

ADVISORY COMMITTEE FOR PHARMACEUTICAL SCIENCE
March 12-13, 2003

CDER Advisory Committee Conference Room
5630 Fishers Lane
Rockville, MD

Day 2: Thursday, March 13, 2003

1:30 Bioequivalence / Bioavailability of Endogenous Drugs

Roxane Laboratories would like to pose the following questions to the panel discussing Bioequivalence / Bioavailability of endogenous Drugs:

Questions:

1. Please clarify method of correction for baseline for bioequivalence studies with endogenous compounds, e.g. Calcitriol.
2. A pilot BE study for calcitriol soft gel capsules meets the criteria for bioequivalence between Test and Reference using plasma concentrations, not corrected for baseline. On applying correction for baseline by subtracting pre-dose concentration from all post-dose concentrations, the study fails to meet the bioequivalence criteria. In the same study if baseline correction is applied by using the pre-dose concentration as a covariate (ANCOVA) the bioequivalence criteria is met.

In such a situation, is it appropriate that a correction for baseline level be applied using baseline as a covariate (ANCOVA), vs. simple subtraction of baseline across all subsequent levels?