



## 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 for moisture measurement in pharmaceuticals are slow and cumbersome, which can lead to damaged or degraded product. The ability to monitor the residual moisture content of powders 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 NIRS. The 2060 *The* NIR Analyzer from Metrohm Process Analytics offers fast, reagent-free, nondestructive moisture analysis in powders. The analyzer can be used with a fluid bed probe specifically designed for these applications.

## はじめに

Powdered APIs (Active Pharmaceutical Ingredients) and excipients are important in pharmaceutical formulation. They are easy to use and allow for accurate dosing. Additionally, they help ensure consistent formulation. They are fundamental in achieving precise drug delivery and efficacy.

The fluid bed dryer is essential in the manufacturing process for removing moisture from wet granules or particles. This step is of paramount importance as it enhances the stability and shelf-life of the final pharmaceutical product.

Additionally, the moisture content during the fluid bed drying stage significantly impacts particle size [1]. Therefore, meticulous control over moisture levels in the fluid bed dryer is imperative in pharmaceutical manufacturing.

If over-drying occurs, the granules can fracture [2], resulting in fine particles which can adversely affect the final formulation. If the product is too moist it can clump together. This causes flow blockages as well as other manufacturing problems.

The moisture content of the powder is generally determined via slow offline laboratory techniques. Often, this is done with loss on

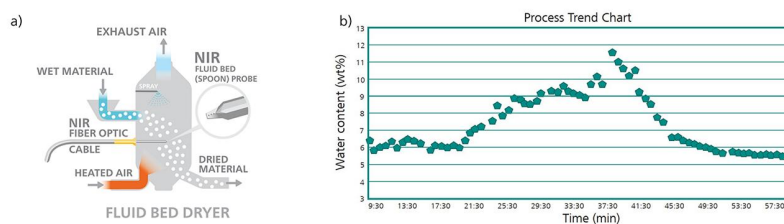
drying (10–30 minutes) after physical removal from the process with a sample thief.

Manual sampling results in delays which can cause problems whenever critical processing decisions must be made. Here, stopping the drying process at the optimal point is key.

Real-time moisture analysis in powders can be performed inline via near-infrared spectroscopy (NIRS). NIR spectroscopy fits well within the Process Analytical Technology (PAT) initiative as recommended by the FDA [3].

NIRS can determine the residual moisture inline without manual intervention. This leads to better process understanding, optimization, and more precise determination of the end of drying. NIRS technology for moisture control is an excellent fit due to its sensitivity to the -OH functional group.

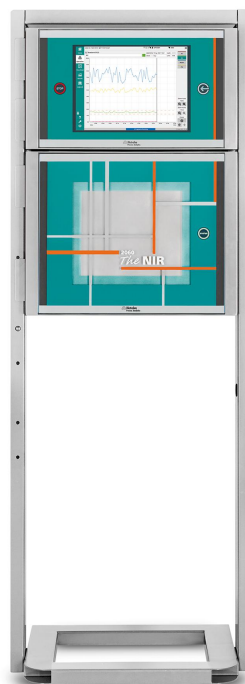
The development of a calibration model which properly correlates NIRS results to a laboratory reference method is necessary. A fluid bed «spoon» probe designed specifically for this purpose is inserted directly into the dryer (Figure 1a). After data is collected, air purges the probe tip through integrated ports to clear the «spoon» for a new sample. Each scan takes 30 seconds, ensuring there is always an accurate



**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 with inline NIRS analysis. Determination of the end of the drying process is made when the moisture level asymptotically approaches a lower limit. The operator is aided in making the decision to end the drying operation before the product is damaged or degraded.

Output from the 2060 *The* NIR Analyzer (Figure 2) 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 manufacturers time and money. Improvement in the product quality can lead to even higher profits.



**Figure 2.** 2060 *The* NIR Analyzer from Metrohm Process Analytics.

## アプリケーション

Wavelength range used: 1100–1650 nm. Inline NIRS analysis is possible directly in the fluid bed

dryer using a micro interactance reflectance probe with purge on collection tip.

**Table 1.** Parameters to monitor in fluid bed dryer.

Analyte	Concentration (%)
Moisture (H <sub>2</sub> O)	0–60%

## 備考

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. More NIRS probe types can be found in **Table 2**.

**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 flange
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
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

## 参考文献

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2. De Leersnyder, F.; Vanhoorne, V.; Bekaert, H.; et al. Breakage and Drying Behaviour of Granules in a Continuous Fluid Bed Dryer: Influence of Process Parameters and Wet Granule Transfer. *Eur. J. Pharm. Sci.* **2018**, *115*, 223–232.  
<https://doi.org/10.1016/j.ejps.2018.01.037>.
3. Aoki, H.; Hattori, Y.; Sasaki, T.; et al. Comparative Study on the Real-Time Monitoring of a Fluid Bed Drying Process of Extruded Granules Using near-Infrared Spectroscopy and Audible Acoustic Emission. *Int. J. Pharm.* **2022**, *619*, 121689.  
<https://doi.org/10.1016/j.ijpharm.2022.121689>.

## OTHER PROCESS NIRS APPLICATIONS RELATED TO THE PHARMACEUTICAL SECTOR

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

### さらに詳しい情報 関連アプリケーション

[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](#)

### プロセス用近赤外分析計の利点

- 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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## システム



### 2060 The NIR Analyzer

2060 *The NIR Analyzer* は、Metrohm Process Analytics 製の次世代プロセス分光法措置です。その独自で定評のある完全な設計により、10 秒ごとに正確な結果を出します。この装置は、光ファイバーまたは接触式フローを用いた、プロセスラインまたは反応容器における直接液体または固形物の非破壊分析を提供します。五 (5) つまでのフローおよび/またはフローセルを接続できるように設計されています。弊社独自開発の多機能な組込ソフトウェアを使用して、5 つのチャンネルをすべて互いに独立して設定することかできます。

2060 フラットフォームの一部として、2060 *The NIR Analyzer* はモジュール式コンセプトを有し、他の三つのバージョンで使用可能です: 2060 *The NIR-R Analyzer*、2060 *The NIR-Ex Analyzer*、および 2060 *The NIR-REx Analyzer* です。