

Near Infrared Spectroscopy in Pharmaceutical Manufacturing

Your up to date information source for the latest in NIRS equipment from Control Development, Inc

The pharmaceutical industry has used Near Infrared Spectroscopy (NIRS) in laboratory based applications for several decades primarily to inspect incoming raw materials and testing of finished product, and more recently for on-line and in-line measurements during production. NIRS can be used to monitor moisture and solvents during drying, powder blend uniformity, particle size, coating thickness, as well as other properties. The information obtained can be used to determine end-points of several unit operations like blending, drying and coating. NIRS is non-invasive, fast and provides real-time data for improved process understanding and control.

The FDA has recognized the need for the pharmaceutical industry to implement real time analysis and control in various stages of manufacturing of pharmaceutical products. In a new initiative, *"PAT-A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance"*, the FDA has outlined the direction that it would like the manufacturing side of the pharmaceutical industry to move towards. This new guidance **encourages** (note: this initiative is **voluntary**) the use of modern process analytical technologies (PATs) in pharmaceutical production and quality control which will help move the industry away from empirical, and towards science-based standards for manufacturing control. Some of the goals of the PAT initiative are:

- Incorporate up to date concepts of risk management
- Use latest scientific advances
- Risk based approaches that encourage innovation
- Efficient use of resources
- Continuous **real time** QA

Control Development, Inc. has developed and is developing on-line and in-line NIR based instrumentation for several manufacturing unit operations, such as:

- Blending
- Drying
- Coating (Pan coaters and Wurster)
- Wet and dry granulation
- Content Uniformity Analysis for Tablets
- Crystallization

Control Development, Inc. provides complete solutions that include custom hardware and software design, pre-production support and validation services.

Product Highlight Blend Uniformity Monitor



Features:

- On-line and real time
- Fast, InGaAs diode Array technology
- No moving parts
- Built in Reference Sources for wavelength, amplitude calibration
- Wireless 802.11g
- Battery Operated
- Class I, Div II (EP available)
- Software included

Benefits:

- Get it right the first time
- Improve yield, reduce cost
- Control your process
- Increase process knowledge
- Minimal operator involvement
- Low maintenance
- No sample preparation

Blend Uniformity Analysis Experiment

The experiment described here was conducted on a 16 quart laboratory blender, with a CDI Blend Monitor mounted close to the bottom on of the shell. Blend components were Acetaminophen - 25%, Cellulose - 25%, Talc 0.2%, and Magnesium Stearate - 0.5%. The blend monitor was triggered externally to take spectra when at the bottom. Total acquisition time was 48 msec for 32 co-added spectra. Blender speed was 5 RPM. 350 sample points were collected. **Data Analysis:** Several wavelengths unique to each material in the blend were monitored. The only data pretreatment was to take the 1st derivative of the spectra.



New Product Announcement



This **Self-Referencing Probe** can be connected to CDI Spectrometers via a fiber optic cable and a power cord. The head produces a beam of light approximately 25mm in diameter. The materials being measured can be in contact with the window or several inches away. Several fibers pick up the diffuse reflectance signal and transmit them to the spectrometer. It has built in references for wavelength and amplitude calibrations.
Part #: PNIR-1000

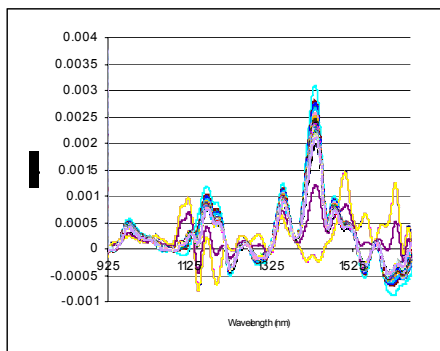


Fig 1. 1st Derivative spectra

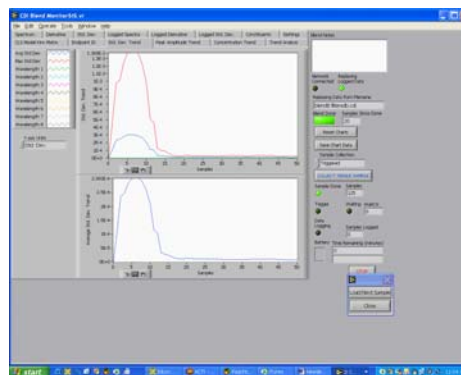


Fig 2. Standard Deviation Plot

A moving block standard deviation was calculated on pre-selected wavelengths representing the different materials in the blend. From Fig. 2, which shows two wavelengths, 1174nm representative of Acetaminophen and 1352nm representative of cellulose. As one can see from the graphs, the standard deviation gets smaller as blending progresses. One can say the materials are blended when the standard deviation is a small, predetermined number.

Quantitative Analysis: A different approach would be to determine blend uniformity by a more quantitative method, such as spectral comparison. One can determine endpoint when the spectrum of material in the blender matches spectrum taken from a sample that has previously been blended. Several spectral matching techniques and algorithms exist that make this approach relatively easy to implement. CDI Blend monitor software makes this approach easy to implement, too. **Summary:** With the availability of NIRS equipment as described above, one can determine blend uniformity in real time and on-line. The cost savings are potentially huge and immediate. This is one more step on the way to **“real time release”**, a stated goal of the FDA PAT initiative.

Publications of Interest

“We all Know PAT Means Progress and Product Improvement; But, Do We Really Have to Change How We Do Things?”. Emil W. Ciurczak. *PAT Journal Volume 2, Issue 3, May/June 2005*

“Improved Understanding of Factors Contributing to Quantification of Anhydrate / Hydrate Powder Mixtures”. Rantanen, Wikstrom, Rhea and Taylor. *Applied Spectroscopy, Vol. 59, No. 7, 2005*

Collaborations:

Dr. Rodolfo Romanach at UPR, Mayaguez, has a CDI Blend Monitor in his laboratory. For a product demonstration please call: Dr. Romanach at (787)-832-4040 Ext.3122 or send email to rromanac@uprm.edu

Tradeshows (2005)

IFPAC INDUNIV Puerto Rico, Sept. 7-8
CVG Toronto, Oct. 6-8
AAPS Nashville, Nov. 7-10, Booth # 643

Resources

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Free Demos

Call (574) 288-7338 to setup a free demo of any of our NIRS equipment.