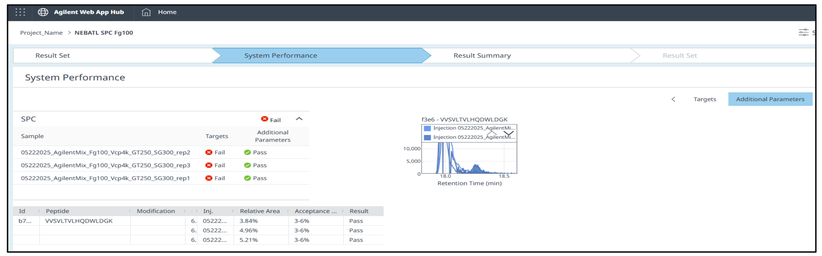
Methods

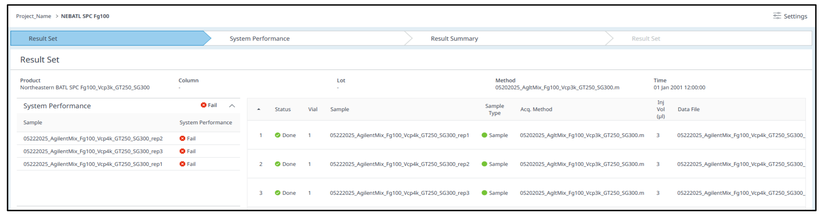
1. **Samples: Agilent MAM Sample Mix**
2. **Instruments: Agilent 6560**
3. **Platform Features:**
   - **Built-in SPC for LC and MS.**
   - **Simultaneous monitoring of multiple CQAs (e.g., glycosylation, deamidation, oxidation).**
   - **Real-time anomaly detection with root cause insights.**
   - **Visualization of historical performance data and automated reporting.**
4. **Comparative Analysis: Compared performance, precision, and efficiency with manual workflows.**

Results and Discussion









Results and Discussion

Benefits and Observations:

- **SPC reduces downtime and variability by ensuring optimal instrument performance.**
- **Assessing system readiness is strengthened by a diverse set of peptides, inclusive of representative CQAs**
- **CQA Visualization: Enables monitoring of attribute trends for better process control.**
- **Dynamic results viewing to quickly assess Pass/Fail criteria**
- **Anomaly Detection: Flags abnormal peaks and results to streamline troubleshooting and root cause analysis, expediting investigations.**

Implications:

This platform will support robust, real-time, and automated MAM implementation, optimizing product characterization and QC efficiency.

Major Findings

- **Automated SPC enhances system reliability in MAM workflows.**
- **Compliance-ready infrastructure supports seamless QA/QC processes.**
- **Fragmentor voltage gradient (70V vs 100V) was used on Agilent 6560 system in lieu of skimmer voltage optimization due to instrument specifications.**
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- **Real-time data access and visualization improve decision-making.**

References

1. Millán-Martín et al. (2023) Crit Rev Anal Chem 54:3234-3251
2. Jakes et al. (2021) J Am Soc Mass Spectrom 32:1998-2012
3. Yang et al. (2023) mAbs 15:2197668

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