LS-10-P-5728 Adaptation of JADAS as an Automatic Particle Acquisition Tool for Quantitative Analysis of Vaccines by Transmission Electron Microscopy

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NIBSC routinely employs imaging, including; electron microscopy (EM) in the testing and evaluation of biological medicines. However, as biological medicines develop so do the challenges of ensuring their safety. Today’s emerging and postulated therapies present an ever-moving target with greater demands on basic research, control and standardisation. The largely artefact free, high-resolution information threshold provided by cryo-EM techniques has been core to the evaluation of a number of current and postulated therapies [i.e., human papilloma virus (HPV) vaccine, measles vaccine, gene therapy vectors, Bordetella pertussis and Meningitis vaccines]. However, each of these studies, despite offering higher information thresholds than were achievable with more traditional room-temperature processing techniques remain demanding in operator time and lack quantitative robustness able to inform against variation in vaccine state.

EM remains a powerful tool for evaluation of these biological medicines due to its lack of bias in identifying variations in samples. If this “catch-all” analytical capability could be extended to allow automated acquisition of larger data sets with digital classification of particles it is theoretically possible that EM could be employed as a “gold standard” quality control procedure for biological medicines. This could have a significant impact on novel vesicle type vaccines which are sensitive to osmotic variation.

NIBSC has adapted an automated particle acquisition software suite; JEOL Automated Data Acquisition System (JADAS) which was developed to acquire images of ice-embedded macromolecular complexes under low dose conditions with the intention of further processing the data for 3D macromolecular reconstruction. The software offers the facility to acquire large quantities of high quality data without operator intervention. We have adapted the software to allow for both room temperature and cryo-EM data acquisition and have carried out extensive evaluation of the HPV and Neisseria meningitides, group B, outer membrane vesicle vaccines. The data shows for the first time the potential of EM as a quantitative analytical tool for the quality control of complex biological medicines and vaccines.