

## Turnable Diode Laser Absorption Spectroscopy for Pharmaceutical and Bulk Powder Dryer-End Point Detection

Pharmaceutical manufacturers use a combination of approaches to remove the solvents from their products. The most common method requires that the drying process be stopped and a sample manually removed for Loss of Drying (LOD) analysis. If the product is not dry, the process is restarted and allowed to run for an indeterminate period. This time-consuming process is repeated until the LOD achieves a predetermined value.



Large-scale drying involving thousands of pounds of product can take many hours to complete. Repeated interruption of the process to accommodate manual product analysis can add hours to that process. Online dryer end-point detection works by monitoring solvent vapors driven from the product during pressure or vacuum drying, and, most importantly, avoids the need for pharmaceutical manufacturers to stop, analyze and then restart the drying process.

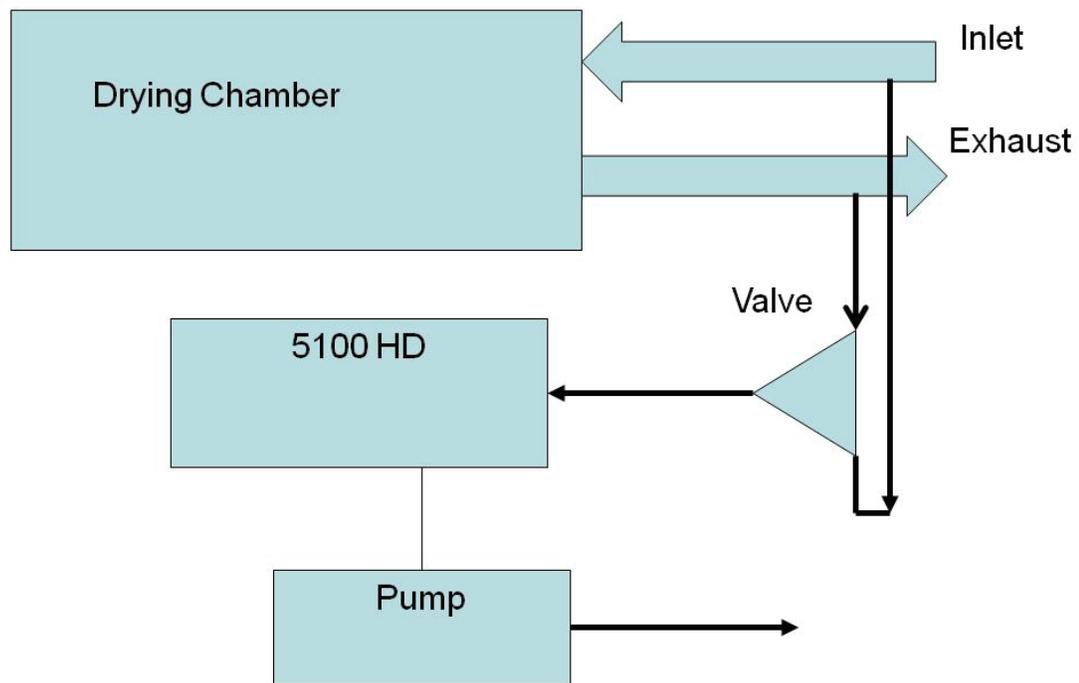
### Features and Benefits

- ▶ **Noncontact Measurement**  
Noncontact measurement offers low maintenance
- ▶ **All Digital Signal Processing**  
32-bit microcontroller capable of sophisticated signal processing
- ▶ **Web-Based Interface**  
Connect through a remote PC using standard web browser
- ▶ **Connectivity**  
Modbus, Ethernet and analog
- ▶ **Real-Time Performance Monitoring**  
Laser line-lock verification using internal reference cell
- ▶ **TYPE 4X Enclosure houses the electronic components**  
Designed for production environments
- ▶ **Fully-Integrated Sample Handling**  
Standard feature

### Trial Demonstrates Effectiveness of TDLAS in Water Solvent Drying

AMETEK, working with a pharmaceutical manufacturer, set up a production trial using its Model 5100 HD analyzer to monitor the batch production of a widely prescribed medication, whose synthesis involves the use of water as the final rinse agent.

Over the course of the trial, the Model 5100 HD recorded moisture concentrations at the drying chamber inlet and outlet, yielding results that clearly indicated that the drying process was essentially completed during the first four hours of the drying cycle, a far shorter time period than had been anticipated.



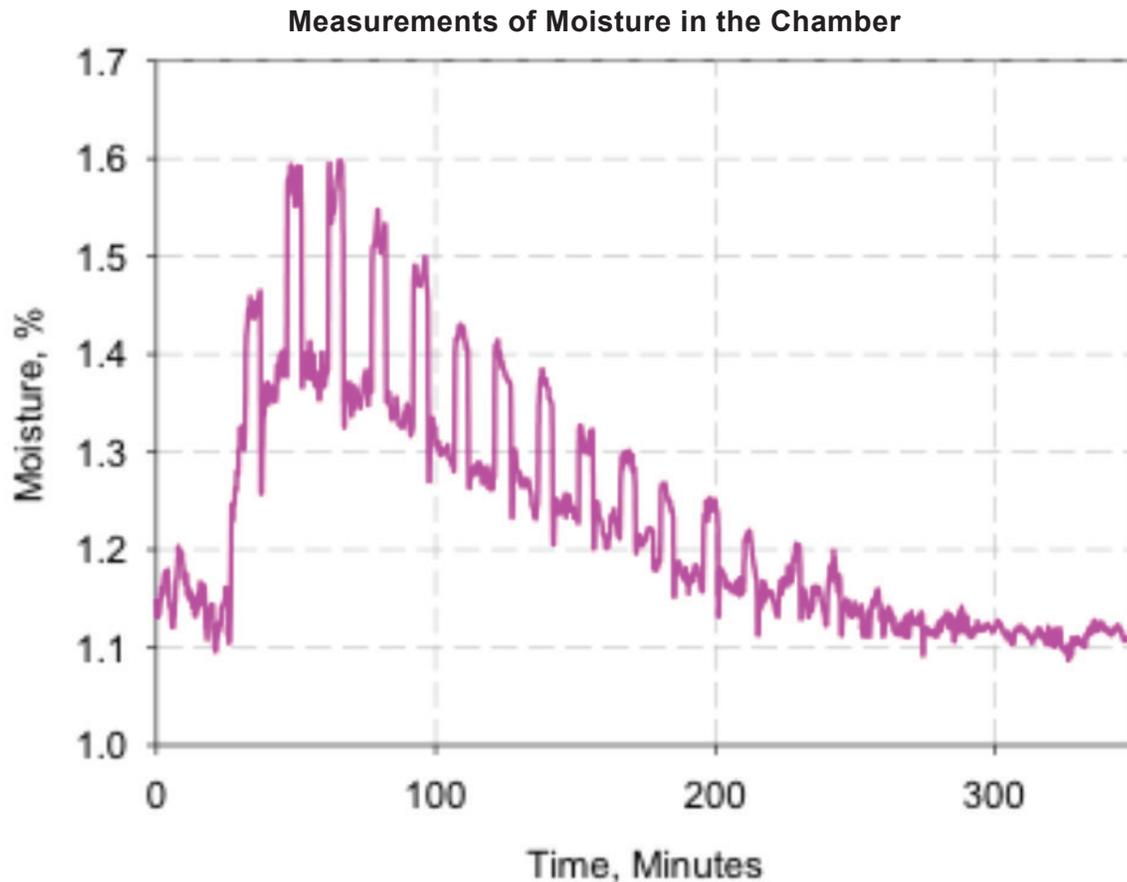
*The installation of the 5100 on a tray dryer*

The air from the inlet and exhaust of the drying chamber was sent to the AMETEK 5100 HD analyzer by using a pump and a two way valve. The inlet and exhaust of the drying chamber were connected to the valve with 1/8" stainless steel tubing using Swagelok fittings. To avoid condensation inside the tubing, the outlet tubing, valve, and the tubing connecting the valve to the inlet of the 5100 HD analyzer were heated and kept at a temperature of ~70°C. The temperature in the sample cell compartment was 65 °C. The flow rate through the sample cell was ~2 liters per minute. The pressure in the sample cell was 14.3 psia. Standard operating procedure (SOP) for this particular product called for an 8 hour drying cycle before extracting a sample for LOD testing.

The 5100 is capable of providing quantitative measurement of the amount of moisture that is found in the dryer exhaust. While the amount of moisture measured is not that of the product itself, there is a direct correlation between the amount of moisture in the product and the moisture in the dryer exhaust. As the 5100 is sampling the dryer, samples must be removed and testing according to the current validated test to obtain the moisture remaining in the product. These measurements are overlaid onto the 5100 measurements to obtain the linkage between the moisture in the product and the moisture in the dryer exhaust.

An alternative approach is to simply use the picture of the drying curve as the indicator of product dryness. In the case above, the drying was accomplished by the use of the lightly conditioned outside air. Since there was humidity in the incoming air, an assumption could be made that once the measurements of the incoming air and the exhaust

air coincide with the accuracy of analyzer measurements, then no further drying could be taking place. And since this drying process, using the same lightly conditioned air, had been producing product that was dry to the manufacturer's specifications, once the convergence of input moisture to output moisture had been found, the product must be dry.



*As can be seen, input and output moisture numbers converge after 5 hours. This was 5 hours earlier than the standard operating procedure required for loss of drying analysis.*

The trial also demonstrated that TDLAS techniques could be used to continuously monitor and control the solvent drying process online, in real time, without operator intervention or process interruption. That alone represented a significant advance in process analytical techniques for pharmaceutical manufacture.

The results further indicated that TDLAS has the potential to significantly reduce drying times, while improving both production and product quality for pharmaceutical manufacturers and other bulk powder producers who rely on water as the principal solvent in their processes.

# TDLAS - Dry-End Point Detection

## Specifications

### Laser Specification: Class 1m

#### Environment:

**Ambient Temperature:** -20°C to +50°C (-4°F to 122°F).

#### Electrical Classification:

NEC/CEC: Class I Division 2  
Groups A, B, C, D, T3, CE  
IP-65 NEMA 4X (A T5 rating can be obtained by eliminating the oven).

ATEX/IECEX Zone 2, T3  
CE, IP-65, (A T5 rating can be obtained by eliminating the oven).  
II 3 G Ex nA nC ic op is IIC T3 Gc IP-65

INMETRO Certification for Zone 2-  
Ex nA nC ic op is IIC T3 Gb IP-65

**Relative Humidity:** 0% to 90%, non-condensing

**Sample Flow Rate:** 1 to 10 LPM recommended (2 - 20 SCFH)

### Sample Cell Pressure:

70 to 170 kPa absolute (10-25 psia)

### Outputs:

4-line x 20-character alphanumeric VF display.

#### Fast Ethernet (IEEE802.3)

**RS-485** serial port, isolated (supports Modicon Modbus RTU)

**RS-232** serial port (for service use only)

(1) isolated 4-20 mA loop-powered analog output standard (can be configured to output results such as analyte concentration and dewpoint) (a second output is available as an option)

(4) dry relay contacts. Contact rating 30 VAC, 60 VDC, 100 VA resistive

**Speed of Response:** <2 seconds (photometric); <15 seconds to T90 including sample surge. Total system response is dependent on sample flowrate

### H<sub>2</sub>O - Analyte Range

#### (% level ranges):

0-5000ppm  
0-2500ppm  
0-1000ppm  
0-250ppm  
0-100ppm (accuracy ±2ppm)  
0-20ppm (accuracy ±2ppm)

**Accuracy<sup>1</sup>:** ±2ppm or 2% of reading, whichever is greater

### Electrical Requirements:

120 VAC (108-132V); 47-63 Hz, or 240 VAC (216-264), 47-63 Hz  
24 VDC (Consult AMETEK)

### Power Requirements:

450W; 105W without sample cell heater

### Physical: HxWxD:

(5100 HD Div 2 Zone 2 Model)  
67.4 cm x 88 cm x 30.2 cm (26.5" x 34.6" x 11.9")

**Weight:** 60 kg (132 lb)

<sup>1</sup> Consult factory for specifications on other measuring ranges

The AMETEK model 5100 HD is an extractive type analyzer designed for wide range moisture analysis. There is no sample conditioning required for the analyzer system other than particulate filtering and assuring the sample does not condense at the maximum integrated oven temperature of 150°C. The analyzer uses a completely digital implementation of the Wavelength Modulation Spectroscopy (WMS) approach.

A key feature of the Model 5100 HD is the use of sealed reference cells, which contains a known amount of moisture for referencing the emission wavelengths of the lasers. The use of reference cells enables both the ability to line-lock the lasers and to continuously verify the instrument performance.



Model 5100 HD

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One of a family of innovative process analyzer solutions from AMETEK Process Instruments.  
Specifications subject to change without notice.

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