PROCESS DEVELOPMENT

Effectively upscaling bioprocesses

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Success in the biopharmaceutical industry is mainly driven by the ability to innovate, and the continuous development of new products is crucial in that context. Shortening development times is key. The use of comprehensive bioprocessing equipment supports the quick establishment of valid bioprocesses, and facilitates easy and reliable scale-up from lab to production plant. Genmab scientists have demonstrated how powerful methods can accelerate the development of antibody production processes.

Jolanda Gerritsen and her team at Genmab in Utrecht in the Netherlands have used a fourfold DASGIP Parallel Bioreactor System to shorten the development time of an antibody production process up to manufacturing level. In their laboratory, they carried out a screening process for a human monoclonal antibody (mAb) produced by CHO-cells in the 2L scale. Once the production procedure was established in the DASGIP Benchtop Bioreactor System, they successfully scaled-up the process to 100L in a first step (Fig. 1), and finally to the 1000L production scale, retrieving comparable results in regard to protein quantity and quality.

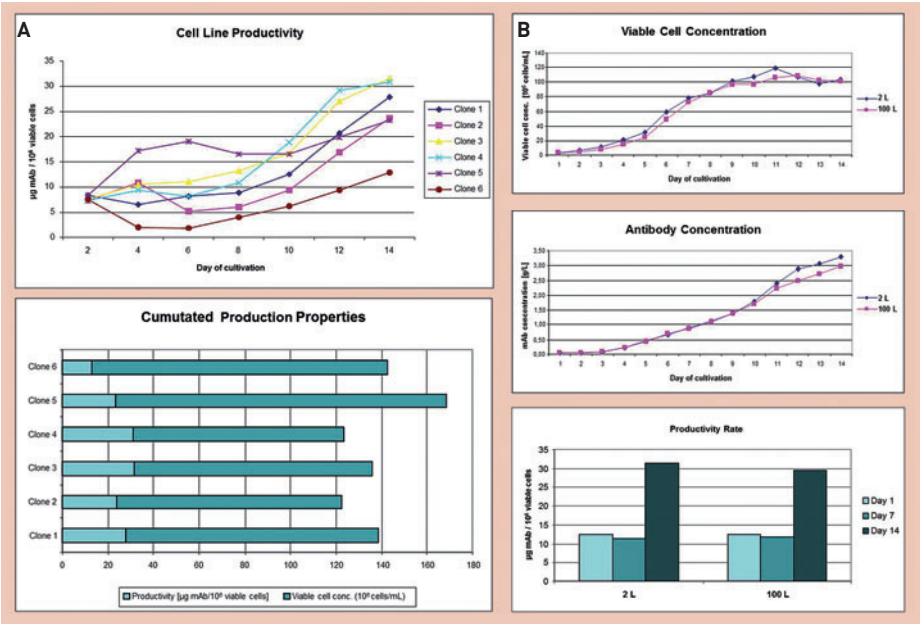

Fig 1. A: Human mAb-producing CHO cell lines were cultured in a fourfold DASGIP Parallel Bioreactor System using CD-CHO basal media with customized feeding. Six independent clones were screened at the 2L scale for cell growth and antibody accumulation. Culturing time was 14 days/batch. B: Clone #3 was chosen for scale up to 100L+ manufacturing scales.

Reliability and scalability are the crucial parameters in accelerating cell culture procedures for antibody production. Strictly parallel operation in cultivation processes facilitates fast process development and saves time during laboratory scale experiments. Using controlled benchtop bioreactors allows direct comparison of single-process parameters relevant in cell line development or optimisation of the antibody production process itself. Comprehensive data management can further promote effective use of time.

The main objective was to establish a screening procedure for monoclonal antibody-producing CHO cell lines with reliable scale-up properties at the Genmab research facilities in Utrecht. The Cell Line Development team aimed to achieve the same antibody titers in large-scale production as were achieved in their small-scale screening cultures, which are fully up and running. They successfully scaled up their process 500-fold.

Impact on the industry

The case study discussed above demonstrates that the use of advanced parallel bioreactor systems can accelerate process development in biopharmaceutical science in a smart and comprehensive way. Parallel operations help save time, and lead to reliable results that are easy to scale up. Parallel design of experiments follows DoE principles, giving an extra plus when aiming for short time-to-market. Depending on the characteristics of the protein of interest, a parallel approach using benchtop bioreactor systems may deliver results that are precisely similar to large scale, allowing operators even to skip a common pilot-scale development cycle.

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