Metrohm NIRSystems

Dedicated near-infrared solutions
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**
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/](http://www.metrohm-nirs.com/Applications/)

Material inspection to in-process monitoring and final product release

- Online, at line
- Offline, at lab

Metrohm order number: 8.108.5026
Pharmaceuticals

NIR spectroscopy has been utilized in the pharmaceutical industry for many years and is recognized by international pharmacopeias like the United States 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
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

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

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 diesel parameters**
- Specific gravity
- Viscosity
- Flash point
- Cold filter plugging point (CFPP)
- Pour point
- Cloud point
- Cetane index
And more ...

**General NIR applications**

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

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/](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**

<table>
<thead>
<tr>
<th>NIR measurement methods</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diffuse reflection</strong></td>
</tr>
<tr>
<td>NIR light penetrates into the sample and interacts with the sample. The NIR energy that is not absorbed is reflected back to the detector.</td>
</tr>
<tr>
<td>• Suitable to measure solid samples without sample preparation</td>
</tr>
<tr>
<td>Cream, paste, granulates, coarse, fine powders</td>
</tr>
<tr>
<td><strong>Diffuse transmission</strong></td>
</tr>
<tr>
<td>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.</td>
</tr>
<tr>
<td>• Suitable to measure solid dosage forms without sample preparation</td>
</tr>
<tr>
<td>Tablets and capsules</td>
</tr>
<tr>
<td><strong>Transflection</strong></td>
</tr>
<tr>
<td>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.</td>
</tr>
<tr>
<td>• Suitable for liquid samples</td>
</tr>
<tr>
<td>Liquids, gels</td>
</tr>
<tr>
<td><strong>Transmission</strong></td>
</tr>
<tr>
<td>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.</td>
</tr>
<tr>
<td>• Suitable for clear liquids, suspensions, and solutions</td>
</tr>
<tr>
<td>Liquids</td>
</tr>
</tbody>
</table>
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**

**Measured 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

<table>
<thead>
<tr>
<th>Sample type</th>
<th>XDS Rapid Content Analyzer</th>
<th>XDS Rapid Content Solid Analyzer</th>
<th>XDS MultiVial Analyzer</th>
<th>XDS MasterLab Analyzer</th>
<th>XDS RapidLiquid Analyzer</th>
<th>XDS SmartProbe Analyzer</th>
<th>XDS Interactance OptiProbe Analyzer</th>
<th>XDS Transmission OptiProbe Analyzer</th>
<th>DS2500 Analyzer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Powders</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Coarse solids/granulates</td>
<td></td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Solids/film/paper</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Tablets/capsules in reflection</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Tablets/capsules in transmission</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Opaque liquids</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Pastes/creams</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Viscous liquids/gels</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Clear liquids</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
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<td>●</td>
</tr>
</tbody>
</table>

● Dedicated systems ▲ With transfectance options ● Temperature controller up to 65 °C ● Optional temperature controller up to 200 °C
• Wide range of measuring options for dedicated applications
• Hot-swappable modules offer 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: at line, offline, inline, and online
• A new level of consistent and reliable instrument performance, integrated diagnostic routines
• Analysis while operating in harsh industrial environments

**Features of Metrohm NIRSystems instruments**

### 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.

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### Process analyzer

<table>
<thead>
<tr>
<th>Sample type</th>
<th>XDS Process Analyzer</th>
<th>NIRS Analyzer PRO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SingleFiber</td>
<td>MicroBundle</td>
</tr>
<tr>
<td>Powders</td>
<td>▲</td>
<td>●</td>
</tr>
<tr>
<td>Coarse solids/granulates</td>
<td>▲</td>
<td>●</td>
</tr>
<tr>
<td>Solids/film/paper</td>
<td>▲</td>
<td>●</td>
</tr>
<tr>
<td>Tablets/capsules in reflection</td>
<td>▲</td>
<td>●</td>
</tr>
<tr>
<td>Tablets/capsules in transmission</td>
<td>▲</td>
<td>●</td>
</tr>
<tr>
<td>Opaque liquids</td>
<td>▲</td>
<td>▲</td>
</tr>
<tr>
<td>Pastes/creams</td>
<td>▲</td>
<td>▲</td>
</tr>
<tr>
<td>Viscous liquids/gels</td>
<td>▲</td>
<td>▲</td>
</tr>
<tr>
<td>Clear liquids</td>
<td>▲</td>
<td>▲</td>
</tr>
</tbody>
</table>

▲ 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.
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 certification (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 (wavelength 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.
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.