VALIDATION OF A NEAR INFRARED SPECTROSCOPY METHOD FOR THE QUANTITATIVE DETERMINATION OF AN ACTIVE INGREDIENT IN NON-COATED PHARMACEUTICAL PELLETS

J. Mantanus[1], E. Ziemons[1], P. Lebrun[1], E. Rozet[1], S. Rudaz[2], R. Klinkenberg[3], B. Streel[3], B. Evrard[1], Ph. Hubert[1]

[1]*University of Liège, CIRM, Belgium;* [2]*University of Geneva and Lausanne, Switzerland;*[3]*Galéphar Research Center M/F, Belgium.*

Purpose: The aim of the present study was first to validate a near infrared (NIR) method for the active content determination of non-coated pharmaceutical pellets. The second aim was to select the prediction model which was the most fitted for purpose. Further, the reliability of the selected model was tested.
Method: To meet the requirements of routine analysis, variability sources such as batches, operators, days and different temperature conditions were included in the calibration and validation set. PLS regression on the calibration set was carried out for the development of prediction models of which ability to quantify accurately was tested with the validation set.
Results: A preliminary selection of 3 models was accomplished by checking the R^2, the Root Mean Square Error of Calibration and Prediction (RMSEC and RMSEP). However, none of those commonly used criteria were able to distinguish the most fitted model for purpose among the 3 selected ones. Accordingly, a novel approach based on tolerance interval and total error measurements was followed: accuracy profiles based on the validation results. Following that approach, the prediction model using signal pre-treatment Multiplicative Scatter Correction (MSC) was chosen as it showed the best ability to quantify accurately the active content over the chosen active range (80-120 % of the targeted content).The reliability of the selected model was then successfully tested with new pilot batches of non-coated pharmaceutical pellets containing 90 and 110 % of the labeled active content, with blends of validation batches and Industrial batches.
Conclusion: In the face of the limit of interpretation of the classical and common-used criteria, the use of the accuracy profile based on the validation results as a decision tool has allowed to choose the best model in full accordance with the very final goal of the NIR method: to quantify accurately the active content (acceptance limits: ± 5%). The adequacy of the NIR method and its interchangeability with its HPLC reference method was confirmed by mean of Industrial batches.