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

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Title: Qualification and stability monitoring of reference standards in the U.S. animal health industry and current challenges

Introduction: The USDA has specific guidance outlining expectations for the qualification and stability monitoring of reference standards used in potency testing of veterinary vaccines. The reference standard used in a relative potency assay is correlated, directly or indirectly, to host animal immunogenicity. The stability monitoring requirements for reference standards are dependent on the product licensure status as of January 1, 2011. Reference standards may be allowed up to 15 years, or continuous dating, based on the approved reference monitoring plan.

Challenges: Merck Animal Health has approximately 30 reference standards reaching their 15-year expiration within 5 years, which will require qualification of new reference standards. This phenomenon is impacting the entirety of the U.S. animal health industry. According to USDA regulations, the qualification study must use the same animal model and efficacy study design that supported initial licensure or the most recent reference qualification. The industry expects to encounter numerous challenges with these *in vivo* qualification studies including the identification of seronegative animals, confirming viability of existing challenge strains, and replicating intricate animal study designs.

Current Approach: To maintain 15-year dating, serial release testing data is trended and reference monitoring reports are supplied to USDA at 2.5-year intervals. For reference standards of newly licensed products, licensed in 2011 or later, a freeze-thaw degradation study must be successfully performed to attain 15-year dating. In addition, firms can elect to develop one qualitative and one quantitative test to monitor the reference, which could support indefinite dating for the newly licensed product reference. The ability to detect and correlate degradation across assays is a key component during validation; however, reference standards are often product-matched, containing multiple antigen components as well as adjuvant which makes such method development challenging.

Conclusions: Qualification of reference standards and the development of reference stability monitoring assays are lengthy and resource-intensive processes for the U.S. animal health industry.