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

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FDA's Process Analytical Technology (PAT) aims at "improving the pharmaceutical development, manufacturing and quality assurance through innovation in product and process development, process analysis and process control" [1]. Taking into account its non-invasive, non-destructive character and fast data acquisition, near infrared spectroscopy is more and more integrated in the PAT system. However, implementation of a NIR quantitative method is performed using an iterative heuristic approach that will ultimately build a model allowing the prediction of the analyte of interest according to the product specifications.

In this context, the aim of the present study was to develop an innovative approach based on the tolerance intervals and desirability indexes to select the most appropriate prediction model from a models plurality instead of using conventional criteria such as R^2, RMSEC, RMSECV and RMSEP [2-3] without objective decision rule. This new approach was performed on different steps of a real pharmaceutical manufacturing process: water and Active Pharmaceutical Ingredient (API) determination 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.

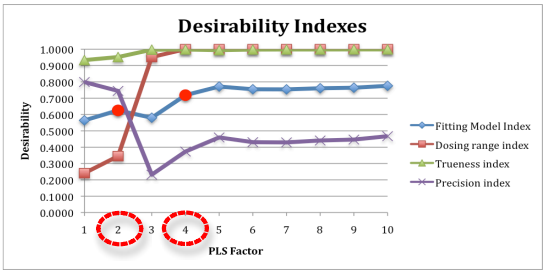

Figure 1. Desirability indexes of a calibration model according to the PLS factor number.

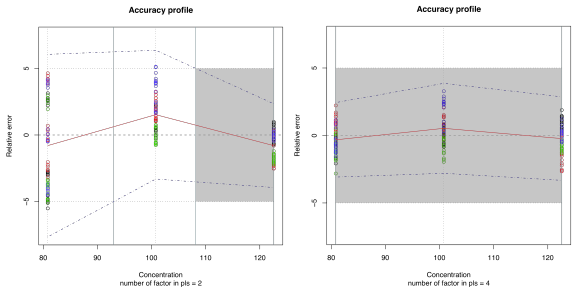

Figure 2. Accuracy profiles of a calibration model according to the PLS factor number: a) 2 PLS factors (left) b) 4 PLS factors (right).

As can be seen from figure 1 and 2, this innovative approach based on desirability indexes 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.

References

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(3) Rozet E. et al., Ana. Chim. Acta, 591, 2007, 239-247.