NIR Modeling for Potency of a NTI Drug Product

Seetha Ananthaiah, Ph.D. - BMS
John Peragine - BMS
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NIR Modeling PAT Project - Objectives

- Assess feasibility of NIR as alternate content uniformity method in tablets (9 potencies)
- Eliminate the need to analyze each drum of tablets via HPLC
- Replace HPLC assay method with NIR method
- Realization of an at-line real time PAT technique

NIR Modeling PAT Project - Background

- A Bruker Optics FT-NIR MPA (Multi Purpose Analyzer) was evaluated for determination of API content in tablets of a NTI drug product
- Two Bruker units were purchased (one for lab modeling; one for the manufacturing lab)
- An experimental plan was devised to develop NIR calibration model
- NIR spectra of 1,300 tablets (1 mg to 10 mg potencies) were collected

NIR Modeling PAT Project - Instrumentation

Source: Bruker Optics website http://brukeroptics.com

NIR Modeling PAT Project – Materials and Methods

- Experimental - Samples
  - 9 different potencies of API - namely 1, 2, 2. 5, 3, 4, 5, 6, 7.5 and 10 mg
  - 4 different expired finished stock lots of each potency
  - Tablets at target thickness but varying hardness
  - Tablets at target hardness but varying thickness
  - Placebo tablets
  - Tablets containing ± 15% of theoretical values for 1, 6, and 10 mg potencies
  - 2 rejected lots (32 drums each)
  - Tablets representing current formula/new formula
  - Tablets made using current process/new process

NIR Modeling PAT Project – Materials and Methods

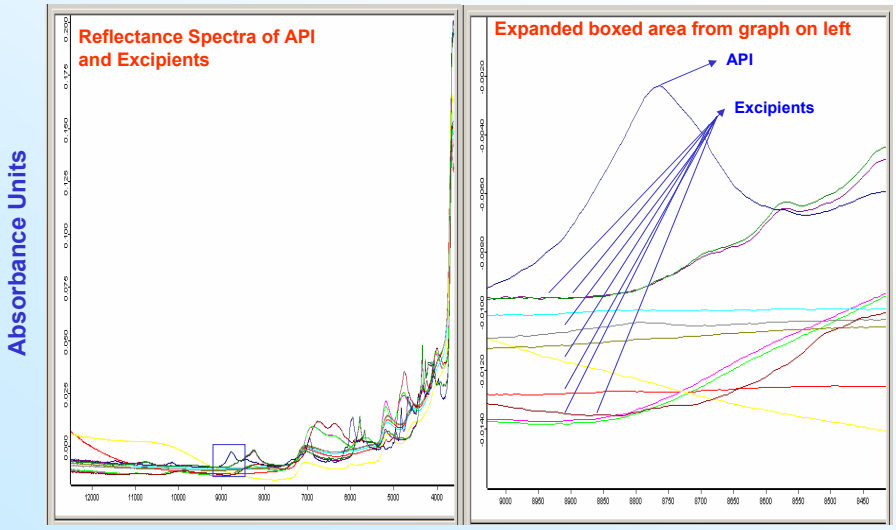
- Experimental – NIR Analysis
  - Between 10 (for lots containing ≤ 100 tablets) and 30 (for lots containing > 100 tablets) tablets were scanned using the Bruker FT-NIR analyzer
  - The 30 position auto-sampling wheel was used
  - Each tablet was scanned in duplicate in transmission mode
  - Scanning range between 8350 and 12500 cm^{-1}
  - Thickness of each tablet was measured before scanning with NIR
- Experimental – HPLC
  - Scanned tablets sent to manufacturing lab for content uniformity analysis of API content
  - HPLC analysis performed on individual tablets

NIR Modeling PAT Project – Materials and Methods

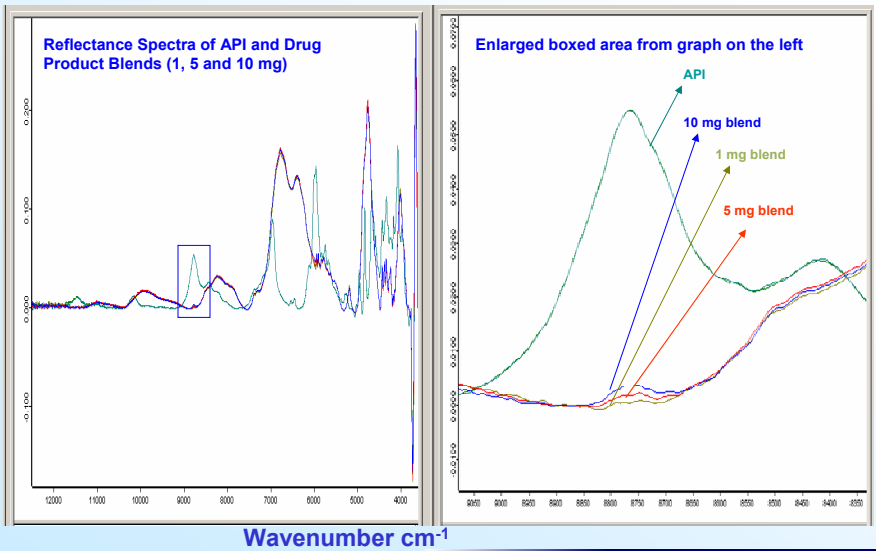
- Experimental – Data Analysis *
  - Partial Least Squares (PLS) modeling using Bruker dedicated “OPUS” chemometrics software
  - Mean centering and vector normalization
  - Spectral range between 8632 and 8864 cm^{-1}
  - Cross validation
  - 160 samples in calibration set and 70 in validation set

* All results reported are for 230 samples for which HPLC data is available

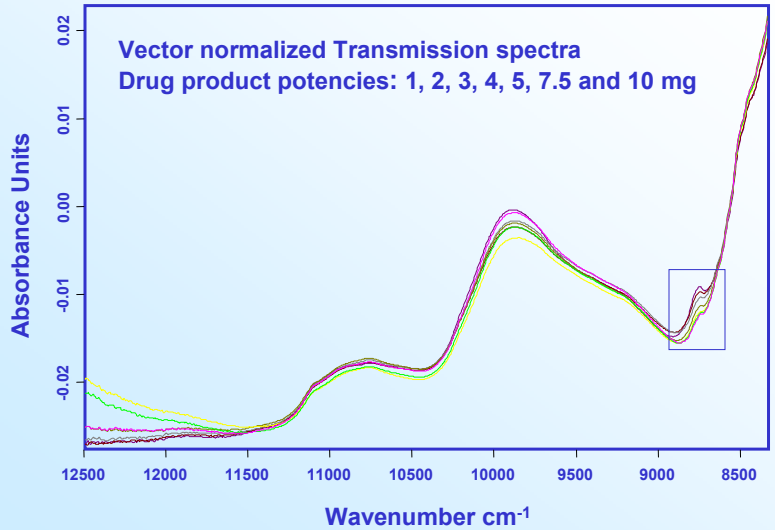
NIR Modeling PAT Project – Results



NIR Modeling PAT Project – Results



NIR Modeling PAT Project – Results



NIR Modeling PAT Project – Results

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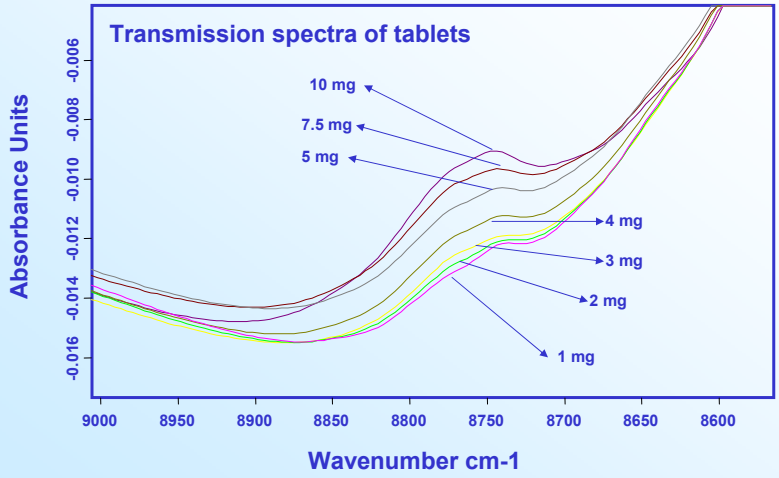

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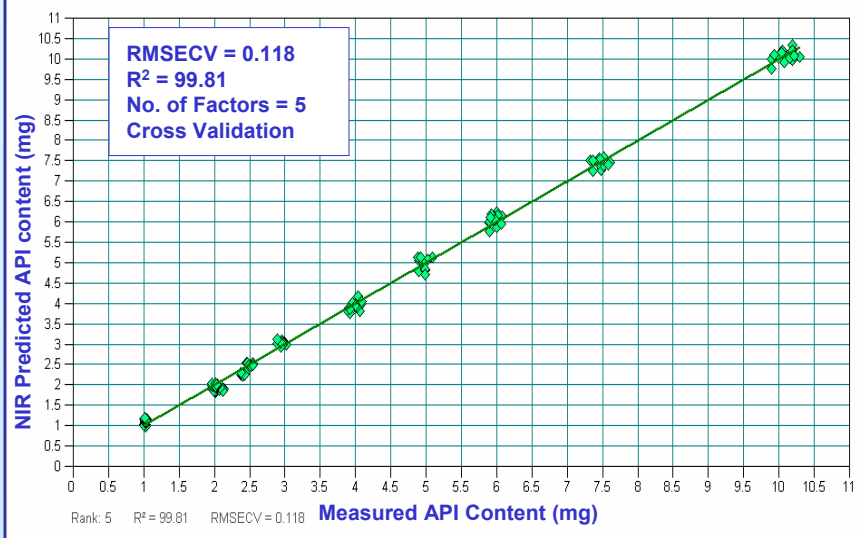
NIR Modeling PAT Project – Results



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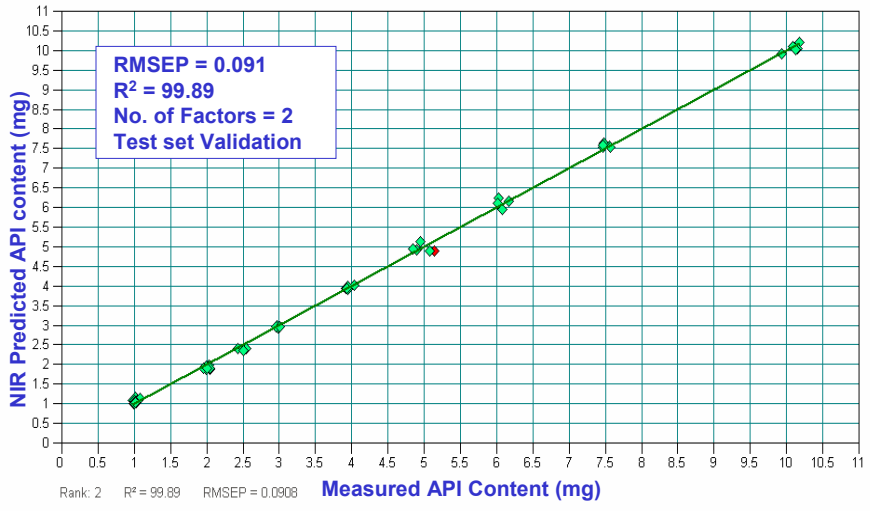

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NIR Modeling PAT Project – Next Steps

- HPLC analysis of NIR scanned tablets ongoing in manufacturing lab.
- Calibration model being expanded as HPLC data becomes available
- Headquarters and manufacturing site functions preparing for tech transfer activities
- Plan being developed for real time NIR monitoring of tablets at manufacturing site

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