

**UP AND DOWN SCALE CONSIDERATIONS FOR THE CONTINUOUS PRODUCTION OF GLYCOOPTIMIZED  
BIOPHARMACEUTICALS**

Steffen Kreye, Glycotope GmbH  
Steffen.Kreye@glycotope.com  
Rainer Stahn, Glycotope GmbH

Key Words: perfusion, single-use, scale-up, scale-down, glycosylation

Product quality especially with respect to glycosylation is a critical product attribute which can have an immense influence on the activity of glycoproteins and should be closely monitored during process development and manufacturing. GlycoExpress™ cells have been developed in this context to provide human host cell lines with robust glycosylation machineries. This work will address challenges in two case studies for up and down scaling of production processes with focus on product quality and continuous processing. In a first section, data of a process transfer from a 200 L stainless steel to a 1000 L single-use bioreactor for a continuous cell culture application is discussed. The impact of engineering aspects for the bioreactor and the cell retention device as well as product quality considerations are addressed. As a second part, a 10 mL down-scale system for perfusion cultivations in a microbioreactor is introduced and its application for process development is evaluated. A GlycoExpress-based Phase II GMP perfusion process for mAb production at the 200 L stainless steel scale was successfully transferred to a 1000 L single-use bioreactor. Growth, productivity and stable glycosylation were maintained during scale up. The developed perfusion down-scale system SAM shows very good comparability to larger scale ATF runs not only for USP characteristics but also for product quality. The system predicts the response to media supplementation better than batch or chemostat approaches. Design of Experiment studies can be easily performed with this system resulting in highly significant models.