A Media Screening Engine for Live Viral Vaccine Process Development: Bridging High-Throughput DoE Screening and Upstream Process Development

Jason Rodriguez, Esther Lim, Chris Daniels, Kent Hamaker

Merck & Co., Inc.
770 Sumneytown Pike
West Point PA, 19486

Cell culture of complex biological molecules such as live viral vaccines (LVVs) requires robust media, which often contain high amounts of serum, to yield enough cell mass to support a strong infection and antigen yield for the final product. Media development can serve as a tool for process development of LVVs by allowing for optimization of critical components such as serum, which can burden LVV programs in terms of cost, raw material procurement, supply, lot-to-lot variability and regulatory concerns. Most importantly, the biggest impact of developing a robust culture media for any particular process lies in enabling higher product quality and/or quantity. To this end, we developed a screening workflow spanning multiple culture platforms to identify basal media and individual supplements that (1) increase cell growth and peak cell densities of a novel adherent cell line used for live viral vaccine (LVV) production and (2) increase viral spread and subsequent antigen yield during the infection process. Central to the screening platform is a high-throughput (HT) robotic screening system from HiRes Biosolutions, which enables screening of up to 2400 individual media formulations for cell growth and virus spread through HT immunofluorescence. Lead candidate media formulations were then tested in small-scale microcarrier culture to test cell growth and antigen yields to enable further process development in bench-scale bioreactors. In summary, our media development efforts identified alternative serum sources that supported LVV production and reduced our overall supply costs. In addition, we identified crucial supplements that increased cell growth and spread of LVV infection in cell culture that could potentially lower our serum demand in the future.