

PAT Analyzer

Fast!! Performance Based Solutions!!



- *High sensitivity NIR diode array spectrometer*
- *Wide spectral range*
- *Fast - Non Scanning Device, Acquire full spectrum in a millisecond!*
- *Wireless and Battery Operated*
- *Self-referencing and self-calibrating*

In September of 2004, the FDA published a guidance document, "PAT – A Framework for Innovative Pharmaceutical Development, Manufacturing and Quality Assurance." PAT is "a system for designing, analyzing, and controlling manufacturing through timely measurement (i.e. during processing) of critical quality and performance attributes of raw and in process materials and processes with the goal of ensuring final product quality".

Blend Uniformity Analyzer

The current practice of blending for a pre-determined amount of time does not take into account physical differences in raw materials (e.g. of excipients) like particle shape, size distribution, inter- and intra-particulate bonding, or humidity in the environment. CDI Pharma's Blend Analyzer provides information related to both physical (e.g., particle size, morphic form, moisture content) and chemical attributes. It addresses limitations of time defined end points. The end point can now be determined based on the desired attributes of the materials necessary for the next unit operation, i.e. blend is homogenous and uniform.

Benefits of Real Time Control

- *Get it right every time*
- *Reduce scrap and improve yield*
- *Improved product quality*
- *Fast analysis at point of manufacture speeds time to market and reduces inventory*
- *Measurements are non-invasive and allows measurements of hazardous materials*
- *Minimal operator involvement*
- *Low maintenance*



Moisture and Solvent Analyzer



NIR in purged explosion proof housing

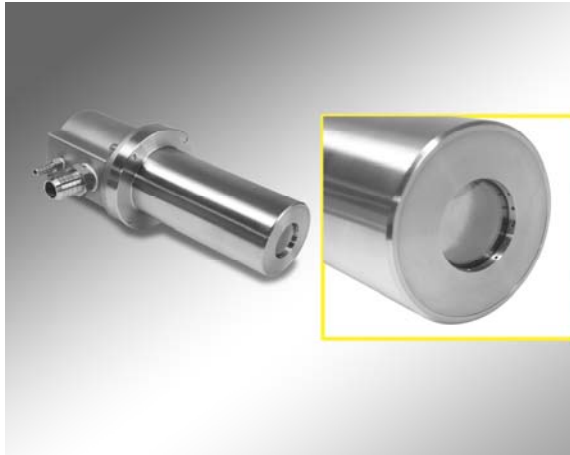
Crystallization or the presence of adsorbed liquids (organic solvent or binder solution or water) in solid pharmaceutical substances can significantly influence properties like chemical decay rate, crystal size, solubility and compaction power. Current direct techniques for moisture determination in dryers are off-line (Karl Fischer, LOD) and require stopping the drying process to remove samples, which

significantly increase cycle times. Manually collected samples are susceptible to changes in physical conditions like humidity and segregation, which will lead to inaccurate moisture analysis. Physical handling of highly potent samples can raise safety and hygiene issues. The other approach is to monitor instrument parameters like airflow, inlet/outlet air or product temperature. This method is not the most accurate as these parameters do not always reflect the critical product properties, i.e. moisture and solvent levels, which can again lead to long cycle times and product degradation (like over drying), or even result in total batch loss. NIRS provides the opportunity to monitor and determine moisture and solvent content on-line and in real time in a fluid bed dryer.

Benefits of measuring moisture in-situ during the drying process

- *Eliminate off-line bench top testing on Gravimetric Analyzers*
- *Reduce drying time by eliminating re-dries*
- *Reduce drying time by factor of ~2X by using higher inlet temperature*
- *Improve Yield, control output moisture to tighter limits*
- *Monitor average particle size using full spectrum NIR spectrometers*
- *Get it right every time*
- *Reduce scrap and improve yield*
- *Improved product quality*
- *Fast analysis at point of manufacture speeds time to market and reduces inventory*
- *Measurements are non-invasive and allows measurements of hazardous materials*
- *Minimal operator involvement*

In-Line Coating Analyzer



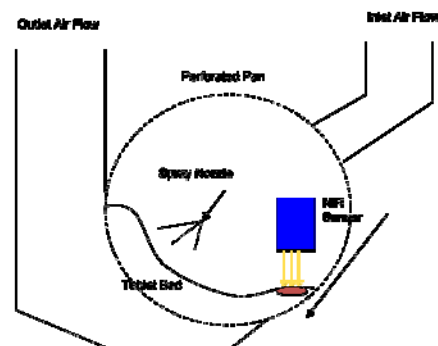
Explosion proof probe with air curtain

weight gain of the tablets determines the amount of film coating a tablet. Near infrared spectroscopy (NIRS) enables in line and real time analysis of film coating on tablets during a pan coating operation. Monitoring the decrease in absorption bands characteristic of the tablet core and monitoring the increase in bands characteristic of the coating material determine the thickness of the film coat. Similarly, active coatings can be analyzed, and end point accurately determined.

Either applying a specific amount of coating material or measuring the

Benefits of measuring coating thickness in-situ during the coating process

- Real time determination of end point
- *Real time determination of coating thickness*
- *Real time determination of amount of coating applied*
- *Eliminated expensive and time consuming methods*
- *No sample preparation*
- *Improve Yield, control output moisture to tighter limits*
- *Get it right every time*
- *Reduce scrap and improve yield*
- *Improved product quality*
- *Fast analysis at point of manufacture speeds time to market and reduces inventory*
- *Measurements are non-invasive and allows measurements of hazardous materials*
- *Minimal operator involvement*



Side-vented pan coater and diffuse reflectance NDR probe equipment setup.

● Product Specifications

Part Number	NIR1000-256L-1.7T1	NIR1000-256L-2.2T2 ^u
Spectrometer		
Spectral Range (nm)*	900-1700	1100-2200
Linear Dispersion (nm/pixel)*	3.125	4.400
Resolution FWHM (nm)*	6.25	8.8
Wavelength Accuracy*	¼ pixel	¼ pixel
Input Fiber		
Core Diameter (microns)	400	400
Material	Ultra Low OH	Ultra Low OH
Connector	905 SMA	905 SMA
Slit Width**	50 micron	50 micron
Optics	f/3	f/2
Grating		
Lines/mm	400	400
Coating Material	Gold	Gold
Blaze Wavelength (nm)	1315	1600
Order Sorting Filter	Yes	Yes
*nominal, **other widths available: slit height is always greater than the fiber core diameter, ^u - upgrade		
Detector		
Material Type	InGaAs	Extended InGaAs
Number of elements	256	256
T.E. cooling	single stage	double stage
Pixel Dimensions (WxH)	50 µm X 500 µm	50 µm X 250 µm
Electronics		
Integration times	10 µs to 16 s	10 µs to 16 s***
A/D Converter	16 Bit, 330 KHz*	16 Bit, 330 KHz*
Read out speed	2 µs per pixel	2 µs per pixel
Readout Noise**	<3.5 counts RMS	<4.5 counts RMS
Offset DAC	Yes	Yes
Flash Memory	On-Board	On-Board
Microprocessor	Enhanced 8051	Enhanced 8051
Strobe	TTL compatible	TTL compatible
Lamp Drivers	Two	Two
** 18 Bit A/D, 16 Bit displayed ** nominal ***typically < 0.5s due to detector limitations		
Probe Head		
Working Distance	Up to 25 mm from window	
Sensing Area	32 mm diameter, custom	
Light Source	Dual Tungsten Halogen Lamps, 5.4 watts each	
Lifetime of Lamps	~ 9,000.00 hours each	
Communications		
Protocol	802.11 G Wireless Ethernet	
Battery		
Type	Li-Ion	
Life	~ 3.5 hrs	
Charger	Built in	
Auto Calibration		
Wavelength Reference	Mercury-Argon line source	
White Reference	Spectralon Disk	
USP <1119> Specifications (Sensor exceeds the following)		
Baseline Noise	<0.3 X 10 ⁻³ for high light flux <1 X 10 ⁻³ for low light flux	
Photometric Accuracy	+/- 1% for all levels	
Wavelength Accuracy	+/- 1 nm	
Standard	NIST SRM 1920 or equivalent	
Physical		
Dimensions	14.95"L X 7.90W X 6.75H	
Weight	8.7 Kg	
Housing	Nema 4X. Class I, Div I/ II, EP and ATEX available	
Documentation	I/Q and O/Q documentation included	
Software		
BlendSpek™		
Spec32™		
Warranty and Support		
Warranty	1 year	
Extended Warranty	Available	
Support	Several support packages available	
Telephone	CDI Pharma Help Desk	

About CDI Pharma

CDI Pharma is a division of Control Development, Inc. The division was formed to serve the unique needs of the pharmaceutical industry. Control Development, Inc., an instrument and sensor maker has a fifteen-year history of innovation in dynamic process analysis. We are one of the largest producers of NIR diode array based spectrometers today, with over 1,000 systems in place globally.

“All our sensors are diode array based, and we pride ourselves as the premier manufacturer of such systems.”

CDI Pharma products include a battery powered and wireless-transmitting NIR blend uniformity monitor designed for PAT applications. The monitor is contaminant-resistant and has a very high optical efficiency. Our product is already in use at several pharmaceutical sites,. The division's software suite includes Spec32™ and BlendSpek™, with their 21CFR11 ready cores tailored for specific blender, granulator, coater and dryer interface requirements.

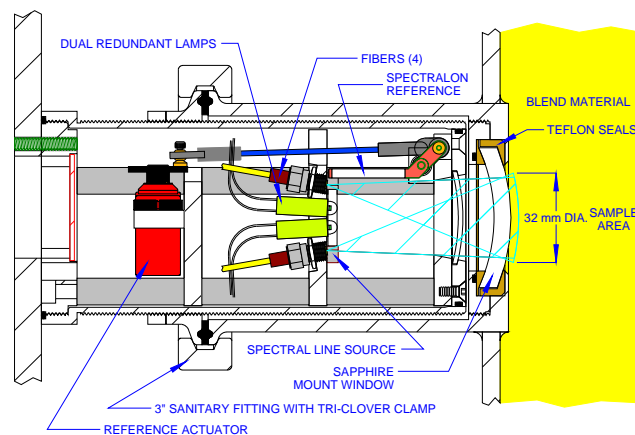
CDI Pharma has trained its staff to professional pharmaceutical standards, instituted GMP-compatible qualification packages and has instituted audit-ready software support programs.

Our Technology

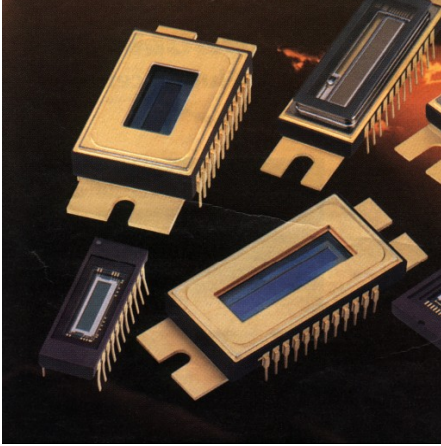
Self calibrating probe head and sampling system

We have a patented (two patents awarded) sampling and illumination system. Our unique design enhances performance, while increasing ruggedness at the same time.

- *Sample is illuminated by dual tungsten halogen lamps*
- *Large 32 mm diameter sample area*
- *Working distance up to 25mm from window*
- *Sapphire double meniscus window reduces back reflection*
- *Spectralon white reference plate*
- *Hg-Ar wavelength calibration source*
- *Fiber optic pickup*



All our NIR spectrometer sensor systems use *T. E. cooled InGaAs diode arrays*. InGaAs arrays performance and packaging have improved over the last 10 years to meet the stringent requirements of the telecommunications industry, and are now available for commercial NIR spectrometers.



These devices feature:

- *Wide dynamic range*
- *Low noise and low dark current*
- *Selectable gain*
- *Anti-saturation circuitry*
- *Correlated double sampling circuitry (greatly reduces reset noise)*
- *Offset compensation circuit*
- *Low cross talk*
- *High resolution*
- *Thermo-electric cooling, single stage for standard InGaAs detectors and dual stage for extended InGaAs detectors*

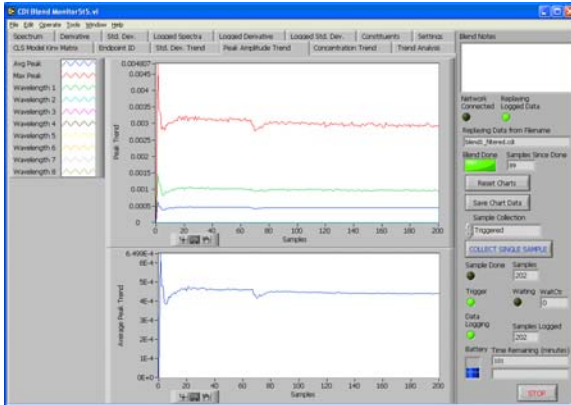
Advantages of NIR Diode Array Spectrometers for Blend Analysis

“Only array based instruments can use variance as it is the only instrument capable of taking a snapshot of sample area. All wavelengths are interrogated simultaneously.”

- *Real Time, On/In-Line*
- *NIR Spectrum provides both Chemical and Physical Information of all components of a sample, from which we can determine homogeneity of all blend types*
- *Direct non destructive method*
- *No sample prep*
- *Minimize assay time*
- *No sampling of the blend, thus no sample error due to sample thief*
- *Improved (process understanding) by optimizing process equipment*
- *Faster response times to customer demands*
- *Better productivity*
- *Lower (manufacturing) costs*
- *Total control of production process*
- *No operator intervention is needed, system is totally automated*
- *For highly potent actives, “non-sampling” has become an important issue*
- *Obtain process information in real-time*
- *Multi-ingredient uniformity can be assessed better than by current technology (HPLC, UV)*
- *Materials blended to uniformity rather than an unchanging pre-set time*
- *Continuous monitoring of the process means more sample points can be taken*
- *Advanced control will give better batch-to-batch consistency, better (product) quality*
- *It should eliminate reworks/rejects (no OOS reports to file)*

BlendSpek™ Software

BlendSpek™ is a software package written specifically for blending applications. This software package is easy to use and allows the user numerous qualitative and quantitative approaches to analyzing data.

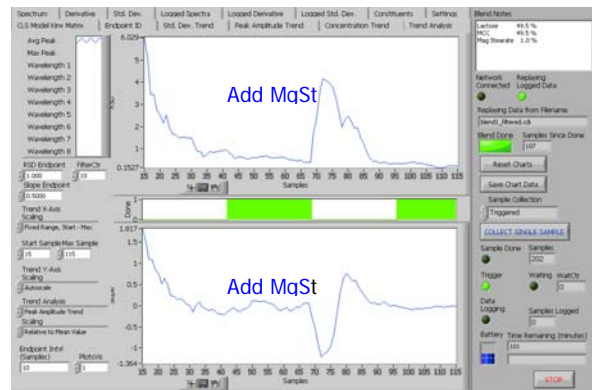


Features

- *Provides real time qualitative and quantitative Analysis of Blend Uniformity*
- *Statistical methods as well quantitative methods supported*
- *Versatile tool allows post processing of data to determine most suitable analysis method*
- *Real time spectral data collection*
- *Real time storage*
- *Real time display*
- *Real time on-line processing*

Endpoint Detection Algorithms

- *Full Spectrum Average (RSD and Slope)*
- *Absorbance at selected wavelengths (RSD and Slope)*
- *Endpoint Spectrum ID Score (RSD and Slope)*
- *Constituent Concentration (RSD and Slope)*
- *Full Spectrum Quantitative Analysis with PLS Chemometric Model*



Sample Collection Modes

- *Automatic triggering with optical proximity sensor*
- *Free-running for continuous collection*
- *Push button control for complete manual operation*

Graphical User Interface

- *Intuitive and easy to use*
- *Post processing of logged data*
- *Model Development*
- *Fine tuning of algorithms*

Flexible Platform

Use the same instrument in the laboratory as well as in production.

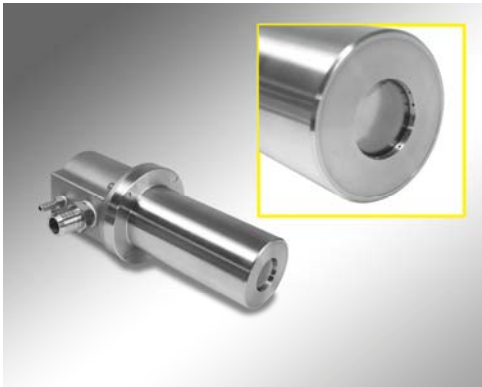


With an available sample stand, use exactly the same sensor in a research environment, product development or production.

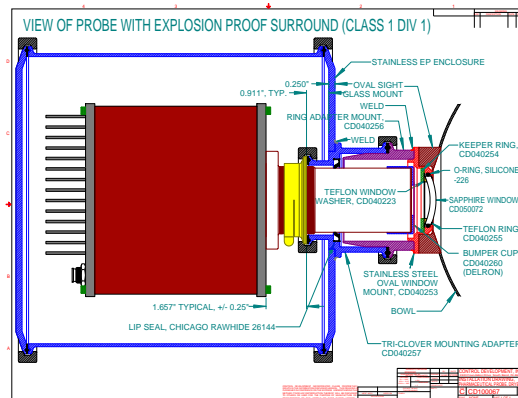
This approach gives reproducible results and makes scale up from development to production easy. The analyzer is easy to move and remove either from the sample stand or a blender.

Other Applications

Explosion Proof Probe for In-Line Analysis of Film Coating in a Pan Coater



Probe in EP Housing for Fluid Bed Dryer



CDI Pharma has solutions for:

On-Line Non-Destructive Determination of Tablet Content Uniformity Using NIRS

End-Point Detection of High Shear Granulation

Real time determination of Content Uniformity, Moisture Content, Compact Density, Tensile Strength, Young's Modulus of roller compacted powder blends