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Virus Characterization by FFF-MALS Assay

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Adequate biophysical characterization of influenza virions is important for vaccine development. The influenza virus vaccines are produced from the allantoic fluid of developing chicken embryos. The process of viral replication produces a heterogeneous mixture of infectious and non-infectious viral particles with varying states of aggregation. The study of the relative distribution and behavior of different subpopulations and their inter-correlation can assist in the development of a robust process for a live virus vaccine. This report describes a field flow fractionation and multiangle light scattering (FFF-MALS) method optimized for the analysis of size distribution and total particle counts. A method using a combination of asymmetric flow field-flow fractionation (AFFFF) and multiangle light scattering (MALS) techniques has been shown to improve the estimation of virus particle counts and the amount of aggregated virus in laboratory samples. The FFF-MALS method was compared with several other methods such as transmission electron microscopy (TEM), atomic force microscopy (AFM), size exclusion chromatography followed by MALS (SEC-MALS), quantitative reverse transcription polymerase chain reaction (RT Q-PCR), median tissue culture dose (TCID₅₀), and the fluorescent focus assay (FFA). The correlation between the various methods for determining total particle counts, infectivity and size distribution is reported. The pros and cons of each of the analytical methods are discussed.