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Determination of culture design spaces in shaken disposable cultivation systems for CHO suspension cell cultures

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Abstract:

Processes involving mammalian cell cultures - especially CHO suspension cells - dominate biopharmaceutical manufacturing. These processes are usually developed in small scale orbitally shaken cultivation systems, and thoroughly characterizing these cultivation systems is crucial to their application in research and the subsequent scale-up to production processes. With the knowledge of process engineering parameters such as oxygen transfer rate, mixing time, and power input, in combination with the demands set by the biological production system, biomass growth and product yields can be anticipated and even increased. However, the available data sources for orbitally shaken cultivation systems are often incomplete and thus not sufficient enough to generate suitable cultivation requirements. Furthermore, process engineering knowledge is inapplicable if it is not linked to the physiological demands of the cells. In the current study, a simple yet comprehensive approach for the characterization and design space prediction of orbitally shaken single-use cultivation systems is presented, including the “classical” Erlenmeyer shake flask, the cylindrical TubeSpin bioreactor and the alternately designed Optimum Growth flask. Cultivations were performed inside and outside the design space to validate the defined culture conditions, so that cultivation success (desired specific growth rates and viable cell densities) could be achieved for each cultivation system.

Keywords: Erlenmeyer shake flask, optimum growth flask, TubeSpin bioreactor, CHO suspension cell culture, process engineering characterization, design space