AMETEK®
PROCESS INSTRUMENTS

APPLICATION NOTE

PHARMACEUTICAL AND BULK POWDER-DRYER ENDPOINT DETECTION USING TUNABLE DIODE LASER ABSORPTION SPECTROSCOPY

5100HD Tunable Diode Laser Absorption Spectroscopy Analyzer

Pharmaceutical manufacturers use a combination of approaches to remove the moisture and 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 for manual product analysis can add hours to the process. Online dryer endpoint detection works by monitoring moisture and solvent vapors driven from the product during pressure or vacuum drying and avoids the need to stop, analyze, and then restart the drying process.

EQUIPMENT

TDLAS is a non-contact analysis technique with long-term stability, high specificity and selectivity. A laser-based water vapor sensor offers the advantage of faster response time, large dynamic range and low drift in comparison with conventional techniques. In applications such as monitoring the water vapor levels in the drying process these attributes help meet the optimal requirements of plant operation.

The AMETEK 5100HD is an extractive laser-based analyzer designed for hot/wet sample analysis. There is no complex sample conditioning required for the analyzer system, reducing complexity, cost and maintenance requirements. The 5100HD uses a sealed reference cell for continuous on-line analyzer verification and offers high specificity, and sensitivity.

AMETEK 5100HD TDLAS ANALYZER

PROCEDURE

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

The air from the inlet and exhaust of the drying chamber was sent to the 5100HD analyzer by using a pump and a two-way valve (Figure 1). To avoid condensation inside the tubing, the outlet tubing, valve, and the tubing connecting the valve to the inlet of the 5100HD analyzer were heated and kept at a temperature of about 70°C. The flow rate through the sample cell was about 2 liters per minute and the pressure in the sample cell was 14.3 psia.

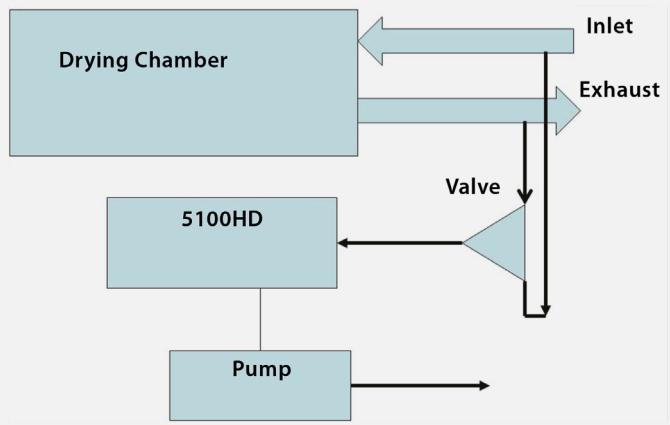

Figure 1. The installation of the 5100HD on a tray dryer

The 5100HD can provide 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 5100HD was sampling the dryer, samples were removed and tested according to the current validated test to obtain the moisture remaining in the product. These measurements were overlaid onto the 5100HD measurements to obtain the linkage between the moisture in the product and the moisture in the dryer exhaust.

RESULT

Over the course of the trial, the 5100HD recorded moisture concentrations at the drying chamber inlet and outlet (Figure 2), yielding results that indicated that the drying process was essentially completed during the first three to four hours of the drying cycle, a far shorter time than had been anticipated. Standard operating procedure for this particular product called for an 8-hour drying cycle before extracting a sample for LOD testing.

The results indicate 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.

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. This also represents a significant advance in process analytical techniques for pharmaceutical manufacture by removing the need to have a human "in the process".

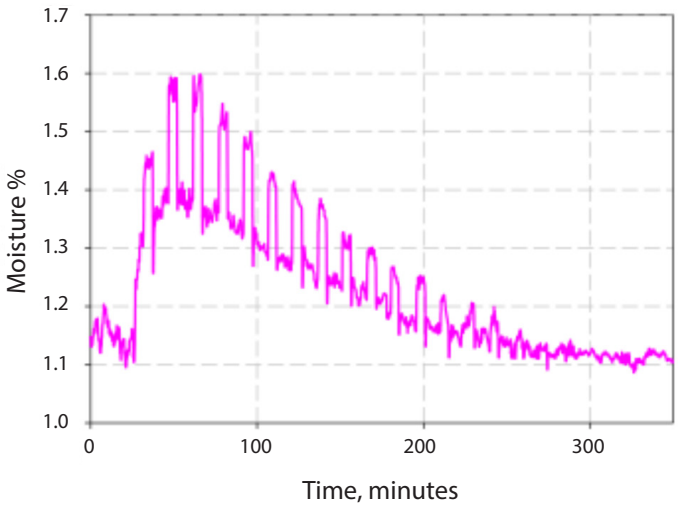

Figure 2. Moisture measurement in the chamber. Input and output numbers converge after five hours, which is three hours earlier than the standard operating procedure required for LOD analysis

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