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

The Future of Reference Standards for Vaccines

***Background*:** Reference Standards have played a critical role in development and quality control of vaccines for over 100 years. For vaccines, these have traditionally been product-specific and focused on assessing bioactivity and critical assay reagents.

***Challenges*:** The COVID-19 pandemic revealed challenges in ensuring vaccine quality, consistency, and availability. It exposed existing vulnerabilities in the supply chain and emphasized the need for a consistent supply of high quality raw and starting materials. The need to respond rapidly to emergence of new variants also challenged traditional paradigms for analytical testing and standard development.

***Proposed Approach*:** An expanded portfolio of novel reference materials could alleviate many of these challenges by providing a benchmark to support analytical testing. Three case studies will be presented to illustrate approaches USP is taking to expanding our portfolio of reference standards and materials to support analytical testing across the entire vaccine development lifecycle:
1) Reference Standards for Raw and Starting materials: CRM_{197}, a carrier protein used in conjugate vaccines, is produced using multiple manufacturing processes and is susceptible to cleavage. Our approach to developing a Reference Standard for CRM_{197} to support qualification of raw materials will be discussed.
2) Reference Standards for Platform Analytical Methods: mRNA-based vaccines have common physiochemical properties, making them amenable to platform analytical methods. Our vision and considerations for development of platform-based reference standards will be shared.
3) Reference Standards of the Future, Digital? Modern analytical methods like NMR and mass spectrometry could enable development of digital standards for vaccines. We will discuss USP's experience with this approach for small molecules and challenges for adapting it to vaccines.

***Conclusions*:** The need for flexibility and speed, coupled with high quality, has resulted in increased emphasis on quality assessment of raw and starting materials and on increased use of platform analytical methods. New approaches to vaccine reference standards are needed to support expanded industry needs.