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## USING SPOT™ AND SLIM™ TECHNOLOGY AND UPSTREAM PROCESS MODULATION TO REDUCE COST OF GOODS OF BIOSIMILARS

Innovative cell line generation and early process development is the cornerstone of the success of a biosimilar antibody, since costs of goods (COGs) needs to be very low. To achieve this, high producing cell lines in combination with a modulatory USP strategy to meet similarity to the originator without limiting productivity are obligatory. The major strategy generally used in USP to optimize productivity, is elevation of viable cell density (VCD) in the fermenter. This USP solution however creates difficulties in DSP, since clarification will be difficult and in addition host cell related impurities will be high. Therefore, we increase specific productivity (Qp) using our SPOT™ technology, already during cell line generation. In addition, upstream process modulation can be used to increase Qp while at the same time improving biosimilar product quality. The high Qp values facilitate high volumetric productivity at low VCD, which enables an efficient DSP process. Alongside we observed that irrespective of the VCDs, cell lines with a high productivity had a very high demand for nutrients and oxygen. Because of the high oxygen requirements, a high-power input is necessary in bioreactors, resulting in hardware limitations, i.e. maximum gas flow and agitation rates. In turn, these hardware limitations ultimately limit innovations that increase productivity further. To avoid this issue, we applied metabolic engineering and developed the SLIM™ technology on our CHOBC® platform. The SLIM™ technology decreases oxygen and feed consumption and therefore decreases gas flow and agitation rates in the bioreactors. Together, SPOT™ and SLIM™ technology in our CHOBC® platform reduce cost of goods of biosimilars.

### Biography

MT Den Hartog received his PhD in Molecular Biology at the University of Amsterdam (NL). Subsequently, he carried out a Post-doctoral Fellowship at the The Palo Alto Institute of Molecular Medicine (Mountain View, US). Thereafter, he was involved in the startup of PanGenetics where he was responsible for Molecular Biology and Protein Expression. In 2003, he was one of the Founders of Bioceros, where he currently holds a position of Director of Cell Line Development. He is Author/Co-author of over 20 papers in international scientific journals in the field of Biotechnology.

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