International Alliance for Biological Standardization

10th Annual Statistics Workshop: Science & Statistics – Elevating CMC through Partnership

November 12-14, 2024
IBBR, Rockville, USA

Shelf-life estimation of pharmaceutical products through tolerance intervals under linear mixed models

Establishing the shelf life of pharmaceutical products is of critical importance in drug development, as it forms the foundation for ensuring proper quality, efficacy and safety throughout their lifecycle. To fulfill this objective, stability studies are undertaken to provide information of the drug quality over time when exposed to various environmental conditions. While the analysis of stability data through tolerance intervals under linear mixed models has been claimed to be an adequate approach for shelf-life estimation, its implementation has been limited by the lack of well-established statistical methods to compute such intervals in the presence of unbalanced datasets. In this talk, a novel method to compute tolerance intervals for unbalanced linear mixed models, based on Generalized Pivotal Quantities, will be presented. Moreover, a practical demonstration of the method for determining shelf life will be shared.

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Session II: Stability Innovations in Manufacturing Biologics

Monitoring products on stability is critical to determine how long they will remain safe and efficacious, and a major area where statistics are used in manufacturing biologics. Traditional stability studies for biologics take years to complete, but work is being done to use accelerated studies to determine or estimate shelf life more quickly. This session will have two presentations on estimating shelf life more quickly, one for mRNA vaccines and therapies, and one for biologics in general. Although regulatory guidance specifies one statistical method that can be used to determine shelf life, other methods are frequently used because of limitations with that method. One presentation in this session will discuss a novel method of using tolerance intervals to estimate shelf life, and discuss a method for estimating tolerance intervals for linear mixed models with unbalanced data, which can also be applicable for other stability analyses.