From: "Flournoy, Nancy"
Date: Thu, 28 Feb 2008 08:52:38 -0600
To: David Allen
Subject: RE: statistical analyses

Dave,

Please forward this to Group B and to Joe Haseman.

In order to be clear about bioequivalence, I have attached a major review article on the subject dated 1996. This article is written for statisticians, so I don't expect the panel to read it, but I think it should be part of the record. I just checked out "Google scholar" and got 7630 hits for "bioequivalence" since 1997 in selected fields of medicine, vet science, chemistry. If I find a good expository article, I will forward it as well.

One topic we did not discuss directly is whether we should require decisions be based on a statistical test instead of, or in addition to, the ratio rule, and if they are to be used in combination, exactly how should this evidence be combined. My position is that we should either (1) recommend decisions be based on a statistical test of bioequivalence or (2) we should recommend a future study of this matter be given the highest priority.

The bioequivalence notion is particularly relevant here, in that it is important to get the null and alternative hypotheses turned around as it appropriate for this testing situation. Because this is a safety issue, the null hypothesis should be that there is an increase in activity relative to the control and the alternative should be that there is none. With this setup, a chemical must be proven safe, not the other way around. This constitutes a major change in the way statistics are currently be used, by those that use them, so far as I can tell and I don't want this very important point to slip by. We have a chance to make a major advance in toxicity testing methodology and I hope we will.

Just recognizing the multiple testing problem is also major. I'll be trying to think of a positive recommendation to make in this regard and I hope you all will too.

See you all very soon,
Nancy Flournoy