Title: **Using R-INLA in Bayesian Adaptive Designs**

Authors: **Lan Tran, PharmaLex**
Arnaud Monseur, PharmaLex
Bradley P. Carlin, PharmaLex
Bruno Boulanger, PharmaLex

Markov chain Monte Carlo (MCMC) methods have made it possible to perform inference for complex Bayesian models. However, it is computationally demanding and due to its random walk aspect, can suffer from long run times and high autocorrelations. The Integrated Nested Laplace Approximation (INLA) is a powerful approximate alternative with substantially reduced computational burden that still yields similar parameter estimates. Bayesian clinical trial designs permit smaller sample sizes, allowing fewer patients to be randomized. Here, R-INLA is evaluated by comparing simulation results of published designs, such as Yin et al. (2012) and Yuan et al. (2021), with RStan. The integrated LaPlace method is shown in the context of a phase II clinical trial, where the Bayesian adaptive design for a comparative arm trial was proposed for analyzing longitudinal data on multiple drug doses. Simulation results permits early stopping of dose arms for either success or futility. Our findings demonstrate the numerical and computational variances in simulations when utilizing Stan or R-INLA, and how employing Bayesian adaptive designs can optimize treatment regiments in early phase trials. These findings can be used to improve success rates and subsequent trial phases and show how INLA enables the evaluation of a wider range of design scenarios and facilitates more comprehensive sensitivity analyses while offering a two-order of magnitude speedup over MCMC. Although our calculations are exploratory, the lessons learned can be utilized in the context of their current impact and potential influence in future of drug development.