Inline moisture analysis in a pilot scale granulation process by NIRS

Summary

Top spray granulation in the pharmaceutical sector is a common method used to form granules from moist powdered materials in fluid bed dryers. The residual moisture must be kept within certain specifications to avoid fracturing of particles or caking (stickiness) of the bulk material. 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 in a pilot scale granulation process with a NIRS Analyzer PRO from Metrohm Process Analytics. The NIRS Analyzer PRO offers fast, reagent-free, nondestructive analysis of residual moisture in powders with a fluid bed probe specifically designed for these applications.

Configuration

A629281120 - NIRS Analyzer PRO – FiberSystem

The NIRS Analyzer Pro is a single point process analysis system based on high resolution diode array technology. It provides non-destructive analysis of liquids, granules, powders, slurries or opalescent substances by using fiber optics microbundles and contact probes for reflectance and transflectance measurements.

Introduction

Top spray granulation is a common method of granulation in the pharmaceutical industry. Powder is fluidized in a fluid bed dryer and a liquid binder solution is sprayed on to the product. After spraying the liquid into the formulation and forming the granule, the product must be dried to the proper moisture level. If the granules are over-dried, movement in the fluid bed can cause their fracture (creating undesirable fine particles) and can damage the formulation due to hydration changes in some active ingredients and excipients. If the granules contain too much residual moisture, the product will not flow properly and may cake. This can cause problems with subsequent processing, including a sticky product and product instability during storage.

Samples are typically withdrawn from the fluid bed with a sample thief during processing and then analyzed offline for moisture content in a laboratory. This delay before the analysis results are available to the operator can cause critical processing decisions e.g., determining when the drying process should end) to be made without optimal product moisture information. Top spray granulation completion is often based on time or product temperature—not moisture content.

Using near-infrared spectroscopy (NIRS) technology, the drying process in a fluid bed dryer can be quickly monitored inline to determine the residual moisture level for better process understanding, control, and end of drying process determination. The figure below shows a trend chart of the moisture content versus time determined by NIRS. A fluid bed probe specifically designed for these applications is used with a «spoon» and purge vents located on the probe tip (**Figure 1a**). After each NIR spectrum is collected, an air purge exiting through the ports in the probe clears the «spoon» for a new sample.

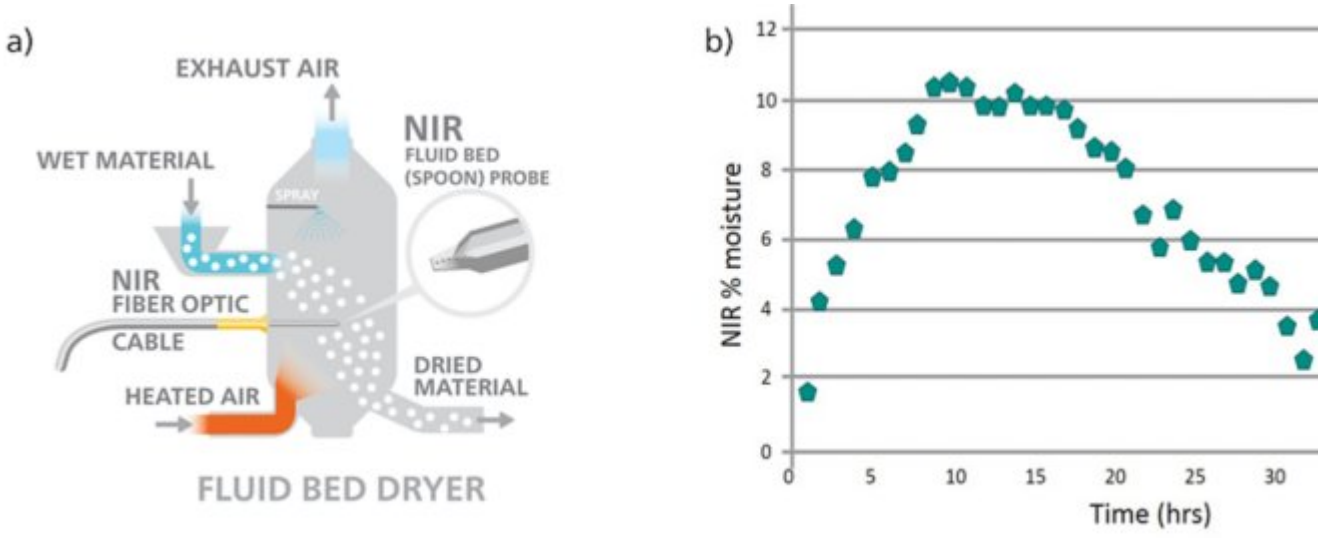

Figure 1. (a) Suggested placement for NIR «spoon» probe in a fluid bed dryer. (b) Trend chart of moisture content as determined by NIRS versus time.

Figure 2. NIRS Analyzer PRO with fiber optic cable and probe.

The 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. The delay caused by waiting for laboratory results before the product can be released for subsequent processing can be minimized or eliminated. Output from the NIRS Analyzer PRO (**Figure 2**) can be used by the fluid bed dryer's programmable logic controller (PLC) or integrated into SIPAT (Siemens Industrial 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.

Spectroscopy offers numerous advantages over many wet-chemical analytical methods. NIRS is economical and fast, enabling in-situ qualitative and quantitative analyses that are noninvasive and nondestructive. As an indirect test method, NIRS is recommended in **all of the key pharmacopoeias** (e.g., Ph. Eur. 2.2.40, USP <1119>) and fits perfectly in the context of continuous processing and the Process Analytical Technology (PAT) initiative of the FDA. Metrohm Process Analytics offers NIRS process analyzers that meet high standards for

wavelength precision, reproducibility, and photometric noise. Numerous reference standards and user-friendly software make it easy to check the instrument requirements specified in the pharmacopoeias.

The pharmaceutical version of the Vision software is fully validated and compliant with **21 CFR Part 11**. Metrohm Process Analytics also offers complete IQ/OQ documentation and instrument performance certification. Documented parameters guarantee that the instrument performs properly. Routine analysis methods can be developed in the software to include qualitative and quantitative analysis methods. Custom trend charts for real-time visual monitoring as well as electronic process control are also implemented.

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.

Typical ranges

Table 1. Parameters to monitor in fluid bed dryer.

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

Remarks

A 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 NIRS 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 flange
Micro interactance immersion probe	Clear to scattering liquids	Solution phase	Direct into process line
	Slurries with < 15% solids	Temperature- and pressure-controlled extrusion	Compression fitting or welded flange
Micro transmission probe pair	Clear to scattering liquids	Solution phase	Direct into process line or reacto
	Slurries with < 15% solids	Temperature- and pressure-controlled extrusion	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, reactor, or process line
	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
- Moisture in Lyophilized Products

Further reading

Related application documents

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

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

AN-PAN-1050 Inline moisture analysis in fluid bed dryers 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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