DEVELOPING A FLEXIBLE AUTOMATED CONTINUOUS DOWNSTREAM PROCESSING SYSTEM FOR RESEARCH TO CLINICAL SUPPLY

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Key Words: Continuous, Downstream, Automation, Control, Flexible

Continuous manufacturing has gained a lot of attention over the last 10-15 years for numerous reasons such as the potential for higher efficiencies, reduced cost of goods, and improved product quality. However, the adoption of these technologies has been slow due to concerns over operating these processes in a GMP manufacturing environment. Some of these concerns relate to the operation of multiple continuous unit operations in an integrated process sequence. This presentation will highlight these concerns and show how these issues were addressed by developing an overarching automated and modular platform which can be easily reconfigured for processing most products.

The developed automation platform is the result of a project funded by Innovate UK that brings together a number of biopharmaceutical companies including Allergan, AstraZeneca, Fujifilm Diosynth Biotechnologies and GSK to identify and address these issues. One objective of the project is to develop a flexible automated biologics downstream process consisting of multiple unit operations that can be rapidly reconfigured for manufacturing different products. To that end the process has been design with modularity in mind with each module having common inputs and outputs. The automation software has also been developed in a way that most typical downstream processes can be implemented in the system with little to no software updates. The ability to rapidly reconfigure the process has been demonstrated by using the system to produce three products with different process sequences.

Another issue that inhibits the adoption of continuous technologies is the concern over simultaneously operating multiple unit operations. This presentation will detail how the automation software was developed to control both the key unit operations such as chromatography and filtration steps but also intermediate operations such as feed conditioning and viral inactivation steps. The automated system reduces the complexity of downstream processes, which can have in excess of eleven unit operations, to a single user-friendly interface. Implementing this control platform enables a single operator to control the entire process.

This presentation will also detail how the automation strategy has been developed to enable a single operator to deal with start-up/shutdown, perturbations in the process and mid-process equipment turnover. It will highlight the challenges that have been faced when developing this system and how these have been overcome.
The aim of this project was to improve efficiency by reducing processing time when compared to the current batch process and this was demonstrated by testing the system with three different products (a MAb and a MAb fusion protein). Furthermore, this presentation with show data from the production of three products that demonstrates comparability between the continuous process and the original batch processes. It will then detail how this was used to demonstrate the production of a large-scale clinical batch run.