Quantitative in-line monitoring of pharmaceutical pellets active content using near infrared spectroscopy

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Purpose: To develop an in-line near infrared (NIR) method able to quantify the active content of pharmaceutical pellets and to validate it for an active content ranging from 80 to 120 % of the usual active content.

Methods: A flow device was designed to recreate a typical particle movement found in the production line. That system was interfaced with a FT-NIR spectrometer. The calibration and validation sets included batches and days as sources of variability. PLS regression on the calibration set was performed to build prediction models of which ability to quantify accurately was tested with the validation set.

Results: A prediction model based on 4 PLS factors and using MSC signal pre-treatment was built. The values of conventional criteria such as RMSEC, RMSECV and RMSEP suggested the overall good accuracy of that prediction model. Further, a novel approach based on tolerance intervals, accuracy profile on the validation results, enabled to visualize and demonstrated the adequate accuracy of the NIR method over the chosen active content range. Moreover, that approach also met the ICH Q2R1 validation criteria.

Conclusion: An in-line quantitative NIR method for the determination of the active content of pharmaceutical pellets was successfully developed and validated. Indeed, the accuracy profile on the validation results gave a complete accuracy report of the NIR method and demonstrated its adequate accuracy. It guarantees that the newly developed NIR method will properly evaluate if the product complies with the active content specifications. Accordingly, this NIR method could be part of a real time release approach.