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Scaling microcarrier-based cell expansion processes

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SCALING MICROCARRIER-BASED EXPANSION PROCESSES

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Therapies utilizing stem cells isolated from various tissues are currently undergoing clinical evaluation. It is predicted that for many indications large quantities of cells will be required to treat the numbers of patients in need of therapy. This requirement represents a challenge because the surface area needed to generate the projected numbers of cells is significant. Microcarriers are a viable platform to meet the surface area requirement for generation of the predicted number of cells.

One challenge when transitioning to larger reactors is the identification of agitation conditions that allow for good suspension of the microcarriers and sufficient kLa and nutrient mixing, without causing mechanical or shear damage to the attached cells. We have used a combination of microcarrier mixing tests in the absence of cell culture, small scale tests on settling time with cells attached, and calculations to narrow the window of empirical testing and increase the probability of success on larger scale cultures in bioreactors. We have characterized settling times, which are a function of both microcarrier properties (density and diameter) and fluid density, and microcarrier mixing data, to define an agitation window for culture testing. This information can be used to guide studies for a wide range of cell/media/microcarrier combinations in multiple types of bioreactors.

We will present a comparison of process optimization data captured in small-scale platforms with multiple microcarriers and medium formulations, and the subsequent transition and further optimization of the best conditions to larger bioreactor platforms. Results obtained demonstrate that conditions for microcarrier-based processes for adherent cell expansion can be optimized at small scale and successfully transitioned to large platforms for further optimization.