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EVALUATION OF A LOW-SERUM MEDIUM FOR GROWTH AND VIRUS PRODUCTION WITH MRC-5 CELLS CULTURED ON CYTODEX 1 MICROCARRIERS

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Scale-up of suspension mammalian or insect cells to large bioreactors is commonly done in industry. However, some developers choose to scale-out adherent systems to produce desired components, since adherent systems are more challenging and costly to scale-up than suspension systems. Serum is often required for adherent cell culture, which can introduce lot-to-lot variability to the production process, can be cost-prohibitive, and raises ethical concerns. Additionally, increased global demand for serum is threatening to cause supply chain issues, which can impact manufacturing at scale. A process which reduces the concentration of serum while eliminating the challenges of scale-up for adherent systems would be extremely desirable to the biopharmaceutical industry. We have conducted scale-up studies using adherent human diploid MRC-5 fibroblast cells cultured with microcarriers with our serum reduced medium (SRM). The Diploid SRM System, is a three-component product with base medium and two supplement formulations optimized for cell growth and virus production, respectively. We evaluated this medium for growth against the current standard for adherent product development, classical medium supplemented with 10% Fetal Bovine Serum (FBS). In past experiments with Vero cells in serum-free medium we have determined optimal conditions for bead-to-bead transfer as well as scale-up, which informed our methodology in this study. Using 3g/L Cytodex 1 microcarriers in spinner flasks, we cultured MRC-5 cells over a period of 10 days, executing one bead-to-bead transfer after 5 days. We found that the Diploid SRM performed comparable or better than classical medium with 10% serum in terms of growth. Effects on vesicular stomatitis virus production will be discussed. We also plan to carry out more growth performance testing at benchtop bioreactor scale. This process optimization can be used to scale-up adherent MRC-5 cells with a 10-fold reduction of serum without having to adapt existing cell lines to suspension culture.

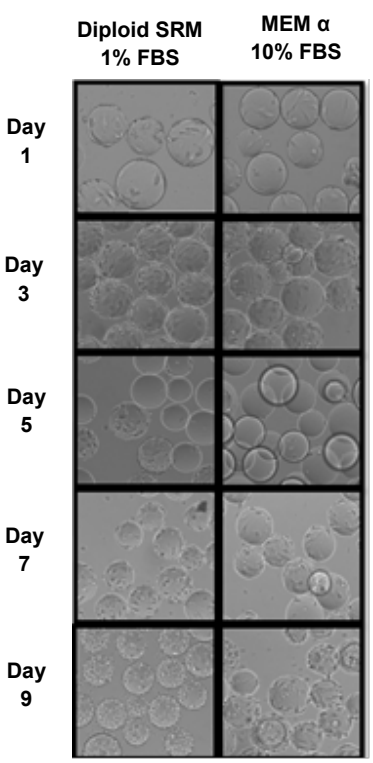

Figure 1 –Micrographs of MRC-5 cells cultured on Cytodex 1

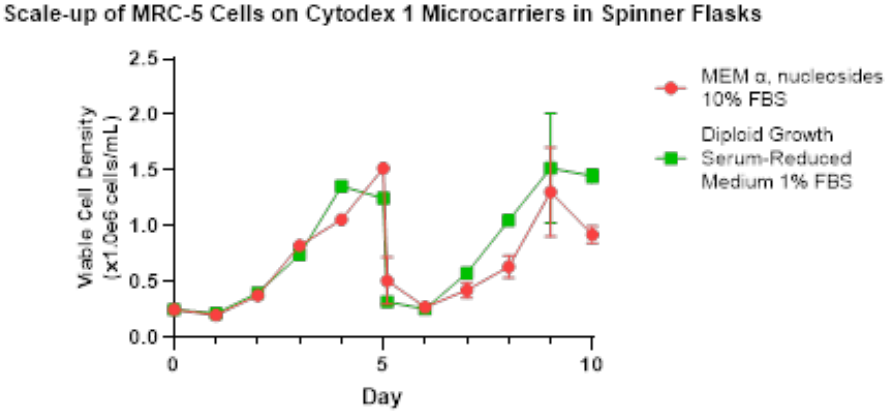

Figure 2 – Viable cell density of MRC-5 cells cultured on Cytodex 1 microcarriers. Bead-to-bead transfer of cells executed on Day 5 of experiment