PROOF OF CONCEPT TRIALS

A. Lawrence Gould

Merck Research Laboratories, West Point, PA USA

Email: goulda@merck.com

The term "Proof of Concept" (POC) appears frequently in the literature, but generally without precise definition PoC trials may be undertaken for many reasons, e.g., screening to identify compounds worth developing or determining the feasibility of potential new uses for approved compounds. Statistical considerations become important for PoC trials when stronger evidence than simply possibility is needed, for example to quantify the risks associated with alternative resource allocation strategies, or when a quantity needs to be estimated with defined variability. This presentation defines PoC trials in terms of predictive probability of "success" with the use of an interim evaluation to provide early evidence of clear futility or effect. Demonstrating PoC would require being able to say with $100\gamma\%$ confidence that the true treatment effect is at least δ , with the ability to terminate early if the predictive probability of making this statement is less than η or greater than ξ . More general decision rules incorporating utilities or costs can be used. The statistical properties are the same as those of group sequential trials with appropriately defined critical values. This approach to PoC trials requires specifying the degree of uncertainty that is tolerable and the magnitude of the treatment effect to confirm, and presents the results in terms that management generally uses in approaching a decision.