Next Generation Manufacturing at Biogen – PAT as an Enabler for Enhanced Process Control in Commercial Antibody Manufacture

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Biogen is among the first biopharmaceutical companies to employ PAT in an active role in the commercial manufacture of biologicals. The implementation of in-process Raman for glucose control, biocapacitance for in-line cell growth monitoring as well as in-line refractive index and other univariate techniques for automatic in-line of process solutions release as key elements of Biogen's Next Generation Manufacturing philosophy is being discussed.

The application of PAT in an active role as part of the control strategy in commercial production in a cGMP compliant environment is not yet done very frequently in the biopharmaceutical industry. This is due to a combination of risk factors which typically involve regulatory challenges, technology maturity and economic benefit. Biogen decided to employ PAT in large scale mammalian cell culture at its new manufacturing site at its newly constructed green-field site in the canton of Solothurn, Switzerland. Biogen's Aducanumab process has shown to benefit significantly from active use of PAT. Inline Raman spectroscopy and inline biocapacitance are used to actively control feed of glucose and nutrients to the production bioreactor. The glucose concentration is predicted using a validated PLS model and is used as input for a closed loop control device that is controlling the addition of glucose solution to the bioreactor in a virtually continuous manner.

Being an essential part of commercial implementation in a regulated environment, the aspects of compliance and life cycle management will be discussed in addition to the technical details of implementation. These include risk assessment, qualification, validation, data integrity as well as maintenance and vendor management. An overview is given on the integrated data infrastructure required to operate a paperless manufacturing plant enabling enhanced process control and paving the way towards Pharma 4.0.