Challenges to Some Multiple Testing Procedures in Regulatory Applications

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ABSTRACT

In regulatory applications, multiple testing problems with clinical trial methodology arise frequently in different shapes or forms, such as multiple doses, multiple endpoints, repeated significance testing of a single null hypothesis, multiple durations of a medical treatment. The null hypotheses are driven from different clinical questions but in practice these hypotheses are almost always handled in the same way by the same kind of statistical multiple comparison procedures. Indeed, the common exercise is treating all null hypotheses as an identical set of mathematical symbols. However, these hypotheses have different clinical implications; for instance, often there is a distinction between primary endpoint and secondary endpoint. Without proper consideration, several multiple comparison procedures such as the widely used sequential gatekeeping strategies often impose too many logical restrictions to make common sense, particularly in testing multiple doses with respect to multiple endpoints, testing a composite endpoint and its component endpoints and testing superiority and non-inferiority in the presence of multiple endpoints. In this presentation I shall highlight the controversies and challenges with such blinded exercise of multiple comparison procedures and invite discussions and comments.