AN INNOVATIVE APPROACH TO SELECT THE PREDICTION MODEL IN THE DEVELOPMENT OF NIR SPECTROSCOPIC METHODS

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Taking into account its non-invasive, non-destructive character and fast data acquisition, near infrared spectroscopy is more and more integrated in production processes to acquire analytical results. Implementation of a NIR quantitative method is performed using an iterative heuristic approach that will ultimately build a model allowing the prediction of the concentration of the analyte of interest.
In this context, the aim of the present study was to develop an innovative approach based on statistical tolerance intervals and the desirability index FMI (Fitting Model Index) to select the most appropriate prediction model from a list of candidate models instead of using conventional criteria such as R^2, RMSEC, RMSECV and RMSEP [1-2] without objective decision rules.
This new approach is illustrated on different steps of a real pharmaceutical manufacturing process: water and Active Pharmaceutical Ingredient (API) determinations in pharmaceutical pellets. Variability sources such as production campaigns, batches, days and operators were introduced in the calibration and validation sets. Partial Least Square (PLS) regression on the calibration sets was performed to build prediction models of which the ability to quantify accurately was tested with the validation sets. Regarding the product specifications, the acceptance limits were set at 20% and 5%, for the moisture and API determination, respectively.

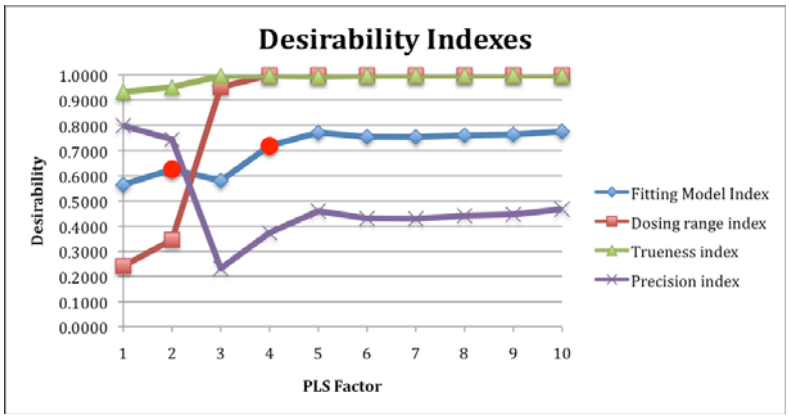

Figure 1. Desirability indexes of a calibration model according to the PLS factor number.

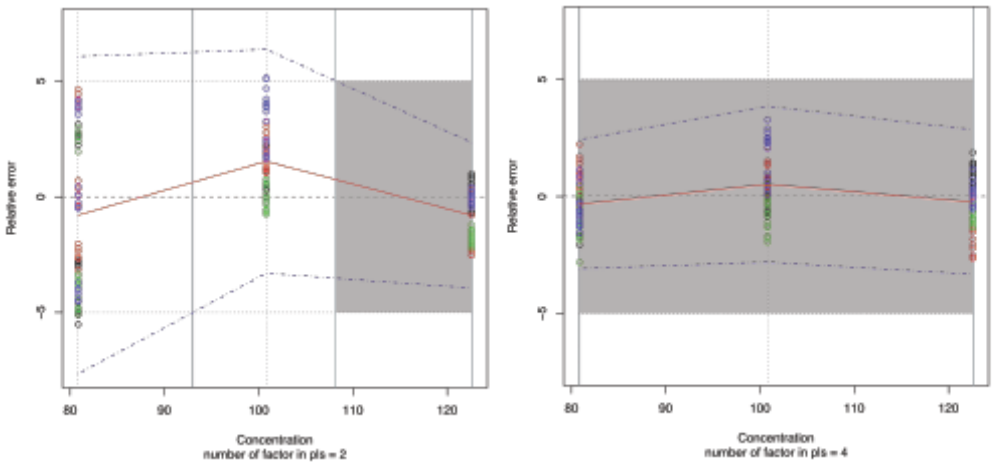

Figure 2. Accuracy profiles of a calibration model according to the PLS factor number: a) 2 PLS factors (left) b) 4 PLS factors (right).

As can be seen from Figure 1 and 2, this innovative approach based on the desirability index FMI of the accuracy profile enabled to build and select the most appropriate prediction model in full accordance with its very final goal, to quantify as accurately as possible the analytes of interest.

[1] Hubert Ph. et al., J. Pharm. Biomed. Anal., 36, 2007, 579-586.
[2] Rozet E. et al., Ana. Chim. Acta, 591, 2007, 239-247.