Comments on

Note for Guidance on Clinical Investigation of Steroid Contraceptives in Women


German Region of the International Biometric Society

Page 4, section 3.1, 2nd paragraph:

"The key studies, carried out in a sufficiently representative population, should normally be at least large enough to give the overall Pearl Index (number of pregnancies per 100 women years) with a 95% confidence interval such that the difference between the upper limit of the confidence interval and the point estimate does not exceed 1 (pregnancies per 100 women years). This may require up to 20,000 cycles."

Comments:

1. The Note for Guidance should state whether the confidence interval for the Pearl Index should be one- or two-sided. It is assumed that a two-sided 95% confidence interval is requested with the consequence that the difference between the one-sided upper 97.5% confidence limit and the point estimate should not exceed 1. The calculations should be based on a pre-specified statistical model and pre-specified distributional assumptions (as, e.g., suggested by Gerlinger et al [1]).

2. Depending on the true Pearl Index, the number of cycles required to obtain a two-sided 95% confidence interval for the Pearl Index of the required precision, i.e. a half-length of less than 1, may be considerably lower than 20,000 cycles (e.g. Benda et al [2]). Since the
number of cycles actually required to fulfill the precision requirement for the estimation of
the Pearl Index has to be determined in a sample size planning under the assumptions of
the specific situation at hand, no absolute number of required cycles should be given in
the Note for Guidance. Therefore, we propose to delete the sentence "This may require up
to 20,000 cycles".

References:
