## Can CombiStats be used to perform Spearman/Kärber calculations?

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## Answer:

Spearman-Kärber calculations are performed on the results of assays depending on quantal responses. Their main advantage is their simplicity. Reed-Münch and Dragstedt-Behrens were developed in a similar way but are not recommended by the European Pharmacopoeia as they are less efficient.

Much has been written about the performance of Spearman-Kärber in comparison with probit analysis (the default method in CombiStats) under various conditions and assumptions. The bottom line seems to be that for all practical purposes, the difference between the two methods is negligible, notably when the tolerance curve can be assumed to be symmetrical, the doses are equally spaced and equal numbers of experimental units per dose are used.

Spearman-Kärber requires a response rate of 0% and 100% at the first and last dose/dilution tested. This means that it is often necessary to increase the number of doses to be tested. However, these response rates provide little information on the effective dose 50 (ED50). Probit analysis is therefore the method of choice for an appropriate use of resources (and in the case of animal assays, for ethical reasons) and for a more precise calculation of the ED50 (consequence of a choice of doses resulting in response rates of between 15% and 85%).

To summarise, probits is the method recommended by the European Pharmacopoeia and the default method in CombiStats for quantal responses. The software package does not allow Spearman-Kärber to be selected. On the other hand, when the doses tested yield a majority of extreme results (close to 0% or 100%), CombiStats will automatically invoke the Spearman-Kärber method. However, this cannot be seen as a valid argument for always using Spearman/Kärber. If this happens frequently, you may have to consider using smaller dilution steps in future assays.