ON-DEMAND, IN SITU MEDIA AND BUFFER PREPARATION IN CONTINUOUS INTEGRATED BIOMANUFACTURING TO REDUCE WATER CONSUMPTION AND CO_2 FOOTPRINT

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Key Words: Process mass intensity; energy; carbon dioxide emission; antibody; media on demand

Currently, common practice is to integrate perfusion culture with continuous counter-current loading. The floor space and the size of unit operations are substantially smaller than those needed for batch processing. This size reduction then enables the implementation of single-use technology for full-scale manufacturing in continuous mode. It is often overlooked that this transformation only “shrinks” the unit operations itself, while the necessary auxiliaries, such as hold tanks, media and buffer tanks, and the demand for process materials, remain unchanged or even drastically increase. Concentrated media and buffer stock solutions are constrained by the relatively low solubility of media and buffer supplements. Hence, the supply chain faces an increase in demand for process materials and the necessity of handling significantly larger volumes. Media and buffer are always prepared in excess to mitigate the risk of campaign failure due to shortages. On a company level, but even more on a global level, this is an enormous waste of resources. We have previously shown that water consumption is the major contribution to energy demand and CO_2 emissions in a bioprocess. This link is described by the so-called metric WARIEN (Water-Related Impact of ENergy), which is also related to the metric PMI (Process Mass Intensity). The reduction and optimization of water consumption has the highest potential to improve the environmental footprint of biomanufacturing, by reducing both energy consumption and CO_2 emissions. Here, we show a single-use device that continuously reconstitutes chemically defined media on demand and buffers directly from solids, resulting in the same quality achievable by conventional batchwise preparation (Figure 1). One has to consider that a medium or a buffer consists of only 2% solids but 98% water. The long-term cultivation of CHO cells over a duration of 12 hours demonstrated that such on-demand medium production is robust and precise. We also demonstrated the ability to prepare complex buffers for chromatography directly from solids. This technology, with on-demand reconstitution directly from solids, will make obsolete the repeated preparation of cell culture media and buffers and intermediate hold tanks and thus significantly reduce floor space requirements. We present an economic and environmental analysis showing how on-demand production improves economics and the environmental footprint. We will present two strategies to produce antibodies with a PMI lower than 1000. Our economic analysis, based on the Biosolve and SuperProDesigner models that were already built from industry data, shows that the expenses that could be saved yearly on a global scale by reducing only the medium and buffer is almost $2.8 billion, assuming that only 20% extra buffer is prepared for each of the bioprocesses considered. This crude estimated number—probably an underestimate—demonstrates the potential and impact of on-demand and in situ media and buffer preparation. The savings by reducing the floorspace are not considered by this economic evaluation. The single-use technology and process intensification toward integrated continuous biomanufacturing is the perfect combination for improving the sustainability of biomanufacturing.

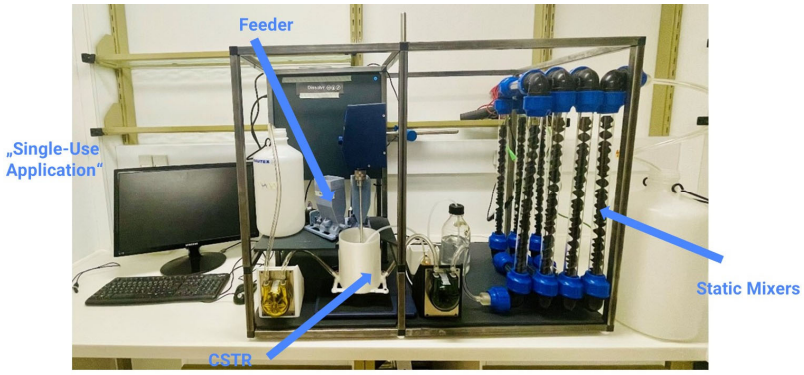

Figure 1 – Pilot scale device for in situ preparation of cell culture media on demand directly from solids.