

## INTENSIFIED BIOPROCESSING ENABLING SINGLE-USE TECHNOLOGIES

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Implementation of single-use technology in the biopharmaceutical industry has evolved from its first integration more than a decade ago to the new state-of-the-art. The successful adoption of single use continues to be driven by the industry seeking for more flexible and cost-effective production platforms. In recent years, the rise of biosimilars and multiple drug entities becoming available for similar diseases has significantly increased the pressure on manufacturing costs. At the same time, production is more and more shifting towards smaller batches in highly flexible multiproduct facilities to adapt to the rapid and dynamically changing market demands. Driven by these needs, the industry has witnessed an upsurge of interest in intensified and continuous bioprocessing. Many companies are developing integrated continuous bioprocessing platforms by leveraging existing technology and combining it with novel, innovative single-use solutions. Intensified processing and single-use technology thereby go hand-in-hand: continuous or intensified operation reduces the overall size of the manufacturing equipment which enables single-use technology in steps where the sheer size of an equipment has previously been a limiting factor. Instead of processing drug material as one single, large batch, an intensified platform moves the product through integrated unit operations either at a continuously low flow or in cycles of smaller sub-lots. Additionally, in intensified manufacturing, a carefully sized equipment enables producers to utilize it to produce various batch sizes and decrease the labor, costs, time and risks for up- or downscaling. A variety of fully continuous or hybrid batch/continuous manufacturing platforms for biologics have been created thus far, all of them predominantly based on single-use technologies. In these platforms, the focus of process intensification lies on four aspects: 1) the primary product flow, 2) the materials and buffer flow, 3) flow of information and 4) portability (scaling and Tech Transfer). A multitude of concepts and technologies have been successfully implemented to intensify the primary product flow, including perfusion upstream platforms,

multicolumn chromatography systems, continuous virus inactivation and high-performance chromatography sorbents or membranes. In addition, the material and buffer preparations are a significant and often underrated contributor to process optimization. The recently developed single-use buffer management systems dilute process buffers from concentrates for the entire downstream platform both at point of use and just in time. Intensified processing has gained traction in the industry. Data from early adopters is promising, with first manufacturers moving their integrated platforms into cGMP environments. The ongoing adoption of intensified and continuous manufacturing concepts is enabling a more widespread use of single-use technology. In combination, the two concepts are a powerful and mutually enabling duo that may permit the biopharmaceutical industry to deliver essential drugs to larger patient populations at lower cost.



Figure 1: Industry trends that drive single-use and process intensification; two mutually enabling technologies.

This presentation explores drivers that advance the intensification of manufacturing platforms through single-use technologies. It shows where the industry has adopted hybrid manufacturing platforms, highlights the lessons learned and where further potential for process intensification can be created.