



Application Note AN N503

On-line analysis of tablets including content uniformity with FT-NIR spectroscopy

FDA's Process Analytical Technology (PAT) initiative requires pharmaceutical manufacturers to improve the critical quality performance monitoring for ensuring final product quality. PAT concentrates in particular on the NIR technology as the most important analytical procedure for the on-line control, as NIR is unrivalled in the sum of its possibilities. Bruker Optics has seized the PAT initiative by introducing products specifically designed to the requirements of the Pharmaceutical Industry.

Bruker Optics has developed the TANDEM system, which combines on-line NIR content uniformity with conventional tablet testing on weight, thickness, hardness and diameter. Traditionally content uniformity analysis has been performed by HPLC. This high volume, time-consuming, labor-intensive process requires that test samples be taken from the production area to the QC/QA laboratory where they are prepared and analyzed. Pharmaceutical companies are striving to implement new process analytical technologies that can help improve product quality and to reduce manufacturing costs. Near-infrared spectroscopy has proven to be rapid, cost and time-effective, convenient, non-destructive, alternative for routine content uniformity analysis. TANDEM provides a comprehensive solutions for the pharmaceutical industry. It provides a full set of tablet characterization parameters including weight, size, thickness,

hardness, diameter, and NIR content uniformity is a single analyzer. TANDEM can be integrated with existing tablet pressing systems for automated analysis. Additionally, the analysis information can be used immediately to adjust production parameters to improve product uniformity. Methods can be developed on the TANDEM or they can be transferred from a Bruker Optics MPA FT-NIR spectrometer.

Instrumentation

The TANDEM system comprises the Sotax AT4 tablet tester and a Bruker Optics MATRIX FT-NIR spectrometer. The TabStat software provides an easy to use software interface for operators. The software package is fully 21CFRpart11 compliant when operated in a compliant environment. Software wizards are provided to make OQ/PQ testing an easy task.

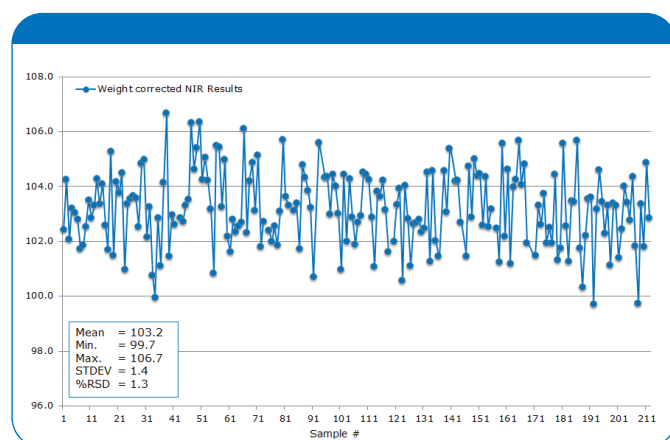
Tablet manufacture - compression

During compression, tablets are delivered from the tablet press to the TANDEM system fully automatically. The TANDEM system then performs weight and thickness analysis on each tablet. Depending on the pre-configured analysis sequence, tablets are either taken to the diameter and hardness station for full completion of conventional

tablet testing or they are taken to the NIR reading head. Different sampling strategies can be implemented to customize the test routines.

Real time data

The process control window of the TabStat software provides a clear overview of the positions of all tablets delivered from the tablet press. In addition all results produced by the TANDEM on the current run are displayed on the screen. For NIR results, a graphical display of the potency of each tablet and the pre-defined averages is shown. The same information is given in a table format. After completion of the batch, a full batch report is available.

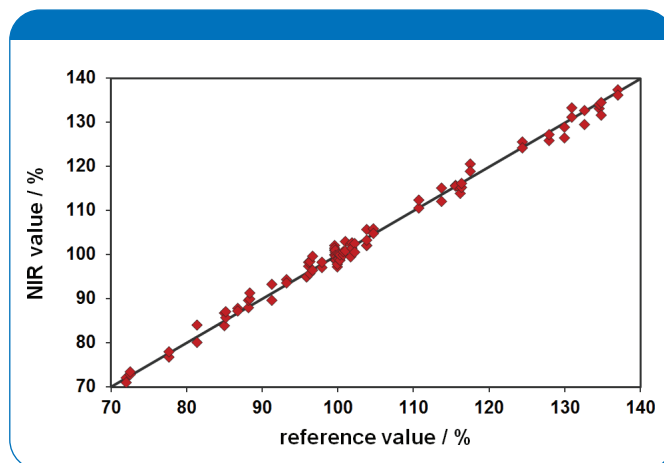


Display of the weight-corrected FT-NIR results of API concentration.

Quantitative Analysis

Near-infrared spectra result from combination and overtone bands of C-H, N-H and O-H vibrations. Since most actives and excipients contain at least one of these bonds, they are ideal for near-infrared analysis.

The OPUS/QUANT quantitative analysis software package uses partial least squares (PLS) to develop quantitative models. Calibration model development requires measuring the FT-NIR spectra of multiple samples containing a range of concentrations of the components of interest.



Validation results of a PLS-based quantification model for the percentage of API showing excellent correlation.

Implementation

The TANDEM has been developed for use in a process environment next to a tablet press. The system has a robust design with a built-in FT-NIR spectrometer, which is insensitive to vibrations from the tablet press. The TANDEM comes in an IP 65 rated stainless steel enclosure and is sealed against dust and sprayed water. The TANDEM has an open architecture for easy cleaning and product changeover.

Operation Modes

The TANDEM can be used in two different configurations:

Stand-alone mode:

- no connection to a tablet press
- manual feed of the tablets into the system
- OPC output interface

Integrated, automatic mode:

- connected to a tablet press
- automatic feed of the tablets into the system
- controlled by the tablet press

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