Application Note AN-NIR-063

# Content uniformity test of pharmaceutical solid dosage forms using NIR spectroscopy

## Pharmaceutical quality control performed within seconds

Quality control is an indispensable part of pharmaceutical manufacturing. One key quality parameter as part of the testing requirements is the uniformity of dosage units. According to the United States Pharmacopeia USP<905>, a minimum of 30 samples of a specific batch must be tested. This procedure usually involves high performance liquid chromatography (HPLC). Prior to HPLC analysis, each dosage unit must be dissolved. The main disadvantages of this procedure are the time and high running costs (due to using solvents) involved. Near-infrared (NIR) spectroscopy allows for significant cost and time savings compared to the standard HPLC method. NIRS gives results in a short time and does not require any chemicals. Furthermore, the simultaneous quantification of APIs and excipients is possible when using NIR spectroscopy for analysis.

This drug content uniformity feasibility study was based on 38 customer-provided samples. The error of the reference method was in the range of 1–2%. The spectra were collected in diffuse reflection mode with a Metrohm near-infrared spectroscopic analyzer for solid samples.

From the total 38 samples (**Figure 1**), 33 samples were used for method development, whereas 5 samples were used to validate the quantification models for ceftazidime, starch, and sodium carbonate. The quality of the calibration models was evaluated using correlation diagrams which display a good correlation ($R^2$ > 0.94) for all parameters between the NIRS prediction and the measured HPLC content. The respective figures of merit (FOM) show that NIRS is excellently suited for content uniformity analysis of ceftazidime solid dosage forms.

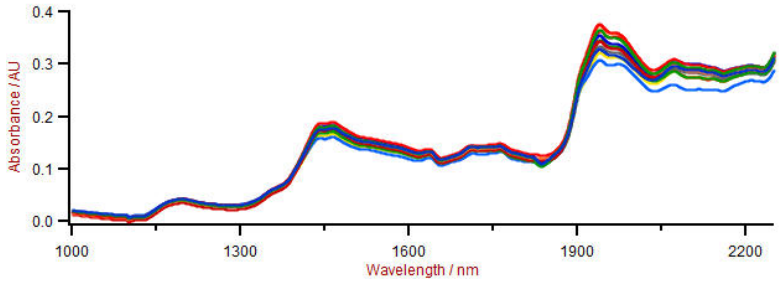


**Figure 1.** Selection of Vis-NIR spectra of ceftazidime samples used to create the calibration model.

## RESULT CEFTAZIDIME CONTENT

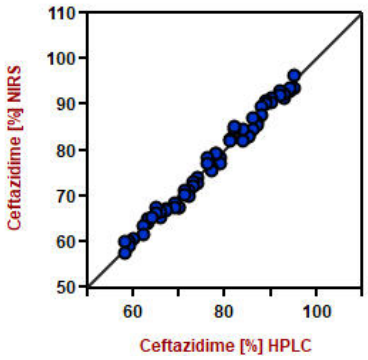


**Figure 2.** Correlation diagram and the respective figures of merit for the prediction of ceftazidime content with NIRS. The lab values were determined using HPLC analysis.

| Figures of Merit | Value |
|---|---|
| $R^2$ | 0.984 |
| Standard Error of Calibration | 1.5 (%) |

| | |
|---|---|
| Standard Error of Cross-Validation | 1.9 (%) |
| Standard Error of Validation | 2.1 (%) |

## RESULT STARCH CONTENT

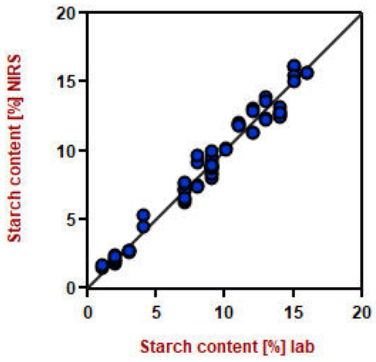


**Figure 3.** Correlation diagram and the respective figures of merit for the prediction of starch content with NIRS.

| Figures of Merit | Value |
|---|---|
| $R^2$ | 0.944 |
| Standard Error of Calibration | 1.0 (%) |
| Standard Error of Cross-Validation | 1.1 (%) |
| Standard Error of Validation | 1.7 (%) |

## RESULT SODIUM CARBONATE

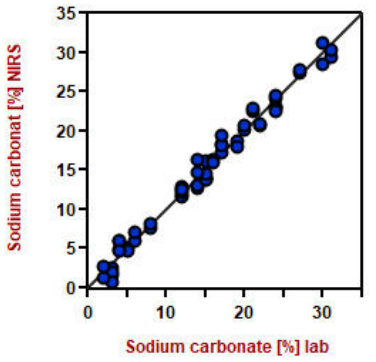


**Figure 4.** Correlation diagram and the respective figures of merit for the prediction of sodium carbonate content with NIRS.

| Figures of Merit | Value |
|---|---|
| $R^2$ | 0.966 |

| | |
|---|---|
| Standard Error of Calibration | 1.7 (%) |
| Standard Error of Cross-Validation | 1.8 (%) |
| Standard Error of Validation | 2.4 (%) |

## CONCLUSION

This Application Note demonstrates the possibilities of NIR spectroscopy for the quality control of pharmaceutical intermediates and final products. Compared to standard HPLC analysis (Table 1), NIRS measurements are reagent-free, and only take a few seconds.

Additionally, it should be noted that similar NIR methods can be developed for other pharmaceutical solid or liquid dosage forms.

**Table 1.** Analysis time for the determination of ceftazidime content using the standard HPLC method.

| Parameter | Method | Time to result |
|---|---|---|
| Ceftazidime content | HPLC | 60 minutes per sample |

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