IMPLEMENTATION OF N-1 PROCESS INTENSIFICATION IN BIOPROCESS DEVELOPMENT AND PRODUCTION

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In recent years, significant progress was achieved in bioprocess intensification, both with respect to scientific understanding but also in terms of implementation. This contribution aims to provide our development and manufacturing perspective with a focus on perfusion in the N-1 step.
We will describe the basic N-1 and N-stage concepts investigated, technical and engineering aspects relevant for (commercial) implementation, as well as scientific approaches that support understanding and design of intensified bioprocesses [1][2]. This includes systems biotechnology approaches (e.g. gene expression profiling, metabolomics, flux balance analysis), comprehensive equipment characterization (e.g. CFD) [3][4] and (mechanistic) bioprocess modeling. Emphasis will be on the cell culture process and cell culture media development. PAT aspects will also be included [5].
Specific examples for intensified processes will be presented for CHO cells producing therapeutic antibodies. This comprises data from the cell culture process but also downstream and product quality data to ensure required quality and impurity profiles while increasing productivity. Economic (plant / cost modeling) and sustainability aspects will also be addressed.
Process intensification in an industrial environment is complex and many factors need to be considered beyond increase of productivity. Here, we will focus on examples for process intensification in mammalian cell culture process development that are the result of an evaluation process in our specific development and manufacturing set-up, acknowledging that this will further evolve as new factors need to be considered or will be weighed differently as technology further develops.

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