PII-108

"TRUNCATED SIGMOID E_{max} MODELS": A REPARAMETERIZATION OF THE SIGMOID E_{max} MODEL FOR USE WITH TRUNCATED PK/PD DATA. WJ Bachman PhD and WR Gillespie PhD, GloboMax LLC, Hanover, MD.

The parameters of the sigmoid E_{max} model are poorly estimated when the range of PK/PD data available is limited to $<0.95E_{max}$ [Dutta et al. J Pharm Sci 85:232 (1996)]. The following reparameterized form of the sigmoid E_{max} model has improved parameter estimation properties:

$$E = E_0 + \frac{(\beta^\gamma + 1)(E^* - E_0)C^\gamma}{C^{*\gamma} + \beta^\gamma C^\gamma}$$

where E is the effect measure and C is a measure of drug exposure (e.g., concentration or dose). The parameter E^* is the estimated effect resulting from C^*, γ is the usual "sigmoidicity" parameter, and E_0 is the baseline effect. β is a measure of the degree to which the function deviates from linearity in C^γ. One approach to applying this parameterization is to fix C^* (or E^*) at a value and estimate the remaining parameters E_0, E^* (or C^*), β, and γ by nonlinear regression. The properties of this approach are evaluated by application to simulated PK/PD data that is truncated at various fractions of E_{max}. When C^* (or E^*) is chosen within the range of the observed data, then the parameters E^* (or C^*) and β are more precisely and accurately estimated than EC_{50} and E_{max} of the standard parameterization.