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Continuous manufacturing of a biologic drug product is the most efficient method for production in the biopharmaceutical industry. By avoiding batch reactors, sensitive proteins are able to minimize the amount of time where conditions may degrade or denature the molecule. While small molecules drugs also adopt continuous manufacturing systems, large molecule pharmaceuticals have paved the way for this process due to the instability of some proteins during production. Process analytical technology (PAT) is an important system in biopharmaceutical companies to measure critical quality and performance attributes during continuous manufacturing.

Judicious choice of analytical methods are required to validate the integrity of the drug product as it is being produced. On-line or at-line measurements of appropriate quality attributes can minimize negative release testing results on the end product. Many companies are adopting real-time release testing (RTRT) protocols to reduce the amount of testing on the end product or in some cases to completely remove end product testing.

Two of the most important quality indicators for protein therapeutics are aggregation and charge heterogeneity. Protein aggregation can be an indication of mis-folded proteins, which has implications in safety and clearance. Charge heterogeneity can be a symptom of poor process control meaning post-translational modifications are resulting in acidic and basic protein variants. Because of these important quality features, aggregation and charge heterogeneity are often chosen in process analytical technology for real-time monitoring.

As can be inferred, for effective RTRT data acquisition and analysis needs to be rapid. Chromatography is the preferred technology for analysis of aggregation and charge heterogeneity through size exclusion chromatography (SEC) and ion exchange chromatography (IEX), respectively. The advent of sub-2 µm SEC particles has streamlined aggregation analysis by UHPLC for rapid, high flow methods. On the other hand, rapid IEX analysis is challenging due to high flow constraints, a result of bio-inert column hardware limitations. Phenomenex recently released a bio-inert titanium column hardware that alleviates the pressure constraints of traditional IEX columns. As such, charge variant analysis (CVA) to determine acidic and basic variants is attainable at high flow rates.

To read more about Phenomenex's contributions to SEC and IEX for high flow analysis of protein critical quality attributes and Process Analytical Technology, click on the link below:

https://www.genengnews.com/magazine/november-15-2018-vol-38-no-20/chromatographic-analysis-for-pat/

> Chromatographic Analysis for PAT

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Summary

Article Name

Process Analytical Technology (PAT) and Chromatographic Methods

Description

Discover process analytical technology (PAT) and how it is an important system in biopharmaceutical companies to measure performance attributes during continuous manufacturing.

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