Biopharmaceutical Emerging Best Practices Association

Primer on dose-response curve comparison in potency assays

BEBPA Technical Note

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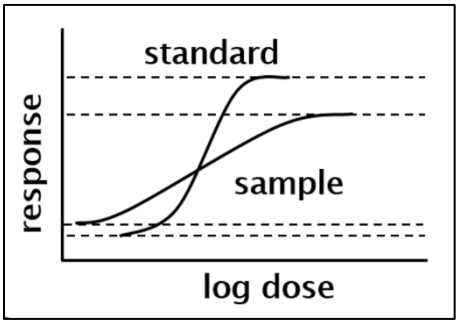
Assessing the similarity of the reference and test sample dose-response curve is a critical step which needs to be accomplished prior to calculating potency of the bioassay. (If you are curious as to why: Check out the following graph…..would the test sample be more or less potent than the reference material? Well…..it would depend on which drug concentrations you were testing.)



The approach to assessing similarity 10 years ago, when the USP <1034> chapter first recommended switching from difference testing, as out-lined in the EP Chapter 5.3 to an equivalence approach. Now that 10 years have passed, the difficulties of the equivalence approach have become more apparent. These problems include:

- Collection of sufficient reference vs. reference dose-response curves is time and resource intensive.
- The above dataset does not incorporate the variability seen during lot-to-lot manufacturing.
- The use of early clinical material to establish similarity might include non-representative or unstable samples.
- The need for interim similarity values during method development and how this should be procedurelized.

References about assessing similarity

1. **Characterizing Non-Constant Relative Potency.** Gregg E. Dinse and David M. Umbach. Published online 2011 May 13. doi: 10.1016/j.yrtph.2011.05.002 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3134169/
2. **Approaches to Parallelism in Bioassays.** Fleetwood K, Bursa F, Yellowlees A. Parallelism in Practice: PDA Journal of Pharmaceutical Science and Technology. 2015 Mar 1;69(2):248-63. https://www.quantics.co.uk/biostatistics-services/bioassay-development-2/parallelism-in-practice-approaches-to-parallelism-in-bioassays/
3. **A Bayesian Approach to Parallelism Testing in Bioassay.** Steven J. Novick, Harry Yang & John J. Peterson. Pages 357-374. Received 01 Jun 2011. Accepted author version posted online: 05 Jul 2012, Published online: 01 Oct 2012
4. **Essentials in Bioassay Design and Relative Potency Determination.** Thomas A. Little, PhD BioPharm International Volume 29, Issue 4, pg 49–52. http://www.biopharminternational.com/essentials-bioassay-design-and-relative-potency-determination