Reviewer's report

Title: Adaptive Clinical Trial Designs for European Marketing Authorisation - A Survey of Scientific Advice Letters at the European Medicines Agency

Version: 1 Date: 27 March 2014

Reviewer: Michael Krams

Reviewer's report:

Well written paper, helpful to audience of designers working in pharmaceutical drug development, with an interest to explore the deployment of adaptive designs in phase 2 and 3 trials.

Discretionary revision: The sample of trials reviewed is likely not to include adaptive designs for which regulatory review is not routinely required, ie trials for company internal decision making, including trials to establish POC or to learn about dose-response. It might be worth highlighting that there would be value in sharing experience between sponsors and regulators on "Learn" trials, which in some environments constitute the majority of the opportunity space.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I am head of Quantitative Sciences at J&J