Application Note: 50646

Two Case Studies of the Transfer of Near-Infrared Methods for the Analysis of Pharmaceutical Solid Dosage Forms

Key Words

- Antaris
- FT-NIR
- Method Transfer
- Tablets

Abstract

The ability to transfer calibration methods from a primary Fourier transform near-infrared (FT-NIR) instrument to a target instrument is assessed using two sets of tablets with varying physical characteristics.

Introduction

The use of near-infrared (NIR) spectroscopy in the pharmaceutical industry has been rapidly increasing over the past decade, with particular interest in the analysis of tablets and capsules. The development of NIR applications for tablets has been successful, however the technology to execute these applications has yet to be extensively implemented.

As tablet applications gain wider acceptance, an important performance requirement will be the ability to transfer calibration methods from one spectrometer to another. The advantage of an internal laser to precisely calibrate the frequency position (Conne's Advantage) affords FT-NIR superior x-axis stability. This x-axis invariance between instruments contributes substantially to overall instrument sameness, facilitating the transfer of methods. Instrument component matching and production controls are also important in maintaining instrument sameness.

Numerous studies demonstrating NIR calibration transfer have been described in literature. Most involve either application of algorithms to "match" instrumentation or difference compensation between the primary and target instruments. Ideally, NIR users would take methods developed on a primary instrument and transfer them directly to a target instrument. Such a convenience would avoid both diagnosing and solving instrument mismatch problems. Additional complications would exist in highly regulated industries such as the pharmaceutical industry because recalibrated methods may have to be re-validated.

In this work, we have used clinical tablets and released tablet products to demonstrate the potential for method transfer on a Thermo Scientific Antaris™ FT-NIR analyzer (Figure 1). The data was collected non-destructively in transmission and reflectance modes.

Figure 1: Antaris Method Development Sampling System

Experimental

Diffuse reflectance and transmission spectra were acquired on the Thermo Scientific Antaris FT-NIR Method Development Sampling System. Tablets were analyzed using the tablet detector and integrating sphere modules to allow both transmission and reflection sampling without moving the samples.* Reflectance sampling parameters were 50 scans per tablet at 8 cm^{-1} resolution from 4000 to 10000 cm^{-1}. Transmission parameters were 100 scans per tablet at 8 cm^{-1} resolution from 6000 to 12000 cm^{-1}. One set of tablets consisted of small, thin, round tablets with less than 10% of weight due to the active component. The small tablets were measured using transmission mode. A second set consisted of larger, thicker oval tablets with greater than 40% of weight due to active component. The large tablets were measured using reflectance mode.

The method used for the larger tablets was Partial Least Squares (PLS) with 3 factors using a second derivative pretreatment and a Norris 11 point segment. The range used for the method was 4181 – 9169 cm^{-1}. The PLS method for the smaller tablets was also used with 4 factors using a second derivative pretreatment and a Norris 25 point segment. The range for the transmission method was 8924 – 11209 cm^{-1}.

** All reflectance measurements were on the unscored side of the tablets.*

Results and Discussion

Transmission and reflectance measurements were attempted for both sets of tablets. For the small tablets, transmission provided better results based on comparison of the method errors. This is typical for smaller, more transmissive tablets with lower percentages of active ingredient. The calibration plot for this model is shown in Figure 2. The error residual is shown in Figure 2a. The correlation coefficient was

.9996 while the Root Mean Squared Error of Calibration (RMSEC) was .247 mg/tab. This method distinguishes all of the clinical levels of active ingredients in the tablets, which was the goal of this particular experiment.

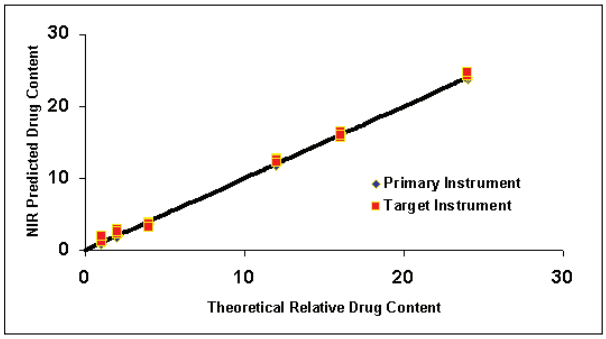

Figure 2: Results for transmission analysis of the small tablets

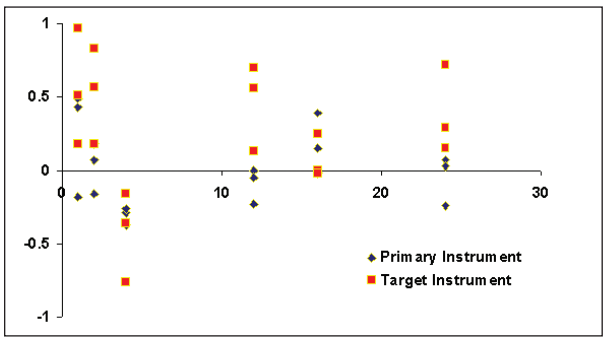

Figure 2a: Residual plot of transmission analysis of small tablets

This method was transferred to the target instrument and the model applied to the same set of tablets. The results of the transfer are also shown in Figures 2 and 2a. The Root Mean Squared Error of Prediction (RMSEP) was 0.486 mg/tab. No bias was found upon analysis of the data on the second instrument.

For the larger set of tablets, reflectance proved a better technique. This is often the case for larger, less transmissive tablets with a high percentage of active ingredient. The results are shown in Figure 3 with the residual in Figure 3a. The correlation coefficient was 0.9864 and the RMSEC was 1.65%.

The large tablet model was transferred to the target instrument. The RMSEP was 1.64% indicating successful and seamless transfer. The scored side to unscored side bias for the reflectance measurements was 3.5%. This is an important caveat when employing reflectance measurements for tablet samples.

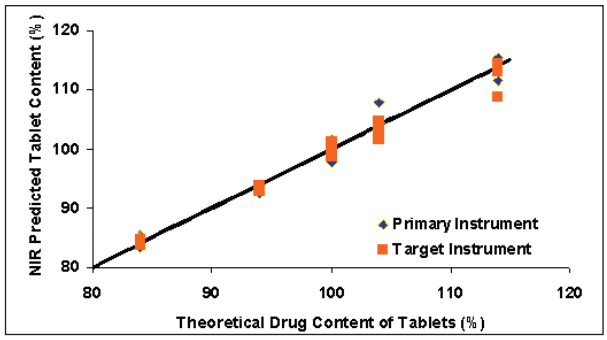

Figure 3: Results of tablet reflectance for larger tablets

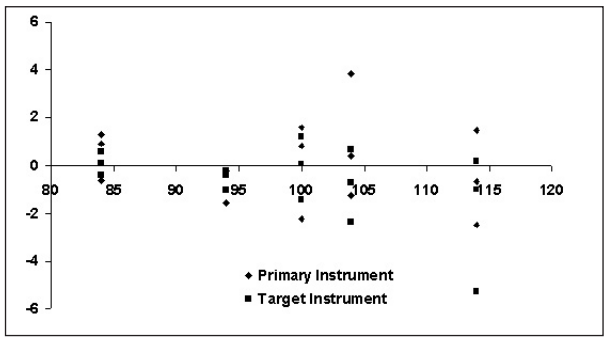

Figure 3a: Residual plot of reflectance data of larger tablets

Table 1 shows the data comparing the analysis of the exact same tablets on the primary and target instruments. Examination of this table shows the similarity of the data obtained from the two instruments.

DRUG CONTENT (% LABEL CLAIM)	PRIMARY INSTRUMENT	TARGET INSTRUMENT	%DIFFERENCE FROM PRIMARY
84	85.7	85.4	-0.35
94	93.2	93.6	0.43
100	100.1	99.8	-0.30
104	104.7	102.8	-1.81
114	112.5	111.0	-1.33

Table 1: Performance of primary and target instruments on the larger tablets

Conclusion

With traditional NIR systems, the transfer of NIR tablet methods may be complex. However, with the Thermo Scientific Antaris FT-NIR instrument's stability, sensitivity, repeatability and matched instrumental design, seamless method transfer has been demonstrated. With the Antaris FT-NIR and proper chemometric modeling complex NIR tablet methods can be readily transferred from system to system.

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