OPTIMIZING SCALE-UP OF VERO CELLS CULTURED ON MICROCARRIERS IN SERUM-FREE MEDIUM FOR VACCINE PRODUCTION

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Key Words: Vero, microcarriers, scale-up, vesicular stomatitis virus, serum-free

Vaccine production with adherent cell lines faces multiple challenges which include selection of a suitable vessel, detachment of cells for scale up, optimization of infection, as well as harvest of virus particles. Microcarriers greatly increase the surface area for adherent cells and offer flexibility for expansion to bioreactors, but scale-up methods require optimization of bead-to-bead transfer. Even though the majority of cell culture based vaccines are produced with adherent cell lines, literature provides limited information in regards to optimization of adherent cell line processes. Some process improvements have been achieved; for example, recent advances in serum free media which no longer require medium exchange prior to virus infection. In this study we focus on the production of the rabies virus surrogate, vesicular stomatitis virus, in Vero cells. Using Cytodex-1 microcarriers in spinner flasks, we evaluated effects of intermittent and continuous stirring, detachment of cells, variation in the addition of new microcarriers on the growth of Vero cells, and effects on vesicular stomatitis virus production. Viable cell density measurements revealed that initial intermittent stirring resulted in increased cell densities compared to continuous stirring after microcarrier addition. In an effort to further simplify the process, we demonstrate that detachment of cells was not required to facilitate bead-to-bead transfer on Cytodex-1 microcarriers.