Measuring Parallelism in Nonlinear Bioassays and Immunoassays

There is often a need to determine parallelism or dilutional linearity between pairs of dose-response datasets for various biological applications. This poster describes a technique based on a modification of Finney’s well-characterized extra-sum-of-squares approach to calculate the Maximum Likelihood Estimate of nonlinear curves for parallelism analysis. The traditional extra-sum-of-squares method uses an F-distributed ratio as a statistic, which does not directly measure the parallelism between the two curves and can occasionally vary in opposition to actual parallelism. An approach using the confidence intervals of the linear regression slope parameter in an equivalence range has been suggested as an alternative method for determining parallelism. This method cannot be used for nonlinear dose-response curves because the confidence regions cannot be separated into simple intervals. Instead the confidence region must be determined jointly for all 4 or 5 parameters, an almost intractable numerical problem.1,2 However, a metric based on the extra-sum-of-squares statistic is perfectly suited for nonlinear curves. The method requires a curve model that accurately fits the datasets, typically a five or four parameter logistic curve, and a good weighting model. This chi-square distributed statistic is a direct measure of the amount of nonparallelism between the two curves. The statistic is zero when the two curves are exactly similar, and becomes larger as the two curves become more nonparallel. The method has been widely used in other fields, and is well characterized in the literature.

REFERENCES