Fall 11-3-2015

Integrated continuous bioprocessing – opportunities and challenges

Mats Akesson
Cell Culture Technology, Novo Nordisk A/S, mtsa@novonordisk.com

Martin Heitmann
Cell Culture Technology, Novo Nordisk A/S

Ditte Skipstrup
Cell Culture Technology, Novo Nordisk A/S

Peter Tiainen
Cell Culture Technology, Novo Nordisk A/S, ptii@novonordisk.com

Recommended Citation

[1] Tiainen et al., End-to-end continuous production of complex recombinant proteins – integration of perfusion cultivation and automated multi-step purification [Abstract presented at Integrated Continuous Biomanufacturing I, Barcelona, Oct 2013] [2] Åkesson et al., Integrated continuous production - a bench-top factory framework for rapid preclinical supply of fragile proteins [Abstract presented at Cell Culture Engineering XIV, Quebec City, May 2014] [3] Tiainen et al., Why Continuous Protein Production Is Protein Friendly – an approach to adapted a process to the protein and not the other way around [Abstract presented at PepTalk, San Diego, 2015]

INTEGRATED CONTINUOUS BIOPROCESSING – OPPORTUNITIES AND CHALLENGES

Mats Åkesson, Cell Culture Technology, Novo Nordisk A/S, Novo Nordisk Park, DK-2760 Måløv, Denmark
mtsa@novonordisk.com
Martin Heitmann, Cell Culture Technology, Novo Nordisk A/S, Novo Nordisk Park, Måløv, Denmark
Ditte Skibstrup, Protein Purification Technology, Novo Nordisk A/S, Novo Nordisk Park, Måløv, Denmark
Peter Tiainen, Protein Purification Technology, Novo Nordisk A/S, Novo Nordisk Park, Måløv, Denmark
ptii@novonordisk.com

Key Words: integrated continuous bioprocessing, perfusion culture, continuous purification, monitoring, product quality, holistic process development

We have developed an integrated continuous processing framework for end-to-end production of complex fragile proteins based on perfusion cultivation and automated multi-step purification [1,2,3]. Upstream, the integrated system consists of a stirred tank bioreactor with an ATF cell retention system. The clarified harvest directly enters an off-the-shelf ÄKTA chromatography system converted into a continuous purification unit. Two alternating capture columns precede an automated multi-step purification train with full flexibility and control of individual columns.

The integrated set-up enables compact automated bench-top factories converting cell culture media to purified protein in an efficient manner without intermediate storage. It provides monitoring of the production progress, allowing for “just-enough” production and better use of resources, and it also supports monitoring of product quality attributes. The latter aspect is obviously relevant in a manufacturing setting but perhaps even more so for process development. Importantly, the integrated approach facilitates assessment of how final product quality will be affected of changes in one or several individual process steps thereby enabling holistic process development.

Benefits for process intensification as well as process development will be demonstrated by case studies from production of fragile proteins for pre-clinical supply. Furthermore, challenges encountered when integrating upstream and downstream processes in the continuous framework will be discussed and shared.

References

[1] Tiainen et al., End-to-end continuous production of complex recombinant proteins – integration of perfusion cultivation and automated multi-step purification [Abstract presented at Integrated Continuous Biomanufacturing I, Barcelona, Oct 2013]

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