Real Time Release Approach in Terms of Four Pharmacopoeia Tests for Tablets Manufacturing Using NIR Spectroscopy

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Purpose
To develop near-infrared spectroscopy methods as a process analytical technique to evaluate the conformity of Paracetamol tablets in terms of content uniformity, tablet hardness, disintegration time and tablet friability.

Methods
Paracetamol tablets were manufactured by direct compression with an alternative press (AC27, GEA-Courtoy, Belgium). Blends with Paracetamol Compap PVP 3 (Covidien/Mallinckrodt), Avicel PH-102 (FMC), Glycolys (Roquette) and Magnesium Stearate (Fagron) were mixed in a multi-axis revolution mixer (Turbula) during 20 min. Flat face bevel edge tablets were obtained using round punches with a diameter of 10 mm. Targeted tablets weight was fixed at 350 mg. Three different active pharmaceutical ingredient (API) concentrations were manufactured: 80, 100 and 120 % of a predetermined dosage (250 mg of Paracetamol) and three different compaction pressures were used: 25, 45 and 65 kg/cm2. Intact tablets were analyzed by transmission mode with a multipurpose analyzer Fourier transform near infrared spectrometer (Bruker Optics). The spectra were collected with the Opus software 6.5 (Bruker Optics). Each spectrum was the average of 32 scans and the resolution was 8 cm-1 over the range from 3600 to 14000 cm-1. European Pharmacopoeia tests were used as reference methods.

Results
Three Partial Least Squares (PLS) models describing API concentrations (%), tablet hardness (N) and disintegration time (s) determined by reference methods against the collected NIR spectra were developed. The Root Mean Square Error of Cross Validation (RMSECV) models were respectively 0,467 % equivalent to 0,47 % compared to targeted concentration, 5,71 N equivalent to 6,2 % of the expected result and 2,41 s equivalent to 6,6 % of the expected result. A qualitative approach was adopted for the analysis of tablet friability ; a cluster analysis allowed us to detect non-conform tablets.

Conclusion
The tablets NIR analyses successfully allowed the prediction of their conformity in terms of content uniformity, hardness, disintegration time and friability. Compared to the time consuming Ph. Eur. reference methods, the benefit of this nondestructive method is significant especially for reducing batch release time.