International Alliance for Biological Standardization

Maintaining the Quality of Vaccines through the Use of Standards:
Current Challenges and Future Opportunities
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Abstract

Use of Reference Standards to Monitor Product Quality: US FDA perspective

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A biological standard is a reference material which is rigorously characterized using relevant biological assays. There are different types of standards and terminologies used but all are essentially used for monitoring the quality of a biological product, calibration of assays and/or in the evaluation and harmonization of clinical data across multiple laboratories. The FDA recommends use of high-quality standards to ensure the quality of biological products for public health use.

With regards to vaccine development, early adoption of standard use, as soon as a WHO International Standard (IS) or a NIBSC reference material becomes available, is highly recommended by the FDA. Prior to implementation of an International Standard, an in-house developed reference reagent can be used. Such standards are typically a thoroughly characterized vaccine bulk lot that was used in clinical trials and for which immunogenicity has been demonstrated. Eventually the in-house reference standard or NIBSC standard should be calibrated against the WHO IS when it becomes available.

Standards are used in biological assays to ensure that the assay is performing as designed. Vaccine reference standards are used to calibrate the analytical assays to determine the potency in terms of titer, antigen content, immunogenicity and to provide quality control for manufacturing consistency. Standards are also used for the standardization and harmonization of assay data across different laboratories.

Generally, standards are quite stable, but degradation can occur and therefore it is critical to monitor stability, especially for any in-house developed reference standard. Storage and handling conditions should be defined, and trending analysis of the data from the standards are needed to monitor any shifts in activity. When a standard is near depletion, complete information on the characterization and qualification of a new standard and bridging to the old standard is required.