Simulations for regulatory decision making: How many simulations do we need to run?

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Simulations are being used more frequently in statistics and in other sciences, and are an important component of strategic plans of regulators such as the US FDA. Simulations offer scientists the ability to employ complex models which are not analytically tractable. As a statistical programming language *R* is particularly suited for use with simulations. However, an implicit assumption for many simulations is that a fixed number of repetitions of the simulation such as $n = 1{,}000$ or $n = 10{,}000$ is more than sufficient to establish accurate results. Focusing on binomial proportion estimation, we use *R* to establish that simulation of size $n = 1{,}000$ or $n = 10{,}000$ are generally inadequate for commonly used levels of precision in a regulatory context. Using both standard normal approximations and exact methods, we establish the required number of replications can approach $4{,}000{,}000$ for some scenarios of interest. Thus, the number of simulations should be determined by the context of use. Additionally, we show that simple quantile estimation using simulation, a method used with Bayesian estimation as well as confidence interval estimation in conjunction with naive resampling and bootstrap methods, is fraught with potential problems. Finally, we suggest possible methods to enable large scale simulation efforts, with an emphasis on parallel computing methods.