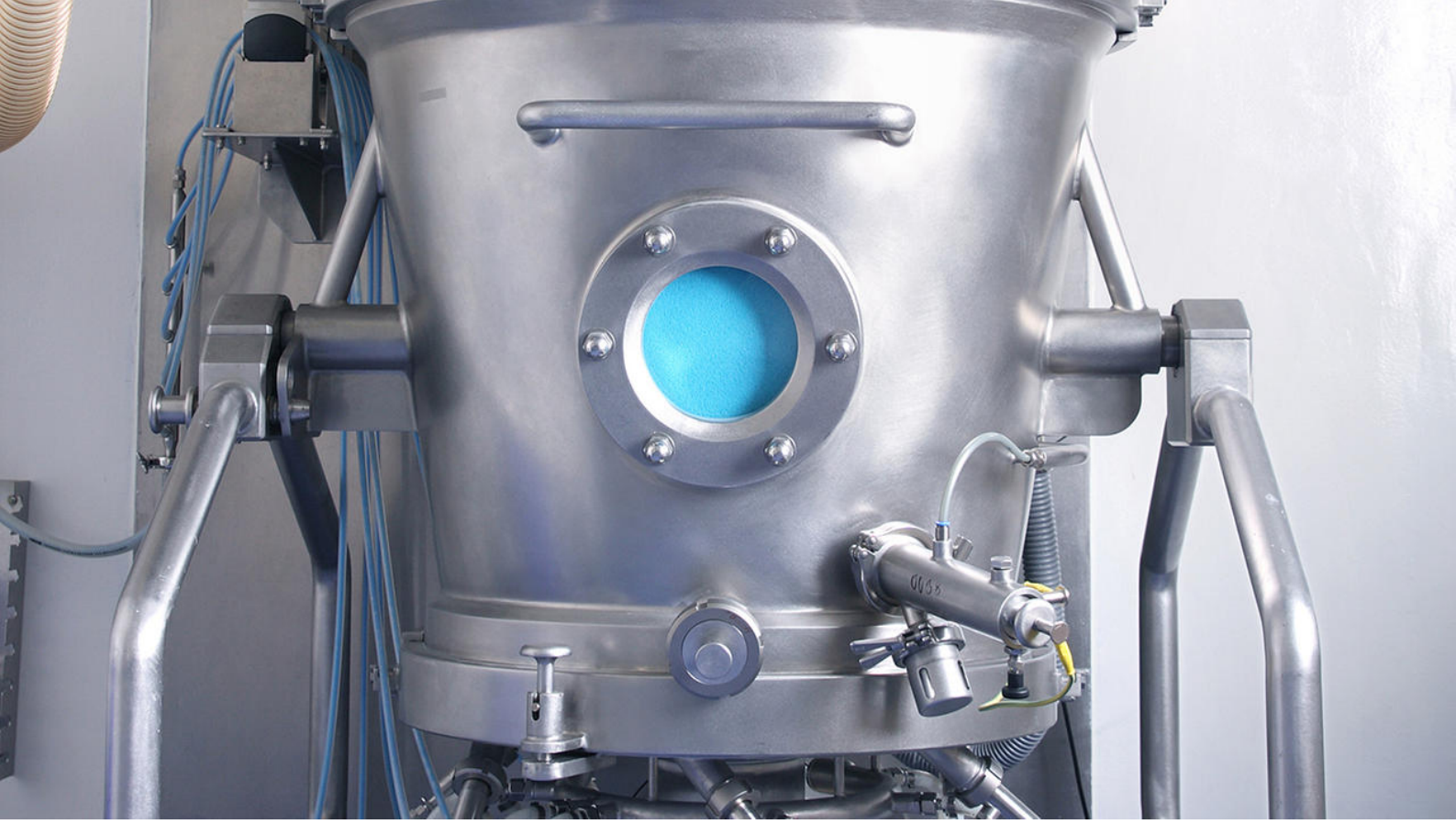

Application Note AN-PAN-1050

Inline moisture analysis in fluid bed dryers by near-infrared spectroscopy

In the pharmaceutical industry, the fluid bed granulator/dryer is an integral point in the manufacture of powdered materials. Residual moisture must be kept within certain specifications to avoid fracturing of particles or caking (stickiness) of the bulk material.

Current methods are slow and cumbersome, which can lead to damaged or degraded product. The ability to monitor the residual moisture content inline after drying is possible with near-infrared spectroscopy (NIRS).

This Process Application Note details the inline analysis of moisture during the drying process with a NIRS XDS Process Analyzer from Metrohm Process Analytics. The NIRS XDS Process Analyzer offers fast, reagent-free, nondestructive analysis of residual moisture of powders with a fluid bed probe specifically designed for these applications.

INTRODUCTION

In the pharmaceutical sector, the fluid bed granulator/dryer is an integral point in the manufacture of powdered materials (active ingredients or excipients). Particle size can be affected by several factors, among them is the moisture content of the product in the fluid bed dryer. If over-drying occurs, the granules can fracture, resulting in fine particles which can adversely affect the final formulation. Product that is left too moist at the end of the process can clump together and cause blockages in the flow, as well as causing other manufacturing problems.

Moisture content of the powder is generally determined via slow offline laboratory techniques such as loss of weight (10–30 minutes), after physical removal from the process with a sample thief. This manual sampling results in a delay, which can cause problems whenever critical processing decisions must be made, such as determination of the end of the drying process. Monitoring the moisture content directly leads to a more informed operator and an efficient drying process.

Real-time analysis of the moisture content in powders can be performed inline via near-infrared spectroscopy (NIRS), which fits well within the Process Analytical Technology (PAT) initiative as recommended by the FDA. The process can be monitored constantly without manual intervention, allowing for better process understanding, control, and more precise determination of the end of drying.

Development of a calibration model which properly correlates NIRS results to a laboratory reference method is necessary first. A fluid bed «spoon» probe designed specifically for this purpose is inserted directly into the dryer (Figure 1a). After each NIR spectrum is collected, an air purge exiting through the ports located in the probe tip clears the «spoon» for a new sample. Each scan takes 30 seconds, ensuring there is always an accurate snapshot of the drying process at any time (Figure 1b).

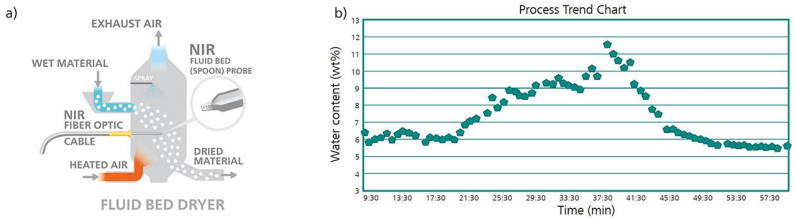

Figure 1. (a) Suggested placement for NIRS «spoon» probe in a fluid bed dryer. (b) Trend chart of water content determined via NIRS versus time.

Product release delays caused by waiting for laboratory results can be minimized or eliminated as determination of the end of the drying process can be made when the moisture level asymptotically approaches a lower limit during the drying cycle. The operator is aided in making the decision to end the drying operation before the product is damaged or degraded. Output from the process analyzer can be used by the fluid bed dryer's programmable logic controller (PLC) or integrated into SIPAT (Siemens Industry Process Analytical Technology) for closed loop process control decisions. The reduction in reprocessing steps saves both time and money, and improvement in the product quality can lead to even higher profits for the manufacturer.

APPLICATION

Wavelength range used: 1100–1650 nm. Inline analysis is possible using a micro interactance reflectance probe with purge on collection tip directly in the fluid bed dryer.

Figure 2. NIRS XDS Process Analyzer from Metrohm Process Analytics.

Table 1. Parameters to monitor in fluid bed dryer.

Analyte	Concentration (%)
Moisture (H_2O)	0–60%

REMARKS

A primary reference method must still be in use. An appropriate range of samples covering the process variability should be analyzed by both methods to build an accurate NIRS model. Correlations are made to process specifications. The correct NIRS probe must be placed in-situ in a manner that provides sufficient sample contact with the probe tip window. Correct probe design and proper placement in process equipment is of high importance.

Table 2. Dedicated solutions for your sampling needs.

Probe Type	Applications	Processes	Installation
Micro interactance reflectance probe	Solids (e.g., powders, granules)	Bulk polymerization	Direct into process line
	Slurries with > 15 % solids	Hot melt extrusion	Compression fitting or welded flang
Micro interactance immersion probe	Clear to scattering liquids	Solution phase	Direct into process line
	Slurries with < 15% solids	Temperature- and pressure-controlled extrusio	Compression fitting or welded flange
Micro transmission probe pair	Clear to scattering liquids	Solution phase	Direct into process line or reactor
	Slurries with < 15% solids	Temperature- and pressure-controlled extrusio	Into a side-stream loop
			Compression fitting or welded flange
Micro interactance reflectance probe with purge on collection tip	Solids (e.g., powders, granules)	Drying of granules and powders	Direct into the fluid bed dryer,
	Environments where sample amount varies		Compression fitting or welded flange

OTHER PROCESS NIRS APPLICATIONS RELATED TO THE PHARMACEUTICAL SECTOR

- Active Pharmaceutical Ingredient (API) content
- Blend homogeneity / Content uniformity
- Solvent purity

FURTHER READING

Related application documents

AN-NIR-016 Near-infrared spectroscopy for monitoring a single-pot granulator

AN-PAN-1048 Inline moisture analysis in a pilot scale granulation process by NIRS

AB-358 Analysis of residual moisture in a lyophilized pharmaceutical product by NIRS

TA-048 Near-infrared spectroscopy for pharmaceutical analysis

BENEFITS FOR NIRS IN PROCESS

- **Optimize product quality** and increase profit by fast response time to process variations
- Greater and faster **return on investment**
- **No manual sampling needed**, thus less exposure of personnel to dangerous chemicals

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