Why is convergence so slow?

Answer:

Typical reasons for slow convergence of 4-parameter models are the presence of outliers or insufficient data in the extreme parts of the curve. CombiStats will issue a notification of slow convergence after 1000 iterations. You can interrupt the iterations by pressing the BREAK key (or CTRL+ESC). When you have interrupted the iterations, you can do a visual inspection of the data and the status of the fit. This will usually reveal the problem. In the case of outliers, you might decide to exclude them or to downweight them. In the case of insufficient data in the extreme parts of the curve, you might decide to use a model that better suits the data. In some cases, you may find that the data show no anomalies and that the fit of the model looks acceptable. This can happen if the improvement in the range of doses tested is very small, but the change of the extrapolated asymptotes at each step is still too large for the iterations to stop automatically. In such cases, it may be justifiable to accept the results as shown after pressing the BREAK key. You might want to check the outcome after different numbers of iterations to convince yourself that the change is indeed negligible.

Remark: The iterative method used by CombiStats (the p+2 technique) is a fairly stable method in the sense that it will converge in many cases where other methods would fail to converge (such as Newton-Rhapson where all parameters are improved at each iteration). However, this is still no guarantee that convergence can be reached even if an optimum exists. The main disadvantage of the p+2 optimisation is that it can be slow when not enough data in the asymptotes are available. Slow convergence can also be regarded as a sign of poor assay quality and might be a reason in itself to reject an assay.