Metrohm NIRSystems

Dedicated near-infrared solutions

Metrohm

Why near-infrared spectroscopy?

Near-infrared (NIR) spectroscopy is a versatile analytical technique and a well-known method for rapid, nondestructive analysis on a wide variety of matrices across many industries.

In the pharmaceutical and chemical industries, NIR analysis has been successfully implemented for many years, with initial applications focused on raw material testing.

More recently, attention has turned to analyzing solid and liquid formulations for final product quality and in-process control (IPC) of manufacturing operations. In this regard, NIR spectroscopy is a main spectroscopic tool used for process analytical technology (PAT) for the pharmaceutical industry. For the chemical markets, NIR spectroscopy provides real-time information for monitoring and control of the chemical production processes and solvent recovery systems.

Benefits of NIR Spectroscopy

Save analysis time, faster time to market
- Results in seconds
- No sample preparation – analyze samples as-is
- Multiparameters measured simultaneously

Greater and faster return on investment
- No reagents, no waste – reduced analysis cost and no waste disposal
- Versatile analyzer – many possible applications

Improved product quality and manufacturing efficiency
- Quality of product can be controlled during all steps of manufacturing
- Fast analysis, real-time monitoring increases productivity and efficiency

Metrohm NIRsystems can be used in all areas of manufacturing, from raw

Incoming raw material	Manufacturing process
Atline, at warehouse	atline, inline, online

Metrohm NIRSystems

Proven precise NIR technology
- 50 patents held by NIRSystems
- Full scanning range, visible plus NIR, 400 nm to 2'500 nm

Confident in application know-how
- 50 years of NIR experience
- Laboratory and process application knowledge
- Global leader in reference analysis method

## Dedicated and well-established software
- Vision software includes data acquisition, method development, and routine analysis in one package

Excellent service and support
- Exclusively represented in more than 80 countries, in more than 40 by Metrohm owned subsidiaries
- Technical support helpdesk and regional support centers

Practical approach to NIR data analysis and further information
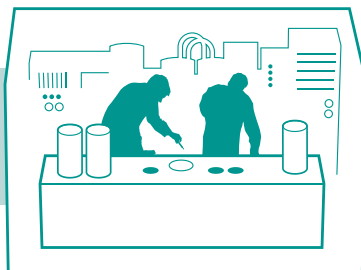
A good overview about NIR spectroscopic analysis and chemometrics in general can be obtained from our written monograph. Theoretical aspects of NIR spectroscopy, as well as many practical tips, are described in the monograph. Order this monograph, free of charge, from **http://www.metrohm-nirs.com/Applications/**
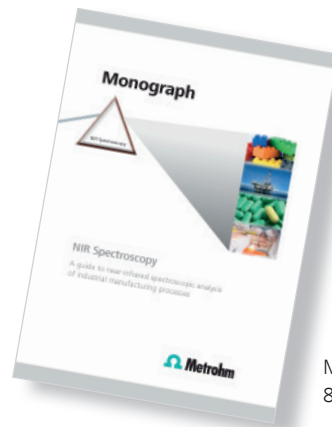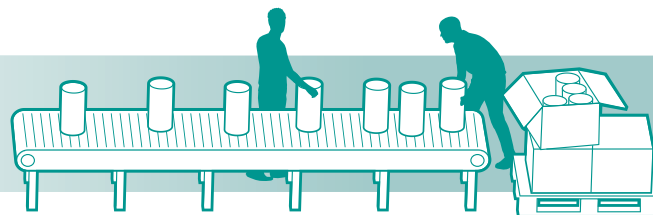
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material inspection to in-process monitoring and final product release

Quality control laboratory	Packaging
offline, at lab	offline, atline

Pharmaceuticals

NIR spectroscopy has been utilized in the pharmaceutical industry for many years and is recognized by international pharmacopeias like the United State Pharmacopeia (USP), European Pharmacopoeia (Ph. Eur) and Japanese Pharmacopoeia (JP). NIR applications can be implemented into several Pharmaceutical processes, from raw materials, to in-process monitoring and control to final product release.

Raw materials inspection
Compliant to GMP regulations, 100% testing of all incoming raw material containers
- Identification of incoming raw materials
- Specification control of raw material quality

Quality control of intermediate products
Less out-of-spec products manufactured, less re-work time
- Determination of blend homogeneity
- Detect the effects of granulation time
- Real-time monitoring of drying process

Quality assurance of finished products
Faster result without sample preparation and reduced workload of reference methods
- Determination of content uniformity
- Moisture determination in lyophilized products without destroying the sample vial
- Determination of active ingredients
- Counterfeit drugs detection

Chemistry

NIR spectroscopy is sensitive to O-H, N-H, C-H, and S-H bonds. Moisture determination is a common NIR application. Reaction monitoring and endpoint determination using NIR spectroscopy provides real-time results to control the process. Many applications that have historically been measured with physical property testing, like viscosity, may be measured with NIR spectroscopy, if the property is dependent on an intrinsic chemical characteristic, such as chain length or cross linking.

Example of NIR applications
- Moisture content
- Acid value
- Hydroxyl number
- Adhesive content
- Antioxidants
- UV inhibitor content
- Cure, melt index
- Melamine content
- Alcohol detection
- Residual solvent detection

Polymers

Due to NIR spectroscopic analysis requiring no sample preparation and being nondestructive, many polymer and plastic attributes can be measured rapidly inline or atline for qualitative as well as quantitative results. Thermoplastics production, raw material purity, and moisture content are common NIR applications.

Control quality of raw materials
Control from first step for less problem in the process
- Hydroxyl number
- Acid, amine value
- Identification of right materials (e.g., HDPE/LDPE)

Polymerisation monitoring
Reducing over-processing of product improving production consistency
- Reaction endpoint determination
- Moisture content determination

Determination of physical properties
Several parameters measured simultaneously
- Molecular weight
- Degree of branching
- Tacticity
- Melting point
- Particle size verification
- Density
- Viscosity

Petrochemicals

In petrochemistry, monitoring of the blending process by NIR spectroscopy has proven huge economical savings, since crucial properties such as water content, density, viscosity, additive content, and hydroxyl number can be measured in less than one minute.

NIR spectroscopy can be used for different applications in petrochemical process starting from crude oil control, blending process and finished product control.

Gasoline parameters
- Research octane (RON, ASTM D 2699)
- Motor octane (MON, ASTM D 2700)
- Road octane number (RdON)
- Volume percentage or mole percent of paraffins,
- Isoparaffins, aromatics, naphthenes, and olefins; PIANO)

Common diesel parameters
- Specific gravity
- Viscosity
- Flash point
- Cold filter plugging point (CFPP)
- Pour point
- Cloud point
- Cetane index

Education and R&D

Although NIR spectroscopy is primarily used in production-related applications, it has found widespread use in research and development facilities. Pharmaceutical R&D often uses NIR methods in pilot plant operations to help evaluate daily processes.

Common R&D parameters
- Moisture content
- Coating thickness
- Roller compaction hardness
- Blend uniformity
- Granulation
- Particle size verification
- Prediction of dissolution profile

And more ...

General NIR applications

Pharmaceuticals	Chemistry	Petrochemicals	Polymers	Others: pulp & paper, textile, ink & paint, etc.
Raw material inspection • Active ingredients • Excipients • Solvents • Packaging	Quality control of raw materials • Substrates • Fillers • Additives • Etc.	Quality control of raw materials	Analysis of polyols	Analysis of lignin in wood pulp
Counterfeit drugs detection, final product determination	Measuring moisture and residual solvent levels in liquid and solid matrices	Monitoring the composition of petrochemical and refining process streams	Determination of additives in polymer pellets	Determination of hardwood/softwood content in wood products
Assay of active ingredients	Quality control of fine chemicals	Lube base oil analysis	Analysis of copolymer levels in polymer pellets	Determination of finish on nylon fibers
Analysis of residual moisture in a lyophilized pharmaceutical product	Real-time reaction monitoring for end-point determination in fine and speciality chemical manufacturing processes	Fuel screening	Determination of finish on nylon fibers	Monitoring fermentation process
Conformity test of solid dosage forms: tablets, capsules	Determining the wet chemical composition of cleaning, etching and stripping baths in the semiconductor industry			

The application specialists of Metrohm NIRSystems have prepared a selection of Application Bulletins and Notes for different industries that show the advantages of the nondestructive NIR method: very fast measurements that require practically no sample preparation and do not need any costly or toxic reagents. This application literature can be downloaded from
http://www.metrohm-nirs.com/Applications/

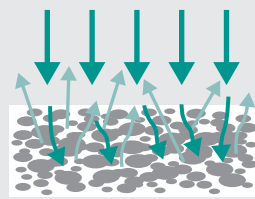# Right choice for successful applications

NIR spectroscopy can be used to analyse different types of samples. Choosing the right measurement method, sampling module, and accessories is the most important step to developing robust NIR methods.
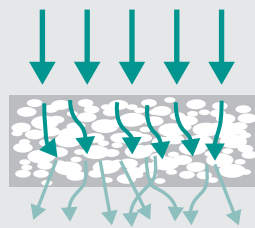
Sample types

NIR measurement methods

Cream, paste, granulates, coarse, fine powders

Diffuse reflection

NIR light penetrates into the sample and interacts with the sample. The NIR energy that is not absorbed is reflected back to the detector.
• Suitable to measure solid samples without sample preparation
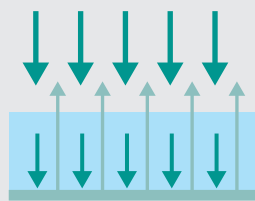

Tablets and capsules

Diffuse transmission

NIR light penetrates into the sample and interacts with the sample. Due to the particles, the light is scattered throughout the sample. The nonabsorbed NIR light is transmitted through the sample reaching the detector.
• Suitable to measure solid dosage forms without sample preparation
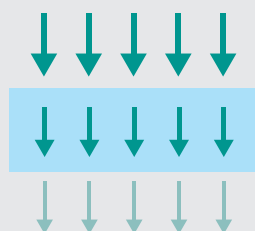

Liquids, gels

Transflection

This measurement method is a combination between transmission and reflection. A reflector is placed behind the sample, used to reflect the nonabsorbed NIR light back to the detector.
• Suitable for liquid samples

Liquids

Transmission

The sample is placed between the NIR light source and detector. NIR light is transmitted through the sample. The nonabsorbed NIR energy continues to the detector.
• Suitable for clear liquids, suspensions, and solutions

Examples of right measuring modules for different sampling systems

The modular design of Metrohm NIRSystems analyzers ensures that analyses are optimized for specific sample types.

NIRS XDS RapidContent, MultiVial, and NIRS DS2500 Analyzer

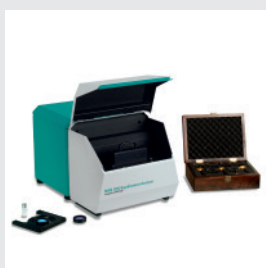**Measured using diffuse reflectance mode**

- The NIRS XDS RapidContent Analyzer and the Solids Module offer analysis of any solid form
- The NIRS XDS MultiVial Analyzer provides the analysis of a tray of solids in vials
- The NIRS DS2500 can analyse materials in bags or sample cups, with a rotation feature for non-homogeneous powders

NIRS XDS MasterLab Analyzer
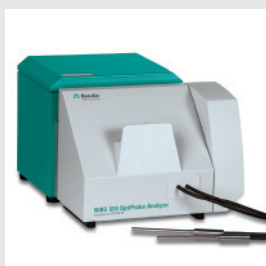
Measured using diffuse transmission

- The NIRS XDS MasterLab Analyzers perform automated transmission and reflectance analysis of a tray of multiple tablets. Automated reflectance analysis of a tray of multiple vials is also possible
- Integrated variable spot size for optimized sample illumination

NIRS XDS SmartProbe, OptiProbe, and RapidContent Analyzer

Measured using transflection mode

- The NIRS XDS RapidContent Analyzer with the liquid sample kit offers liquid analysis using the gold diffuse reflectors
- The NIRS XDS Interactance OptiProbe and the NIRS XDS SmartProbe offer the immersion probe with high energy mirror for liquid analysis

NIRS XDS RapidLiquid and Transmission OptiProbe Analyzers

Meausred using transmission mode

- The NIRS XDS RapidLiquid Analyzer performs temperature-controlled transmission analysis of liquids in cuvettes or vials up to 65 °C
- The NIRS XDS Transmission OptiProbe Analyzer is designed for laboratory monitoring of liquids. The optional Vial Heater Module allows more difficult samples to be analyzed up to 200 °C

NIRSystems overview

Laboratory and atline analyzer

Metrohm NIRSystems laboratory analyzers with their patented monochromator can be operated in QC, R&D, and plant laboratories. Modular sampling accessories allow for analyses of powders, granules, solids, slurries, gels, pastes, and turbid or clear liquids.

The patented design of Metrohm NIRSystems analyzers offer unparalleled performance and precise instrument matching to reduce your method development effort, minimize your implementation time and ensure seamless method transferability.

NIRS XDS series

The next generation of NIR technology offering measurement flexibility through a hot-swappable feature. Each measuring module is easily exchanged, with no downtime, for the best performance of your application or sample type.

NIRS DS2500 Analyzer

The NIRS DS2500 offers the same broad wavelength range, 400 to 2'500 nm as the XDS, but in one dedicated, cost-effective solution. Developed for routine analysis in any environment, the DS2500 is suitable for use atline in the production plant

Benefits

- **Superior analytical performance**

- **Seamless method transferability**

- **Shorten implementation time**

- **Robust & reliable**

Dedicated NIR systems for the best performance

Sample type	Laboratory analyzer, atline analyzer								
	XDS Rapid Content Analyzer	XDS Rapid Content Solid Analyzer	XDS MultiVial Analyzer	XDS MasterLab Analyzer	XDS RapidLiquid Analyzer	XDS SmartProbe Analyzer	XDS Interactance OptiProbe Analyzer	XDS Transmision OptiProbe Analyzer	DS2500 Analyzer
Powders	●	●	●	●		●	●		●
Coarse solids/granulates		●	●	●		●	●		●
Solids/film/paper	●	●	●	●					●
Tablets/capsules in reflection	●	●	●	●					
Tablets/capsules in transmission				●					
Opaque liquids	●	●	▲	▲		●	●		●
Pastes/creams	▲	▲	▲	▲		●	●		▲
Viscous liquids/gels	▲	▲	▲	▲	●	●	●	●	
Clear liquids	▲	▲	▲	▲	●	▲	▲	●	▲

● Dedicated systems ▲ With transflectance options ● Temperature controller up to 65 °C ● Optional temperature controller up to 200 °C

Features of Metrohm NIRSystems instruments

- Wide range of measuring options for dedicated applications

- Hot-swappable modules offers flexibility to expand application anytime with NIRS XDS models

- Precise instrument matching, ensures that both quantitative and qualitative methods can be transferred directly from one NIR analyzer to another

- Gateway to process

- Covers different working conditions: atline, offline, inline, and online

- A new level of consistent and reliable instrument performance, integrated diagnostic routines

- Analysis while operating in harsh industrial environments

Process analyzers

The process analyzers provide near real-time process information while operating in harsh manufacturing conditions. The process sample interface is dictated by the sample type and process conditions. Metrohm NIRSystems offers 2 different types of process analyzers with several sampling options.

NIRS XDS Process Analyzer

The XDS Process Analyzer is available in a variety of configurations with one, four, or nine sampling points. Depending on your sample characteristics, single fiber or microbundle fibers are available. This economical way of performing remote measurements enables the analyzer to be installed in an unrestricted area, reducing installation and operation costs.

NIRS Analyzer PRO

The NIRS Analyzer PRO is a process analysis system based on high-resolution diode array technology. Three configurations are available; direct contact, fiber based, and non-contact.

Sample type	Process analyzer					
	XDS Process Analyzer			NIRS Analyzer PRO		
	SingleFiber	MicroBundle	DirectLight/ NonContact	Window reflectance	Fiber	DirectLight
Powders		▲	●	●	▲	●
Coarse solids/ granulates		▲	●	●	▲	●
Solids/film/paper		▲	●	●	▲	●
Tablets/capsules in reflection						
Tablets/capsules in transmission						
Opaque liquids	▲	▲			▲	
Pastes/creams	▲	▲		●	▲	
Viscous liquids/gels	▲	▲			▲	
Clear liquids	▲	▲			▲	

● Dedicated systems ▲ Different fiber optic probes are available

NIRSystems software

Vision software

Identification, qualitative, and quantitative methods are easily derived with the advanced, user-friendly, network-able Vision software. Precise and accurate analysis is accomplished with the press of a key or click of a mouse.

Dedicated requirement
- Single or multi-user versions are available for different purposes, easily connected to the NIR analyzer via the network or direct connect.
- Basic chemical version of software or compliant pharmaceutical version of Vision is available.

All in one software
- Spectral acquisition, method development, and routine analysis are included in one complete Vision software package.
- Same software package for complete NIRSystems product line: laboratory, atline and process analyzers.

All in one result
- From one spectrum, get multicomponent results. Qualitative identification results and quantitative parameters obtained simultaneously from just one scan!

Fully validated and regulation compliant
- The pharmaceutical version of the software can be fully validated and is 21 CFR Part 11 compliant.
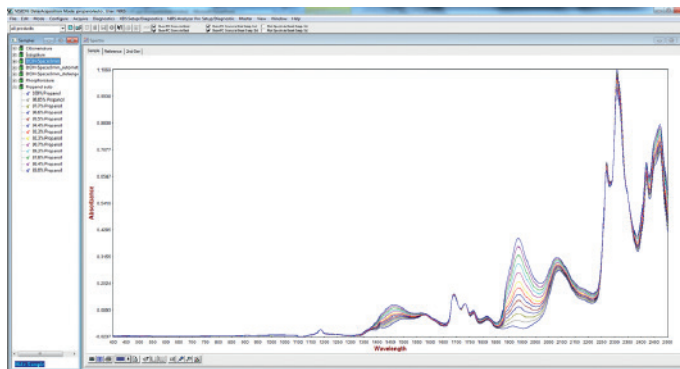
Routine Analysis

Date: 02.10.2013
Time: 15:55:12
Author/Operator: user A
Instrument Model: NIRSystems XDS
Serial number: 3010-1664

Library: Raw materials
Output Project: Pharma Test

Date	Time	Sample ID	Library	Selected	ID as	ID Result	P/F	Qual R.slt	P/F	Constituent	Value	Units
02.10.2013	15:28:31	Unknown ID1	Raw materials	unknown	Calcium Stearate	0.998	Pass	0.990	Pass	Moisture	0.560	%
02.10.2013	15:34:16	C_ID2013_1	Raw materials	Calcium Stearate	Calcium Stearate	0.999	Pass	0.992	Pass	Moisture	0.490	%
02.10.2013	15:42:32	C_ID2013_2	Raw materials	Calcium Stearate	Calcium Stearate	0.984	Pass	0.991	Pass	Moisture	0.490	%
02.10.2013	15:48:15	M_ID2013_1	Raw materials	Mg Stearate	Mg Stearate	0.998	Pass	0.990	Pass	Moisture	1.020	%
02.10.2013	15:50:56	M_ID2013_2	Raw materials	Mg Stearate	Mg Stearate	0.999	Pass	0.988	Pass	Moisture	1.230	%
02.10.2013	15:52:14	L_ID2013_1	Raw materials	Lactose	Lactose	0.997	Pass	0.992	Pass	Moisture	1.150	%
02.10.2013	15:55:30	L_ID2013_2	Raw materials	Lactose	Lactose	0.999	Pass	0.991	Pass	Moisture	1.146	%

NIRSystems reference standards and regulatory compliance

To comply with regulatory requirements, regarding the calibration, qualification, and verification of equipment used for measurement and control of quality, XDS NIR analyzers incorporate instrument performance certifica-tion (IPC™) routines to verify analyzer performance. In accordance with industry recommended methods, all tests are performed using NIST traceable standards placed at the sample plane.

- Traceable standards
- First offered in 1995 to pharmaceutical users
- Designed to meet ongoing IQ/OQ requirements
- Full record of successful testing

Follow USP and Ph. Eur recommendation

Metrohm NIRSystems offer the test for qualification of NIR instruments according to USP and Ph. Eur. recommendation (wavelenght uncertainty, photometric linearity and spectroscopic noise tests). Software and traceable standards are included in the pharmaceutical package.
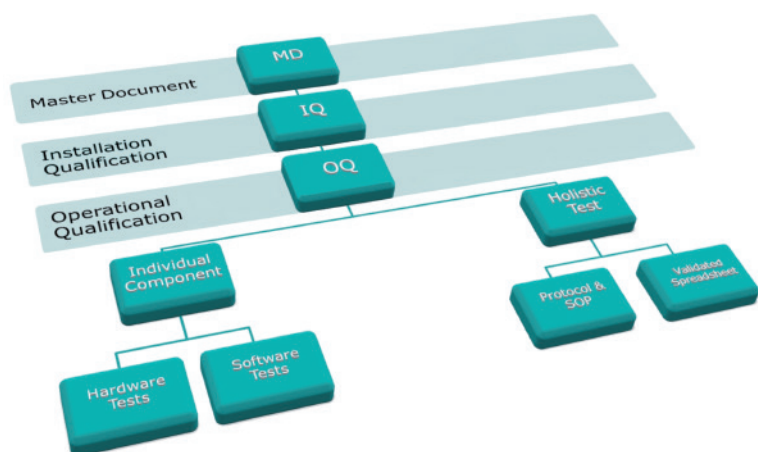
Support

Our worldwide support network of trained scientists, wide range of customer care assistance programs, and comprehensive package of validation support services ensures durable and efficient method development and routine implementation for years to come.

Compliance service

Performed during the installation of your analyzer, Metrohm insures that the NIR analyzer and the Vision software are working at peak performance. This service is provided by fully trained and certified personnel. Full IQ/OQ documentation is provided to the customer at the end of the installation. Additionally, Metrohm provides NIRS Instrument Performance Certification (IPC™) to measure key performance parameters, and to verify their conformance to established specifications.

These support include
• IPC™ provides documented evaluation of parameters important for reliable instrument performance. It is performed at customer sites by a qualified IPC Engineer trained by Metrohm.
• Professional installation and startup of a new instrument by compliant Installation Qualification (IQ)
• Operational Qualification (OQ), guaranteeing that Metrohm instruments meet the equipment specification
• A guideline for Performance Qualification (PQ)
• Work-related training of users with subsequent certification

Metrohm application support and literature

Metrohm strives to provide the best support and service to all of our customers. Need help with determining the best NIR analyzer to fit your needs, or need help creating a library or calibration model? Call us! Metrohm has the most knowledgeable application scientists in the NIR business. With a NIR technical support helpdesk and a dedicated techservices e-mail, we are here to help you with all of your application questions.

Service

Metrohm Quality Service – worldwide

Metrohm is exclusively represented in more than 80 countries, in more than 40 of which we have our own subsidiaries. This guarantees a tight network for sales and service. The Metrohm support team strives to provide our customers with service that surpasses their expectations.

Metrohm Care Contracts

Support plans and preventive maintenance contract are available and represent your company's best protection of its investment and assurance of uninterrupted use of the NIR analyzers.

Metrohm Academy

Training of our customers is critical to the successful implementation of an NIR method. Metrohm offers training in our facilities around the world. If you want to train many users on the NIR analyzers, we can bring the training to you.

www.metrohm-nirs.com

Metrohm
NIRSystems