ELECTRON MICROSCOPY AS AN EMERGING ANALYTICAL TOOL FOR CHARACTERIZING VACCINES

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Characterization of nanoparticles and biologics is a critical step in the development of important new pharmaceutical products and biosimilars. Biologics pose unique characterization challenges that require an interdisciplinary approach in which several orthogonal methods are used to provide a complete picture. The physical characteristics of a biological product include properties such as the size, shape, morphology and aggregation state of the particles. These properties are often dependent on the specific environment of the particles and thus ideally must be assessed under conditions that reflect the final formulation of the pharmaceutical. Electron microscopy (EM) and in particular cryo-electron microscopy (cryoEM), has a unique advantage in that it provides a direct means of observing the individual particles in a sample, preserved in their natural hydrated state (cryoEM), simultaneously providing information on homogeneity, size distribution, titer, morphology, preservation state, flexibility, and aggregation state. For particles with a regular size and shape, particle averaging methods can provide 3D structural information, complementing X-ray crystallography analysis.

We will demonstrate the use of EM as an analytical and structural characterization tool by presenting a number of case studies as highlights. Specifically, we will discuss the characterization of Human Papilloma Virus (HPV) VLPs in GARDASIL®, including the structure of the VLPs alone, on adjuvants, and when interacting with neutralizing antibodies [1]. We will also show how TEM was used as a non-intrusive tool to understand the structure and function of Hepatitis B surface antigen (rHBsAg) VLPs, the active component in the HBV vaccine [2]. We will furthermore demonstrate how TEM can be used to provide supporting information for characterization of a biosimilar drug delivery nanoparticle, a recombinant tuberculosis vaccine antigen, interacting with a lipid-based adjuvant [3], and a bi-specific, tetravalent immunoglobulin G-like molecule [4].

References:

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