CONTINUOUS BIOPROCESSING IN SINGLE-USE BIOREACTORS: BEYOND STIRRED TANK-BASED SOLUTIONS

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Continuous bio-processing opens up new possibilities for single-use concepts. Several mammalian cell culture processes are operated in continuous operation using perfusion technologies to not only ensure product quality and avoid product degradation, but also to reduce costs and working volumes. In combination with single-use bioreactors, the effects on production costs are even higher. The introduction of single-use bioreactors in continuous operation for microbial applications also reduces the costs of producing microbial molecules, e.g. if previously rarely used co-cultivation systems are applied.

Although mainly limited to mammalian cell culture processes, single-use bioreactor concepts have been developed that are also suitable for microbial processes. In addition to stirred tank reactors, two-dimensional rocking bioreactors are well suited for fed-batch and continuous cultivation processes, since no dynamic parts have to be integrated into the bag.

Whether for cell cultures or microbial processes, the robustness of the bag material and the quality of the sensors must be ensured during the longer process times in continuous cultivation. Classic electrochemical electrodes, in this case hybrid sensors of a disposable and a reusable part, can be an option to achieve long-lasting operation without compromising data quality. In addition, it is obvious that continuous processes require specific and appropriate monitoring tools to meet regulatory requirements and to detect process disturbances as quickly as possible to adjust dilution rates and product separation cycles. Therefore, the latest advances in optical density measurement and single cell analysis in combination with single-use bioreactor concepts are presented. Some examples are shown of how the construction of a single-use bioreactor including monitoring tools (*on line* and *in line*) enables continuous processes with a suitable robust control option in the case of cell culture and microbial cultivation processes.

Finally, a cost estimate is made for a specific biosimilar production process to demonstrate the potential of suitable continuous bioprocessing with a single-use bioreactor and downstream processing compared to alternative, conventional concepts.

Literature

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