

Food: a Bayesian Bioequivalence Analysis

Goal: To perform a Bayesian bioequivalence assessment in a food-effect bioavailability study.

Background: The effect of food on drug PK was assessed in a 2-period sequential study (N=12). Single oral doses of a drug were administered first in fasted state (Period 1), then after a meal (Period 2). A sufficiently long washout period was observed between administrations. Blood samples were collected after dosing and non-compartmental PK parameters: AUC, Cmax and Tmax were estimated.

Adaptive design: Not applicable.

Bayesian Model: The log-transformed AUC ratio (Fed/Fasted) was analysed as a normal response with mean μ_0 and inverse variance τ .

Vague priors were set on the mean and precision parameters:

$$\mu_0 \sim \text{Normal}(0, 10E-9), \text{ and } \tau \sim \text{Gamma}(0.0001, 0.0001).$$

Decision: Mean estimates were back-transformed from the log scale and bioequivalence was concluded when the 90% credible interval on $\exp(\mu_0)$ was included in 80 to 125%.

We have also estimated the posterior probability of bioequivalence as

$$\Pr[\text{Bioeq}] = \Pr[80\% \leq \exp(\mu_0) \leq 125\%].$$

Results: The AUC data are presented below.

Table 1. Individual AUC data.

Subject	AUC fasted	AUC fed	AUC ratio Fed/fasted	Log ratio
1	962	830	0.863	-0.148
2	1110	900	0.811	-0.210
3	1130	1510	1.336	0.290
4	1290	730	0.566	-0.569
5	888	680	0.766	-0.267
6	671	810	1.207	0.188
7	1300	2490	1.915	0.650
8	1520	1850	1.217	0.196
9	1040	200	0.192	-1.649
10	2130	5690	2.671	0.983
11	1150	1900	1.652	0.502
12	1480	1620	1.095	0.090
N	12	12	12	12

Subject	AUC fasted	AUC fed	AUC ratio Fed/fasted	Log ratio
Mean	1222.6	1600.8	1.191	0.005
Std	373.3	1444.5	0.659	0.673

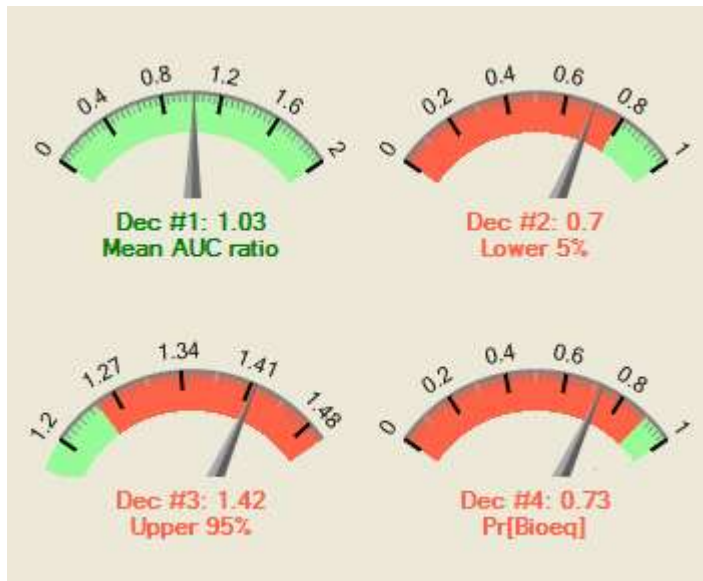


Figure 1. Bayesian Bioequivalence results.

Bayesian bioequivalence decision could not be established yet in N=12 subjects.

Decimaker: The corresponding Decimaker study project may be found [here](#).

References:

- FDA Guidance for industry. Food effect bioavailability and Fed Bioequivalence Studies. <http://www.fda.gov/cder/guidance/5194fnl.pdf>, 2002.