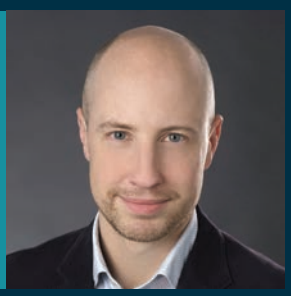
Lining up to deliver continuous processing

There is considerable interest within the biopharmaceutical industry to move from batch to continuous manufacturing processing. Increased flexibility in response to changing demands is just one resulting advantage. Furthermore, a process that runs in a continuous loop rather than in stages involves less storage of work-in-progress and should result in a smaller factory footprint leading to reduced running costs and capital investment. The realization of such a concept needs to rely on an advanced automation, control data handling concept. But how can this be achieved, both in terms of technology and regulatory requirements?



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The Continuous Downstream Processing project, part of BioPhorum's Technology Roadmapping, is looking at this question in relation to multiple scales of operation by leveraging both disposable and stainless steel bioreactors for the commercial production of mAb. Consideration is being given to both continuous perfusion fermentation and fed batch fermentation feeds into the downstream process.

One of the key barriers to continuous downstream processing identified by the workstream is a general lack of consensus within the industry as to how to demonstrate and implement the potential benefits. Companies can see intuitively that it is a good thing to do, but they have difficulty in elucidating how to quantify and measure the detailed benefits for individual cases, with high validation costs raising the perceived risk of implementation. Moreover, most industry studies skip over some of the difficult issues with downstream processing and do not provide a clear idea of the areas where the industry is technologically ready and where there are gaps. To unlock the potential benefits, the industry needs to work collaboratively to reduce the risks and identify the common solutions.

Gap analysis white paper

To address the concerns of manufacturers, suppliers and regulatory bodies, the workstream is creating a comprehensive gap analysis white paper that identifies model processes and considers the impact of continuous biomanufacturing on control aspects such as automation and in-line monitoring. The paper includes a consideration of the upstream inputs to the downstream process, presents case studies of model scenarios and demonstrates the benefits of continuous processing.

This is a huge project, involving more than 50 individuals from 26 member companies comprising – biomanufacturers, supply partners, equipment producers, and engineering companies. The group began in 2017 during a Biophorum Technology Roadmapping meeting, which visited the MoBiDik (Modular Biologics Disposable (K) Continuous) demonstrator laboratory run by Bayer AG in Leverkusen, Germany.

Image credit: Bayer AG

Engin Ayturk, Senior Manager at Biogen, explains: "It is about trying to build a knowledge hub and a clear vision that can be shared with the industry. Although we are working on the process development side we are also trying to engage with other BioPhorum initiatives that can mutually benefit, or indirectly influence, the progress of this project."

One of the unique attributes of the project is the speed with which the workstream is planning to deliver on the project, with the publication of the white paper later in 2018.

The white paper will be reviewed by regional innovation hub partners within the Phorum and will be used to open discussions with regulators to align the thinking around continuous processing – many of which are thought to result from a lack of communication. A regulatory team within the workstream is already preparing a working group.

Moreover, the group has identified that even where regulators do not perceive there to be a challenge, there is a need to bring together industry best practice guidelines. The many different process and control options for a continuous downstream process can sometimes result in a low level of confidence that a planned control strategy is appropriate. The paper will present best practice knowledge in this area, drawing from members who already have related experience.

When the project is completed it will provide considerable benefit to healthcare manufacturing systems worldwide. As Sebastian Teitz, Product & Laboratory Manager at Asahi Kasei, explained: "Through this project we hope to reduce investment in manufacturing costs and thereby lower the price of medicine by ambitious proportions."

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