

DEVELOPMENT OF AN N-1 PERFUSION MEDIUM TO INTENSIFY SEED TRAIN OPERATION

Mona Bausch, Cell Culture Media and Perfusion Systems R&D, Process Solutions, Germany
luis.ayala@merckgroup.com

Caroline Ströder, Cell Culture Media and Perfusion Systems R&D, Process Solutions, Germany
Christian Schultheiss, Cell Culture Media and Perfusion Systems R&D, Process Solutions, Germany
Luis Fernando Ayala Solares, Cell Culture Media and Perfusion Systems R&D, Process Solutions, Germany
Melanie Feigenspan, Cell Culture Media and Perfusion Systems R&D, Process Solutions, Germany
Jana Glawion, Cell Culture Media and Perfusion Systems R&D, Process Solutions, Germany
Jochen B. Sieck, Cell Culture Media and Perfusion Systems R&D, Process Solutions, Germany

Seed train expansion of cells before the final production step is often time-consuming and a major source of process variability. For the intensification of seed train operations there are several opportunities discussed across the biopharma industry today. One of the possibilities is to operate N-1 bioreactors in perfusion mode to shorten timelines and improve bioreactor utilization. In this work, we investigated the influence of using an expansion medium especially designed for N-1 perfusion to gain optimal results in the whole manufacturing campaign.

For screening and designing an N-1 perfusion expansion medium, a scale down model which represents a typical production campaign, including the seed train, was established. Expansion medium prototypes were combined with different production media in the final production step, e.g. EX-CELL® Advanced HD Perfusion as medium designed for high-density perfusion, and Cellvento® 4CHO Medium and 4FEED as exemplary fed-batch process.

After determining a suitable expansion medium formulation, the prototype was evaluated for solubility and streamlined to ensure a simple hydration and robust supply chain. Afterwards, results were confirmed using a simulated manufacturing process using benchtop bioreactor systems, showing that the positive impact of the expansion medium on the final yield is present both when using perfusion or fed-batch as final production stage.

Our results indicate that using the right companion medium in seed train expansion - specifically designed for the purpose - can prepare the cells optimally for the final N-stage and increase productivity while using low CSPRs. Combining these findings with the application of a perfused N-1 step in the manufacturing campaign leads to a great opportunity for the intensification of the whole upstream process.