FAILURE OF OFFICIAL STATISTICAL METHODS TO PROVE BIOEQUIVALENCE OF TWO MELOXICAM BIOEQUIVALENT FORMULATIONS. A NEW, "ETHICAL" STATISTICAL APPROACH

FLORIN ENACHE, CONSTANTIN MIRCIOIU[1]

Application of parametric and non-parametric officially accepted criteria for proving bioequivalence (BE) of two suppository formulations failed mainly from three reasons connected mainly with statistical rules. First two were connected with reference drug. Its pharmacokinetic parameters were nor normal nor log-normal distributed and presented a much higher variability than parameters of tested drug. The third reason was that, the number of subjects was restricted to 24 and only 18 ended the study. The number was not enough great to compensate for high variability of the reference product.

Official rules were considered as not correct and non ethical since their application implies , in the case of highly variable drugs, to impose to tested drug conditions which are not fulfilled even by reference drug or to test BE on unacceptable great number of human subjects.

In this conditions it was considered the alternative of an "ethical" and more rationale method. The method considered scaled, enlarged acceptance criteria starting from intravariability, geometric means ratio and a fixed number of subjects. Essential difference between this method and the method intended as future rule by group of statisticians of Food and Drug Administration (FDA) was that, from ethical reason it was considered instead of estimation intravariability from three periods experiments, the mean square root error obtained in analysis of variance (ANOVA) in standard two period experiment.

Applying the more ethical and essentially more correct rules, the products proved to be bioequivalent.

[1] University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania, e-mail address: constantin.mircioiu@yahoo.com