An Inferential Procedure for the Probability of Passing the USP Dissolution Test

Jen-Pei Liu [(1), (2)*]

[(1)]National Taiwan University, Taiwan
[(2)]Division of Biostatistics and Bioinformatics, Institute of Population Health Sciences, National Health Research Institutes, Zhunan, Taiwan
jpliu@ntu.edu.tw

Abstract

Dissolution is one of the tests that is required and specified by the United States Pharmacopeia and National Formulary (USP/NF) to ensure that the drug products meet the standards of the identity, strength, quality, purity, and stability. The sponsors also establish the in-house specifications for the mean and standard deviation of the dissolution rates to guarantee a high probability of passing the USP/NF dissolution test. However, the USP/NF dissolution test is a complicated three-stage sampling plan that involves both the sample mean dissolution rate of all units and the dissolution rate of individual units. It turns out that the true passing probability of passing the USP/NF dissolution is formidable to compute analytically even when the population mean and variance of dissolution rates are known. It is not clear that previously proposed methods are the estimators of the true probability for passing the USP dissolution test. Therefore, we propose to employ a parametric bootstrap method in conjunction with the Monte Carlo simulation to obtain the sampling distribution of the estimated probabilities of passing the USP/NF dissolution test and hence the confidence interval for the passing probability. In addition, a procedure is proposed to test whether the true probability of passing the USP/NF dissolution test is greater than some specified value. A numerical example illustrates the proposed method.

Keywords: USP/NF test; Dissolution; Bootstrap; Monte Carlo simulation; In-house specifications.