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Abstract

Standardization and implementation of existing international reference standards for high throughput multiplex immunoassays

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Background: Multiplex immunoassays (MIA) such as Luminex x-MAP® and Meso Scale Diagnostics (MSD) offer opportunities for simultaneous quantification of multiple antigens in a single well. Several studies have reported the use of multiplex assays for immunogenicity testing of vaccines. It is important that such multiplex assays are developed and validated by reporting the results in units that are traceable to an appropriate international reference standard. There are challenges as currently available international standards are more suited to monoplex/conventional assays. The development of in-house reference standards for MIA has its own challenges as it requires serum samples with high antibody titers against all target antigens. Approaches based on the utilization of serum pools of vaccinated people may not be practical for all laboratories. This study reports on the implementation of existing international reference standards for use in a multiplex assay for quantification of antibodies against tetanus (T), Diphtheria (DT), Pertussis Toxin (PT), Filamentous hemagglutinogen (FHA) and Pertactin (PRN).

Material and Methods: Characterization of the existing reference standards to evaluate their suitability use for MIA assays are urgently required to develop MIA assays which are traceable to international reference standard. NIBSC/WHO provides three reference standards, namely TE-3, 10/262 and 06/142 which respectively have the unitages for T, D, and acellular pertussis (PT, FHA and PRN) antigens.

Results: The study proposes the unitages to all the five antigens for antibodies against PT, FHA, PRN, DT and TT in the TE-3, 10/262 and 06/142 which can be used to develop suitable reference standard for MIA assays. Using the NIBSC standards, the study describes a case study for development and validation of a 5-plex magnetic bead-based Luminex-based assay to quantify human IgG antibodies to DT, TT, and pertussis antigens.

Conclusions: These unitages will provide opportunities for the use of these reference standards in multiplex assays. Development and validation of an assay against the international reference

standard provides opportunities to harmonize and pool clinical results across multiple studies with good confidence and reproducibility.