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PRODUCTION OF STABLE, IMMUNOGENIC FOOT-AND-MOUTH DISEASE VACCINE IN A CHEMICALLY-DEFINED, SERUM-FREE MEDIUM OPTIMIZED FOR BHK-21 CELLS

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BHK-21 cells are an important bioprocessing host for the production of recombinant proteins and vaccines. The largest application of these cells is the production of Foot-and-Mouth Disease (FMD) and Rabies vaccines for the animal health market. Commercial FMD vaccine production relies on classical cell culture media supplemented with bovine serum. This serum is sourced locally from FMD-vaccinated cattle and thus requires antibody precipitation with PEG to allow supplementation during cell culture scale-up. This step diminishes the nutritional value of sera and also increases variability. To reduce serum use during the virus production phase, the process depends on media supplementation with hydrolysates such as Tryptose Phosphate Broth and lactalbumin hydrolysate. Use of these animal-derived components is unreliable due to lot-to-lot variability and may be unsafe due to potential introduction of adventitious agents. We developed a chemically-defined, protein-free and serum-free medium optimized for high-density growth of suspension BHK-21 cells. This medium allows direct adaptation into serum-free growth with minimal process workflow modifications. FMD virus titers produced in this medium are comparable to those of serum-containing media but show greater consistency in 146S antigen yields. FMD O-serotype monovalent vaccines were formulated with antigen produced at 50L scale in this medium or in classical medium with bovine serum to determine antigen immunogenicity and stability. These vaccines were tested in animals and found to be equally immunogenic; both traditional and serum-free vaccines induced strong FMD-specific neutralizing antibody responses in animals when evaluated by liquid phase blocking ELISA. Our results show that production of FMD vaccine in a serum-free, protein-free, chemically-defined medium is feasible and does not appear to alter immunogenic determinants. Process development related to high cell density at time of infection will be discussed.