Exploring the Impact of Missing Data on the Study Results Using Tipping Point Analysis
Supriya K and Bharath Kumar
Glaxo Smith Kline Pharmaceuticals Ltd., Bangalore.

The impact of missing data on quantitative research can be serious, leading to biased estimates of parameters, loss of information, decreased statistical power, increased standard errors, and weakened generalizability of findings. The potential for bias in study conclusions introduced by missing data has become a major concern of regulatory agencies. This reflects an increasing academic consensus that many widely used statistical analysis approaches make assumptions about missing data that are unrealistic and may not result in appropriate estimates of the effects of treatment. New guidelines and recommendations place a great emphasis not only on the importance of carefully selecting primary analysis methods based on clearly formulated assumptions regarding the missingness mechanism, but also on the necessity to perform a range of sensitivity analyses that stress the results of the primary analysis under different sets of assumptions. There are many methods that could be employed for sensitivity analyses. One of the sensitivity analysis method the Tipping Point Analysis helps us to identify assumptions about the missing data under which the conclusions change. This analysis make a series of fixed assumptions about average values of the primary endpoint among subjects who discontinue the study early. The varying assumptions include outcomes where patients with missing data from the test arms have worse outcomes than patients with missing data on the reference arm. In our trial, we wanted to test whether the new drug is non-inferior to the existing standard drug among patient population. For the primary endpoint analysis, all missing and excluded data was assumed to be Missing at Random (MAR). The Tipping Point analysis was employed to investigate the impact of missing data by using differing assumptions regarding the mean treatment effect. The analysis results were used to explore the conditions under which the conclusion of non-inferiority no longer holds.