



NIR spectroscopy: The efficiency boost for QC labs

Reduce costs, save time, and improve data integrity across a range of QC applications with near-infrared spectroscopy



Introduction

Across the wide range of material and chemical production industries, there is an increasing need for improved quality assurance and quality control processes.

As the regulation and quality requirements become stricter in these industries, there is a stronger focus on developing cost-saving and time-efficient methods. There are three main drivers for companies to voluntarily implement more of these practices:

- **Cost pressure** – testing can reveal costly out-of-spec products, allowing production to be stopped in plenty of time
- **Increased competition** – quality practices provide a competitive edge and can be used as a marketing tool to raise brand value
- **Scarcity of resources** – qualified staff are difficult to find; therefore, checks that can be carried out by non-specialists are invaluable

Near-infrared (NIR) spectroscopy is a method that addresses the above drivers and is particularly suited for making quality control more efficient and cost-effective. This application eBook provides you with an over-

Contents

- How does NIR spectroscopy work
- Application highlight: Petroleum
- Application highlight: Polymer
- Application highlight: Chemical
- Boost efficiency in the QC laboratory
- Data integrity with NIR spectroscopy
- Featured products
- Additional resources

view of the basic principles of NIR spectroscopy and how it works, the benefits of this technique over traditional alternatives, selected application examples in several key industries, plus a detailed evaluation of the cost savings and impact on data integrity.

Understanding NIR spectroscopy and its potential
For over 30 years, NIR spectroscopy has been an established method for fast and reliable quality control within different industries.

However, companies often seem unprepared for the demands of implementing this method, whether due to a lack of awareness regarding application possibilities or a general hesitation to adopt new methods. The white paper [NIR spectroscopy: how does it work and how to implement](#) provides a brief introduction to this fascinating technology, followed by implementation guidelines according to ASTM E1655.

Multiple parameters in just one measurement

One major advantage of NIR spectroscopy is the determination of multiple parameters, in just 30 seconds, with no sample preparation. The non-invasive interaction of light with matter is influenced by the physical and chemical properties of the sample, making NIR spectroscopy a suitable method for the determination of both property types. Here, we provide an array of application notes that outline real application examples across the [petroleum](#), [polymer](#), and [chemical](#) industries.

Reduce your running costs by up to 90%

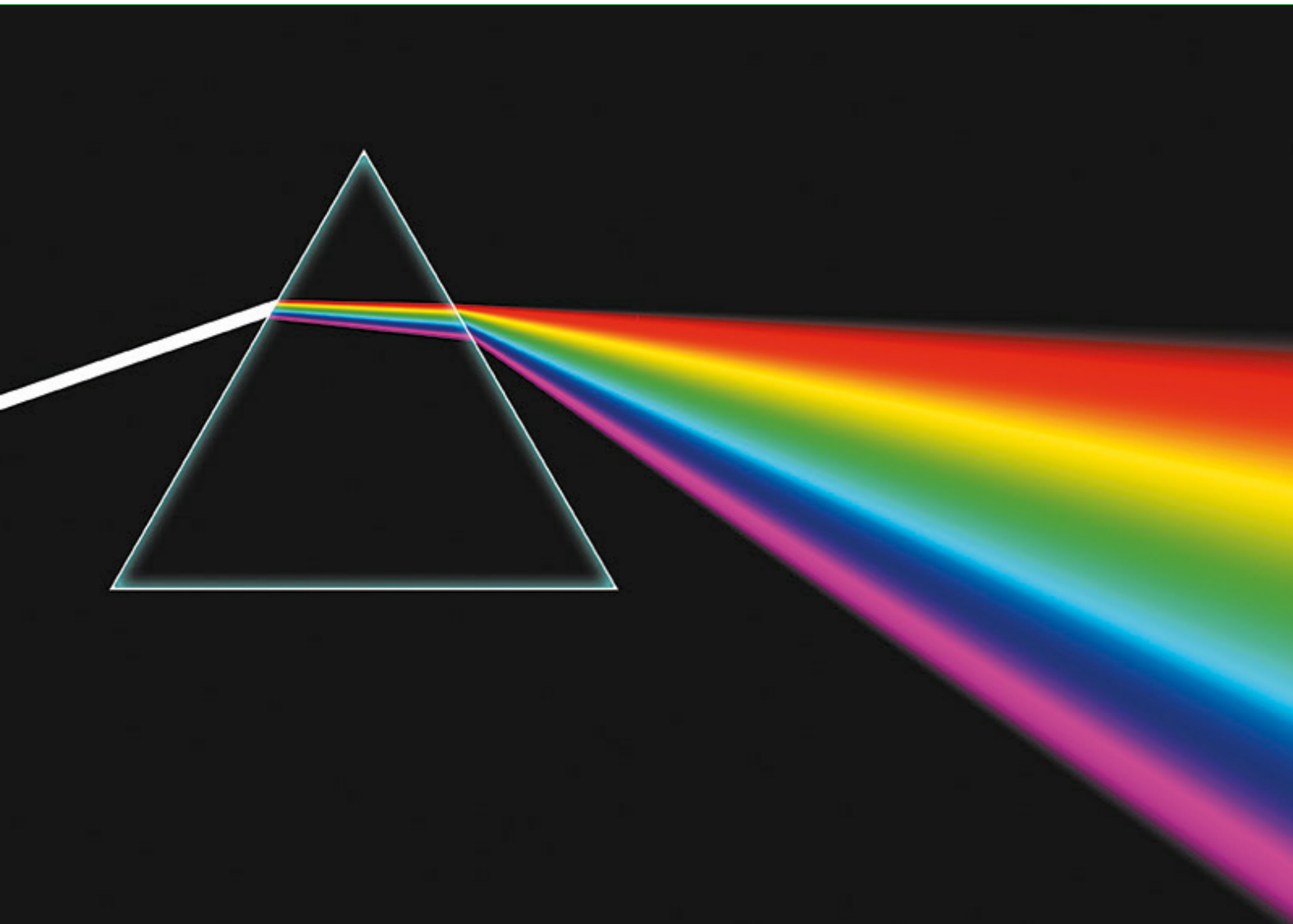
The cost of chemicals and toxic reagents is often a major pain point for those conducting wet chemical analysis. Both the purchasing costs and the process of chemical disposal amount to a significant expenditure

and these factors have an impact on total quality assurance and control costs, which in turn affects overall product margins. As a non-destructive, chemical-free technology, NIR spectroscopy has the potential to significantly reduce these costs. The white paper [Boost efficiency in the QC laboratory: How NIRS helps reduce costs up to 90%](#) explores the economic advantage of NIR spectroscopy compared to more conventional methods.

Data integrity: What does it mean, how can I improve it?

The white paper [Data integrity with NIR spectroscopy](#) provides an overview of the key requirements mentioned by the FDA in its data integrity guidelines, plus a comprehensive presentation on how these individual aspects, summarized within the acronym ALCOA (attributable, legible, contemporaneous, original and accurate) and ALCOA +, are covered by [Metrohm's Vision Air spectroscopy software](#).





WHITE PAPER

NIR spectroscopy: How does it work and how to implement it

1.1 When light hits matter

The interaction between light and matter is well-known process—just recall the last time your skin was sunburned. Depending on the applied light intensity and energy, the interaction can be destructive (e.g. sunburn) or benign (e.g. radio waves). Light used in spectroscopic methods is typically not described by the applied energy, but in many cases by the wavelength. The relationship for both quantities is described by:

$$E = \frac{hc}{\lambda}$$

with E = light energy, c = Planck constant; c = light constant, and λ = wavelength of the light. Since energy and wavelength are inversely proportional, higher wavelengths correspond to lower energies. Therefore UV (ultraviolet) light (10–300 nm) is higher in energy compared to near-infrared (NIR) light (800–2500 nm), which is one of the reasons behind the non-destructive nature of NIR spectroscopy as an analytical method.

A NIR spectrometer such as the Metrohm DS2500 measures this interaction to generate spectra as displayed in Figure 1. NIRS is especially sensitive to the presence of certain functional groups like CH, NH, OH, and SH. Therefore, NIR spectroscopy is an ideal method to quantify chemical parameters like water content (moisture), hydroxyl value, Acid Number, amine content, or octane number to name just a few. Furthermore, the interaction is also dependent upon the matrix of the sample itself, which allows also the detection of physical parameters such as density, viscosity, melt flow rate, or the flash point.

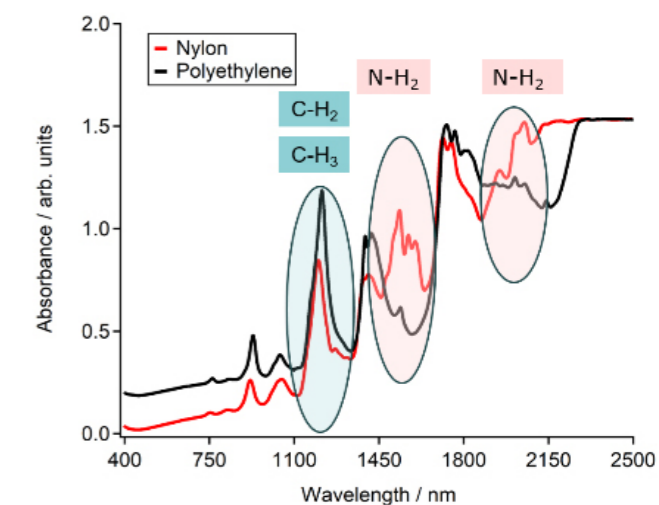


Figure 1. Nylon and polyethylene spectra resulting from the interaction of NIR light with the respective samples.

All of this information is contained in just one spectrum, making this method suitable for quick multi-parameter analysis. The workflow of spectra collection and a more detailed description of the advantages of this technology is given in the next chapter.

1.2 NIR Spectroscopy: sample handling and measurements

A good starting point to understand the benefits of NIR spectroscopy is to look at how these spectra are measured. NIR spectroscopy can be used to analyze different types of samples, such as solids, liquids, creams, and suspensions. However, different instrumentation is required depending on the sample type. Choosing the right measurement method, and respective accessory is the most important step to develop robust NIR operating procedures. Below, the different measurement modes (diffuse reflection, transmission, and transflection) are shown for various sample types.

1.2.1 SOLID SAMPLE MEASUREMENT

Solid samples (such as powders) are secured within an appropriate container or vial (Figure 2a) then placed as-is on the analyzer. Heterogeneous samples, such as polymer pellets, can be analyzed using larger measurement cups (Figure 2b).



Figure 2. Solid sample placement for NIR spectra measurement. a) Direct measurement of powder substance in a vial. b) Large heterogeneous samples can be analyzed using large sample cups.

The measuring mode typically used for these kinds of samples is referred to as **diffuse reflection**, generally an appropriate procedure for analyzing granulates, fibers, flakes, and both coarse and fine powders. For diffuse reflection (Figure 3), the NIR light, which comes from below the sample, penetrates into and interacts with it, while being partially absorbed. Unabsorbed NIR light reflects back to the detector. In less than 1 minute, the measurement is completed and the results are displayed.

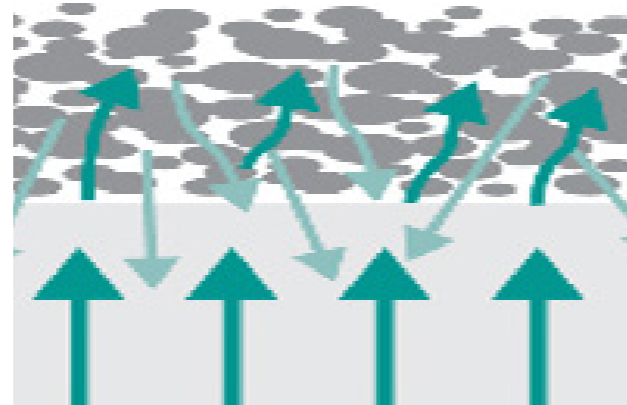


Figure 3. Schematic display of the light path interacting with a sample during diffuse reflection.

1.2.2 LIQUID SAMPLE MEASUREMENT

As Figure 4a illustrates, for liquid measurements with NIR spectroscopy, a vial or cuvette is used as a sample vessel for the analysis. Disposable vials are typically used for convenience reasons, removing any need for sample cleaning, and allowing a full analysis in less than 2 minutes, comparable to the measurement of solid samples. The measuring mode of choice for liquid analysis is known as **transmission**. In this case, the NIR radiation travels through the solution before reaching the detector (Figure 4b).

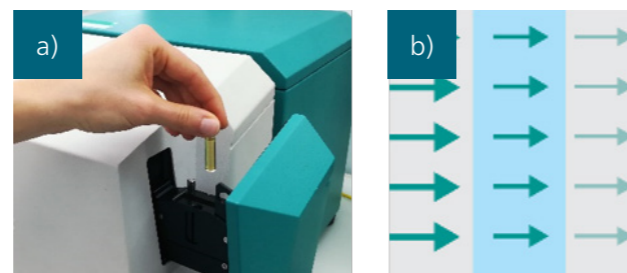


Figure 4. a) Measurement of liquids are typically done in vials. b) The measurement mode is known as transmission, where light travels through the sample while being absorbed (from left to right in the schematic).

1.2.3 A SPECIAL CASE: CREAMS, PASTES, AND GELS

The transflection measuring method is most suitable to measure **creams, pastes, and gels**. This technique is a combination between transmission and reflection. A reflector is placed behind the sample, which reflects any unabsorbed NIR light back to the detector (Figure 5b). Wide open sample cups (Figure 5a) support the eventual cleaning step, which is another important aspect to achieve a fast and convenient analysis.

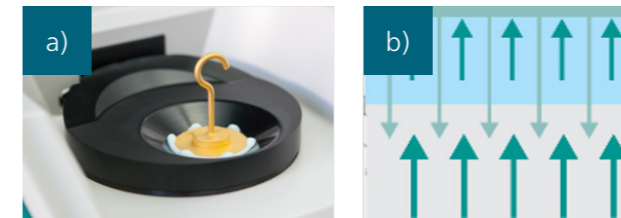


Figure 5. a) Display of setup for measuring creams. The gold reflector is placed on top of the sample to reflect unabsorbed light. b) Illustration of the transflection measuring principle.

1.2.4 SUMMARY

Three different measuring methods are common in NIR spectroscopy, which depend heavily on the sample type. Table 1 displays an overview with suggestions for measurement methods and instruments based on the sample type to be analyzed.

Sample type	Measurement method	Recommended instrument
Solids	Diffuse Reflection	DS2500 Solid Analyzer
Liquids	Transmission	DS2500 Liquid Analyzer
Slurries, Creams	Transflection	DS2500 Solid Analyzer

Table 1. Overview of commonly used measurement methods for different sample types.

The procedure to obtain NIR spectra already highlights two major advantages of NIR spectroscopy: **simplicity** regarding sample measurement and **speed**:

- **Fast** technique with results in **less than 2 minutes**.
- **No sample preparation** required – solids and liquids can be measured in original forms.

Other advantages of NIR spectroscopy are listed below and will be discussed later:

- **Low cost** per sample – no chemicals or solvents needed.
- **Environmentally friendly** technique – no waste generated.
- **Non-destructive** – precious samples can be reused after analysis.
- **Easy** to operate – inexperienced users are immediately successful.

The next section explains in more detail how a NIR spectroscopy prediction model is developed and implemented in the laboratory workflow.

1.3 How to implement NIR spectroscopy in your laboratory workflow

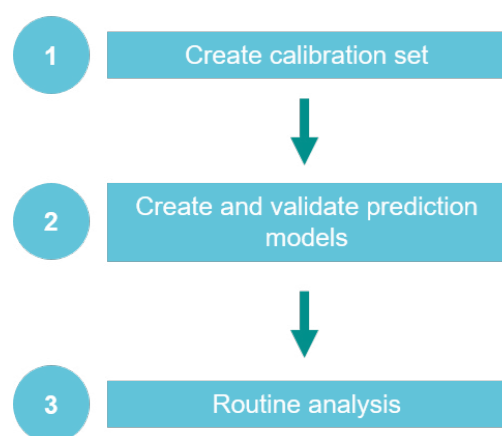
NIR spectroscopy is a secondary technique, which means a prediction model (based on values from a primary technique) is required first prior to beginning any routine analysis. This is similar to other analytical methods, for example HPLC. To quantify a substance with HPLC, a series of standard solutions of the analyte must be prepared and measured to create a calibration curve spanning a certain concentration range. Unknown samples are subsequently measured, and their concentrations are calculated based on their detector response along with the calibration curve.

A similar procedure is required when implementing NIR spectroscopy. Initially, spectra with known concentrations or known parameter values (gathered with a primary method such as titration) are collected. This set of spectra, known as a calibration set, is the basis to create prediction models, which can be done using the provided spectroscopy software, e.g. **Metrohm Vision Air Complete**. The prediction models are then embedded in an operating procedure (OP), which

includes all measurement specific settings such as definition of sample vessel type or number of scans. The usage of such OPs allows operators to conduct their routine analysis at the push of a button with no necessity to run the primary methods anymore.

The following section describes a more detailed workflow for the implementation of NIR spectroscopy in a QC laboratory environment in accordance with the ASTM E1655 guideline. For illustrative purposes, the workflow is described using a real example.

A laboratory at a company which produces polymeric material has purchased a NIR analyzer with the intention to use it for rapid moisture measurements (as an alternative to Karl Fischer titration), and for the determination of the intrinsic viscosity (as an alternative to viscometry measurements). According to chapter 1.2.1, a calibrated Metrohm DS2500 Analyzer measuring in diffuse reflection is the suitable analyzer configuration. The workflow is summarized in Figure 6.



Parameter	Prediction	Reference
Moisture %	3.70	3.69
Relative viscosity	2.425	2.424

Figure 6. Workflow for NIR spectroscopy method implementation.

1.3.1 STEP 1 – CREATE CALIBRATION SET

A calibration set is required to create prediction models, as mentioned earlier. This set is used to “train” the system to correctly interpret spectra (e.g. moisture content and intrinsic viscosity) measured during routine analysis. These calibration set samples must cover the complete expected concentration range of the parameters tested for the method to be robust. This reflects other techniques (e.g. HPLC) where the calibration standard curve needs to span the complete expected concentration range. Therefore, if you expect the moisture content of a substance to be between 0.35% and 1.5%, then the training/calibration set must cover this range as well.

In this example, 10 polymer samples with moisture levels between 0.38–1.43% and intrinsic viscosity values between 2.51–3.60 are measured using both the DS2500 Analyzer and the respective primary methods (KF titration and viscometry). The obtained spectra are then linked with the moisture and viscosity values using the Vision Air Software (Figure 7). Subsequently, this data set (known as a calibration set) is used for prediction model development.

1.3.2 STEP 2 – CREATE AND VALIDATE PREDICTION MODELS

The next step is to identify spectral regions that correlate with the moisture and viscosity value, respectively. To enhance the visibility of these differences, mathematical calculations such as the first or second derivative are applied (Figure 8).

Once visually identified, the software will attempt to correlate the selected spectral regions with the values sourced from the primary method(s). The result is a correlation diagram for water detection along with the respective figures of merit, including the Standard Error of Calibration (precision) and the correlation coefficient (R^2) shown in Figure 9. The same procedure is carried out for the second parameter discussed here, intrinsic viscosity.

Again, this process is similar to the general working procedures with techniques like HPLC. When creating a calibration curve with HPLC, typically the peak height or peak intensity (surface) is linked with a known internal standard concentration. Here, only one variable is used (peak height or surface) there-

Time	Sample number	Intrinsic Viscosity	Intrinsic Viscosity Ref.	Moisture Content [%]	Moisture Content Ref.
3/2/2020 1:10:28 PM	Sample 10	—	2.51	—	0.55
3/2/2020 1:10:17 PM	Sample 9	—	2.71	—	1.35
3/2/2020 1:10:06 PM	Sample 8	—	3.12	—	1.43
3/2/2020 1:09:56 PM	Sample 7	—	3.15	—	1.21
3/2/2020 1:09:46 PM	Sample 6	—	2.70	—	0.45
3/2/2020 1:09:34 PM	Sample 5	—	3.00	—	1.12
3/2/2020 1:09:24 PM	Sample 4	—	3.15	—	0.87
3/2/2020 1:09:13 PM	Sample 3	—	3.60	—	0.96
3/2/2020 1:09:06 PM	Sample 2	—	3.40	—	0.65
3/2/2020 1:08:55 PM	Sample 1	—	3.39	—	0.38

Figure 7. Display of 10 NIR measurements linked with intrinsic viscosity and moisture reference values obtained with Karl Fischer titration and viscometry.

fore this procedure is known as univariate data analysis. To create the correlation for NIR spectroscopy, a spectral range (approximately 1900–2000 nm for the water peak) and therefore multiple absorbance values are used. Therefore, NIR spectroscopy is known as a multivariate data analysis technology.

The ideal number of spectra in a calibration set depends on the variation in the sample (particle size, chemical distribution, etc.). In this example, we used 10 polymer samples, which is a good starting point to check the application feasibility. However, to build a robust model which covers all sample variations,

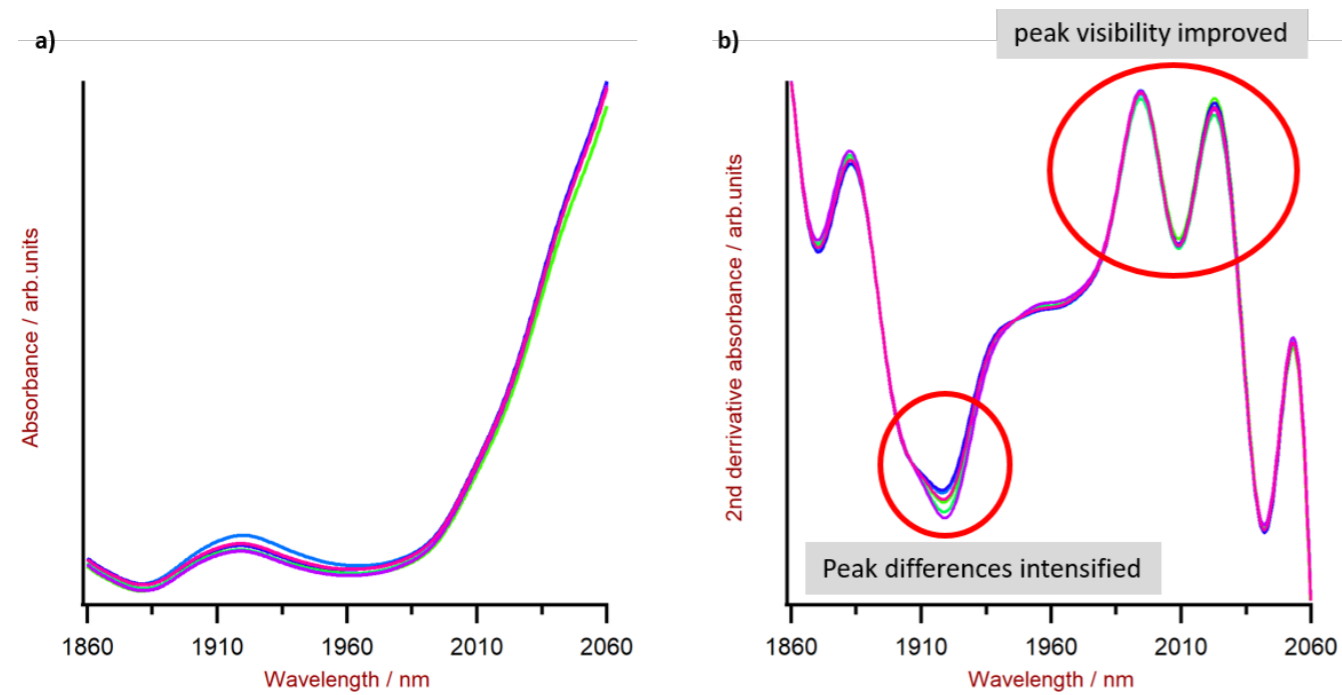


Figure 8. Example of the intensifying effect on spectra information by using mathematical calculation: a) without any mathematical optimization and b) with applied second derivative highlighting the spectra difference at 1920 nm and intensifying the peaks near 2010 nm.

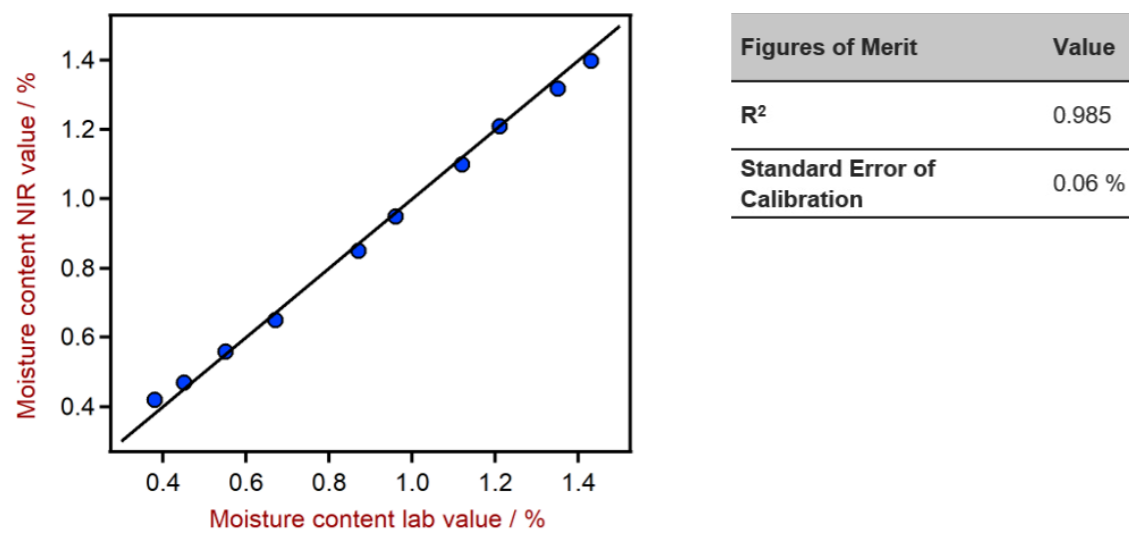


Figure 9. Correlation plot and Figures of Merit (FOM) for the prediction of water content in polymer samples using NIR spectroscopy.

more sample spectra are required. As a rule, approximately 40–50 sample spectra will provide a suitable prediction model in most cases.

This data set comprised of 40–50 spectra is also used to validate the prediction model. This can be done using the Vision Air Complete software, which splits the data set into two groups of samples:

- 1) Calibration set 75%
- 2) Validation set 25%

As before, a prediction model is created using the calibration set, but the predictions will now be validated using the validation set. Results for the polymer samples are shown in Figure 10 and display a correlation plot with the respective figures of merit, which include the Standard Error of Calibration (precision of the calibration set prediction), Standard Error of Validation (precision of the validation set prediction), and R^2 .

Users that are inexperienced with NIR model creation and do not yet feel confident with it can rely on Metrohm support, which is known for its high quality service. They will assist you with the prediction model creation and validation.

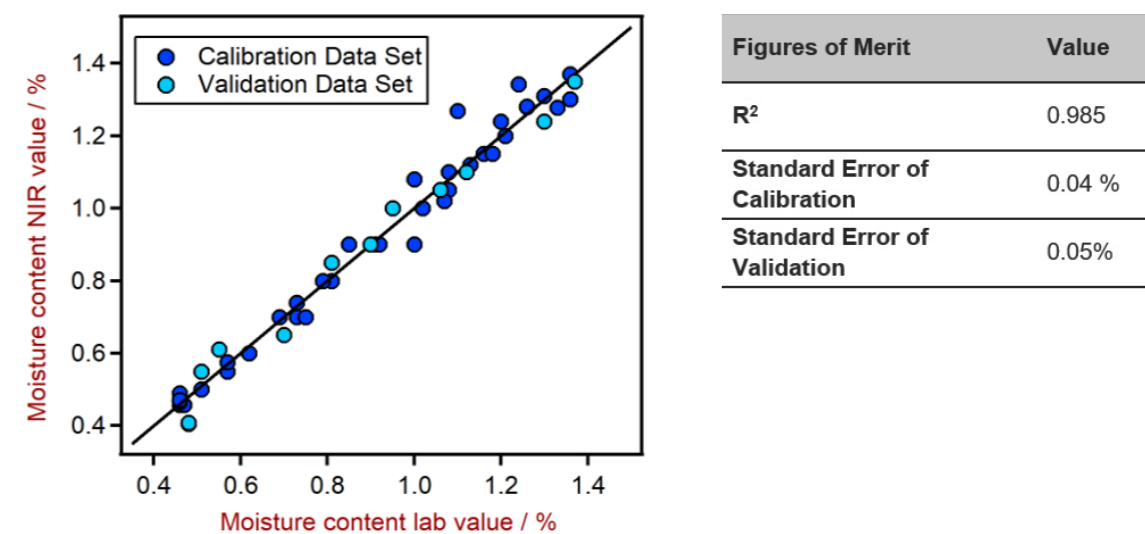


Figure 10. Correlation plot and Figures of Merit (FOM) for the prediction of water in polymer samples using NIR spectroscopy. The split set function in Vision Air Complete allows generation of a validation data set, which is used to validate the prediction model.

1.3.3 STEP 3 – ROUTINE ANALYSIS

The beauty of the NIRS technique comes into focus now that the prediction model has been created and validated.

Polymer samples with unknown moisture content and unknown intrinsic viscosity can now be analyzed at the push of a button. The NIRS DS2500 Analyzer will display results for those parameters in less than a minute. Typically, the spectrum itself is not shown during this step—just the result—sometimes highlighted by a yellow or red box to indicate results with a warning or error as shown in Figure 11.

Another display possibility is the trend chart, which allows for the proactive adjustment of production processes. Warning and action limits are highlighted here as well (Figure 12).

In summary, the maximum effort needed to implement NIR spectroscopy in the laboratory is in the beginning of the workflow, during collection and measurement of representative samples that span the complete concentration range. The prediction model creation and validation, as well as implementation in routine analysis, is performed with the help of the Metrohm Vision Air Complete software and can be completed within a short period. Additionally, our Metrohm NIR spectroscopy specialists will happily support you with the prediction model creation if you require assistance.

At this point, take note that there are cases where NIR spectroscopy can be implemented directly without any prediction model development, using Metrohm pre-calibrations. These are robust, ready-to-use operating procedures for certain applications (e.g. viscosity of PET) based on real product spectra. Visit the Metrohm pre-calibration website or contact your local

Metrohm sales representative for more information. In the next chapter, a selection of handpicked applications from the chemical, polymer, petrochemical, and personal care industry is presented to provide an overview of the many possibilities with NIR spectroscopy.

Operating procedure	Time	Sample number	Intrinsic Viscosity	Moisture Content [%]
Polymer Analysis	3/2/2020 4:03 PM	Sample 19	3.02	1.02
Polymer Analysis	3/2/2020 4:02 PM	Sample 18	2.56	1.20
Polymer Analysis	3/2/2020 4:01 PM	Sample 17	2.94	0.06
Sample event				
! Moisture Content: 0.06% is below operating procedure action limit 0.30%				
Polymer Analysis	3/2/2020 4:01 PM	Sample 16	3.94	0.58
Polymer Analysis	3/2/2020 4:01 PM	Sample 15	3.10	0.80
Polymer Analysis	3/2/2020 4:00 PM	Sample 14	2.90	0.50

Figure 11. Overview of a selection of NIR predicted results, with clear pass (no box) and fail (red box) indications.

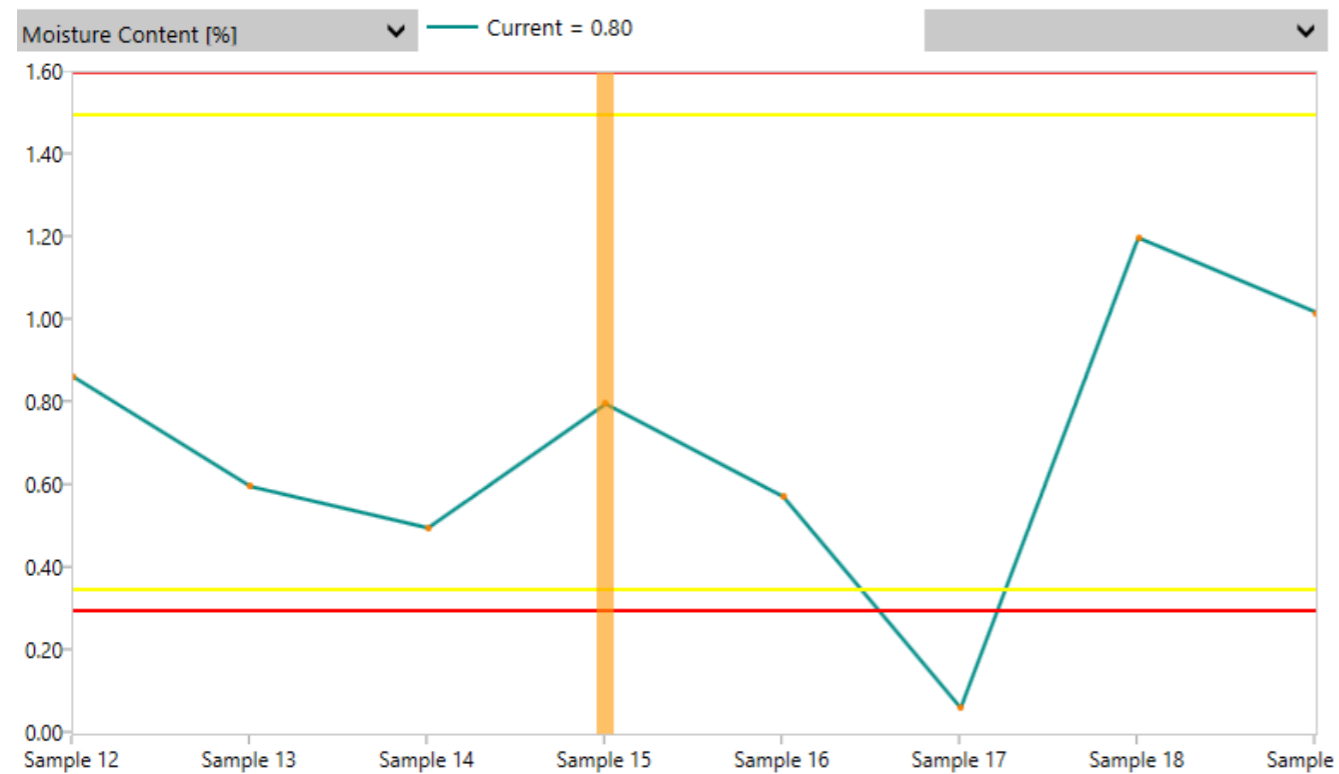


Figure 12. Trend chart of NIR moisture content analysis results. The parallel lines indicate defined warning (yellow) and action (red) limits.



NIR APPLICATION NOTE NIR-022

Quality control of gasoline

Rapid determination of RON, MON, AKI, aromatic content, and density

In recent years, there has been a significant push to reduce the environmental impacts of fuels through improvements to fuel quality. This requires engines to be more efficient, along with increasing the octane content of fuel so higher compression engines can be utilized. The determination of key quality parameters of gasoline, namely research octane number (RON, ASTM D2699-19), motor octane number (MON, ASTM D2700-19), anti knock index (AKI), aromatic content (ASTM D5769-15), and density, conventionally requires several different analytical methods, which are laborious and need trained personnel. This application note demonstrates that the XDS RapidLiquid Analyzer, operating in the visible and near-infrared spectral region (Vis-NIR), provides a cost-efficient and fast solution for the multiparameter analysis of gasoline.

EXPERIMENTAL EQUIPMENT

Gasoline samples were measured with the XDS RapidLiquid Analyzer (RLA) in transmission mode over the full wavelength range (400–2500 nm). Reproducible spectrum acquisition was achieved using the built-in temperature controlled sample holder. For convenience, disposable vials with a path length of 8 mm were used, which made a cleaning procedure unnecessary. The Metrohm software package Vision Air Complete was used for data acquisition and prediction model development.



Figure 1. XDS RapidLiquid Analyzer and 8 mm disposable vial filled with a gasoline sample.

Table 1. Hardware and software equipment overview

Equipment	Metrohm number
XDS RapidLiquid Analyzer	2.921.1410
Disposable vials, 8 mm diameter, transmission	6.7402.000
Vision Air 2.0 Complete	6.6072.208

RESULT

The obtained Vis-NIR spectra (Figure 2) were used to create prediction models for the determination of several key fuel parameters. The quality of the prediction models was evaluated using correlation diagrams, which display a correlation between the Vis-NIR prediction and primary method values. The respective figures of merit (FOM) display the expected precision of a prediction during routine analysis.

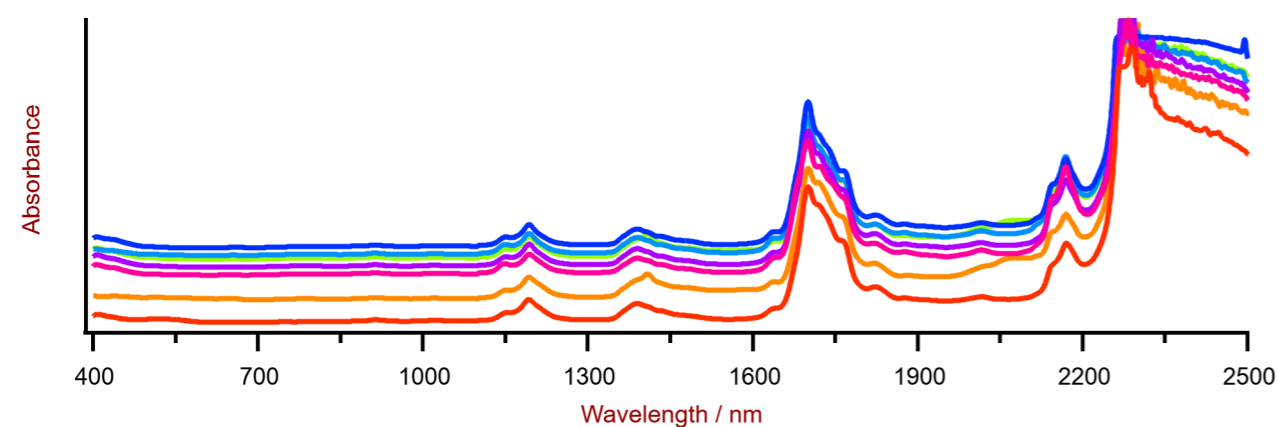
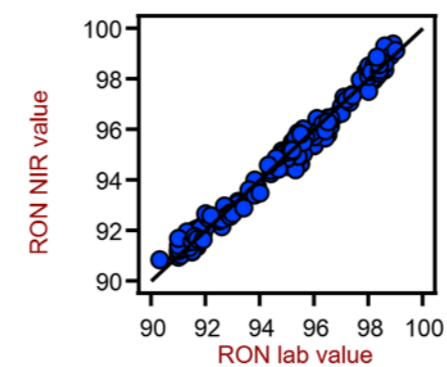


Figure 2. This selection of gasoline Vis-NIR spectra was obtained using a XDS RapidLiquid Analyzer and 8 mm disposable vials. For display reasons a spectra offset was applied.

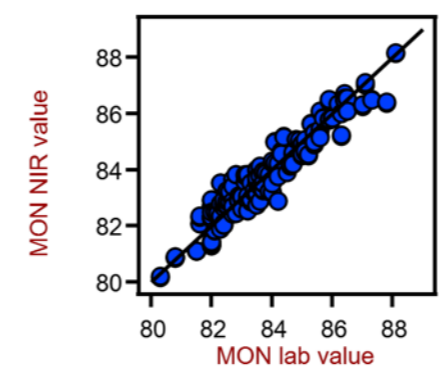
RESULT RON VALUE



Figures of Merit	Value
R ²	0.989
Standard Error of Calibration	0.26
Standard Error of Cross-Validation	0.29

Figure 3. Correlation diagram and the respective figures of merit for the prediction of the RON value in gasoline using a XDS RapidLiquid Analyzer. The reference lab values were determined according to CFR engine tests under controlled conditions.

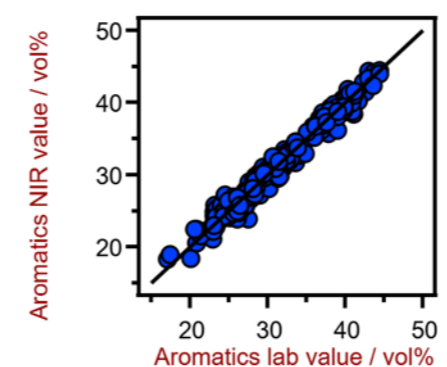
RESULT MON VALUE



Figures of Merit	Value
R ²	0.889
Standard Error of Calibration	0.50
Standard Error of Cross-Validation	0.53

Figure 4. Correlation diagram and the respective figures of merit for the prediction of the MON value in gasoline using a XDS RapidLiquid Analyzer. The reference lab values were determined according to CFR engine tests under controlled conditions.

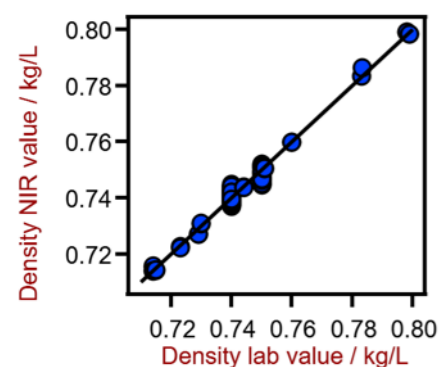
RESULT AROMATICS CONTENT



Figures of Merit	Value
R ²	0.974
Standard Error of Calibration	0.97 vol%
Standard Error of Cross-Validation	1.07 vol%

Figure 5. Correlation diagram and the respective figures of merit for the prediction of the aromatics content in gasoline using a XDS RapidLiquid Analyzer. The lab values were determined with gas chromatography/mass spectrometry techniques.

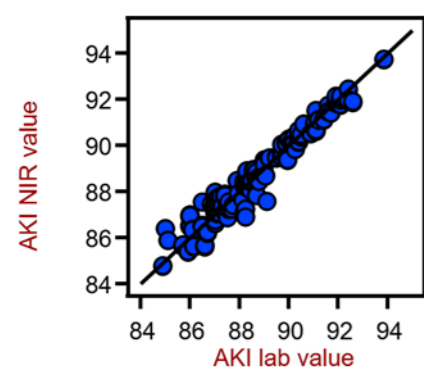
RESULT DENSITY



Figures of Merit	Value
R ²	0.973
Standard Error of Calibration	0.0021 kg/L
Standard Error of Cross-Validation	0.0023 kg/L

Figure 6. Correlation diagram and the respective figures of merit for the prediction of gasoline density using a XDS RapidLiquid Analyzer. The lab values were determined using a density meter.

RESULT AKI VALUE



Figures of Merit	Value
R ²	0.945
Standard Error of Calibration	0.45
Standard Error of Cross-Validation	0.46

Figure 7. Correlation diagram and the respective figures of merit for the prediction of AKI value in gasoline using a XDS RapidLiquid Analyzer. The reference lab values were determined according to CFR engine tests under controlled conditions.

CONCLUSION

This application note shows the feasibility of NIR spectroscopy for the analysis of diene value in pyrolysis gasoline. In comparison to the wet chemical

method UOP326-17 (Table 2), the time to result is a major advantage of NIR spectroscopy, since a single measurement is performed within one minute.

Table 2. Time to result with conventional testing methods

Parameter	Method	Time to result
RON	CFR engine test	~30 minutes per sample
MON	CFR engine test	~30 minutes per sample
AKI	CFR engine test	~30 minutes per sample
Aromatic content	Gas Chromatography	~45 minutes per sample

To view the information for all key parameters and to get the latest information, please check out our pre-calibrations:

www.metrohm.com/pre-calibrations

Analytes: RON, MON, AKI, Aromatics content, Density
 Matrix: Gasoline
 Industry: Petrochemical Industry
 Standards: ASTM D2699, ASTM D2700-19



Quality Control of Polyamides

Determination of viscosity, functional groups, and moisture within one minute

Functional group and viscosity analysis (ASTM D789) of polyamides can be a lengthy and challenging process due to the sample's limited solubility.

This application note demonstrates that the DS2500 Solid Analyzer operating in the visible and near-infrared spectral region (Vis-NIR) provides a cost-efficient and fast solution for a simultaneous determination of the intrinsic viscosity as well as the amine, carboxylic, and moisture content in polyamides. With **no sample preparation or chemicals needed**, Vis-NIR spectroscopy allows for the analysis of polyamides in **less than a minute**.

EXPERIMENTAL EQUIPMENT

Polyamide pellets were measured with a DS2500 Solid Analyzer in reflection mode over the full wavelength range (400–2500 nm). A rotating DS2500 Large Sample Cup was employed to overcome the distribution of the particle sizes and chemical components. This allowed for an automated measurement at different sample locations for a reproducible spectrum acquisition. As displayed in **Figure 1**, samples were measured without any preparation. The Metrohm software package Vision Air Complete was used for all data acquisition and prediction model development.

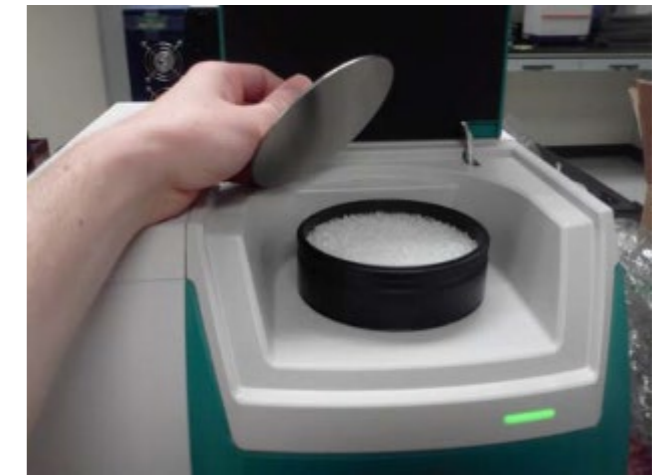


Figure 1. DS2500 Solid Analyzer and polyamide pellets present in the rotating DS2500 Large Sample Cup.

Table 1. Hardware and software equipment overview

Equipment	Metrohm number
DS2500 Analyzer	2.922.0010
DS2500 Large Sample Cup	6.7402.050
Vision Air 2.0 Complete	6.6072.208

RESULT

The obtained Vis-NIR spectra (**Figure 2**) were used to create prediction models for quantification of the intrinsic viscosity and amine end group, carboxylic end group, and moisture content in polyamides. The quality of the prediction models was evaluated using correlation diagrams, which display the relationship between Vis-NIR prediction and primary method values. The respective figures of merit (FOM) display the expected precision of a prediction during routine analysis.

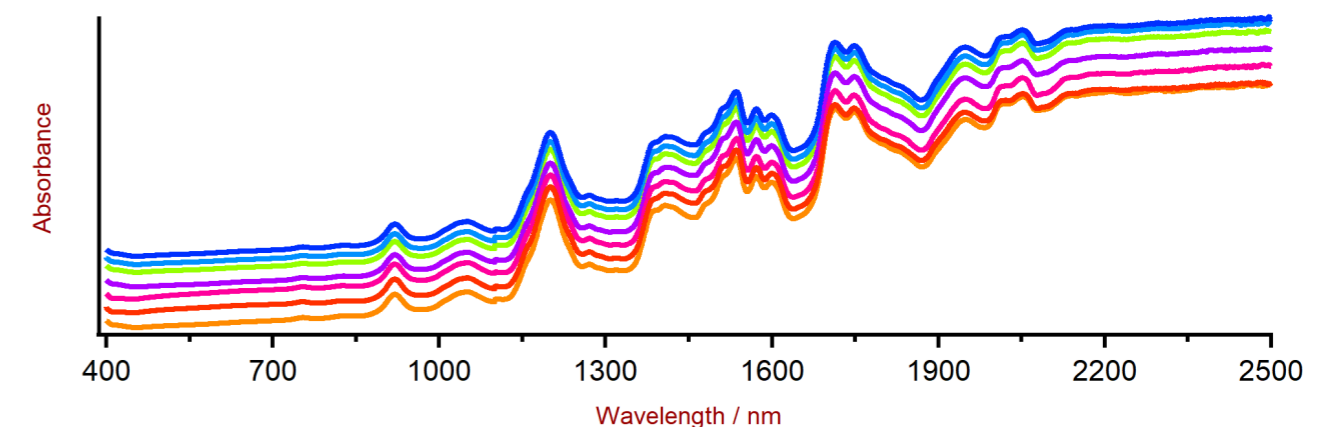
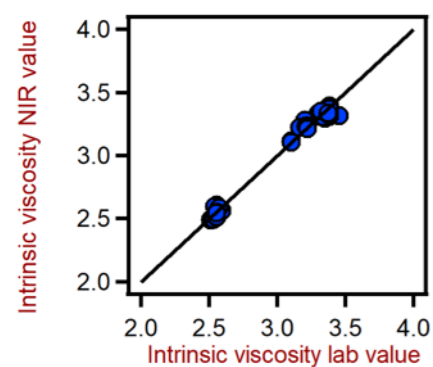


Figure 2. Selection of polyamide Vis-NIR spectra obtained using a DS2500 Analyzer and a rotating DS2500 Large Sample Cup. For display reasons spectra are shown with an offset applied.

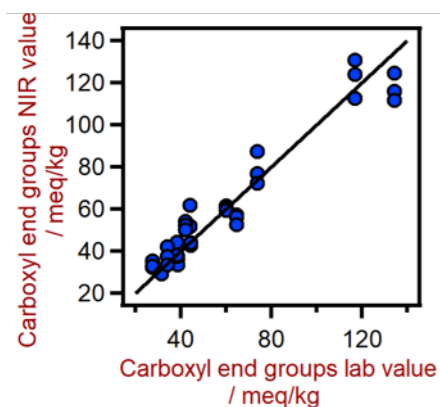
RESULT INTRINSIC VISCOSITY



Figures of Merit	Value
R ²	0.986
Standard Error of Calibration	0.046
Standard Error of Cross-Validation	0.055

Figure 3. Correlation diagram and the respective figures of merit for the prediction of the intrinsic viscosity in polyamides using a DS2500 Solid Analyzer. The intrinsic viscosity lab value was evaluated using viscometry.

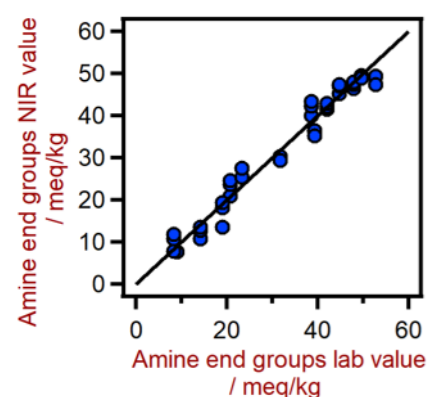
RESULT CARBOXYL END GROUP CONTENT



Figures of Merit	Value
R ²	0.972
Standard Error of Calibration	6.1 meq/kg
Standard Error of Cross-Validation	11.1 meq/kg

Figure 4. Correlation diagram and the respective figures of merit for the prediction of carboxylic end group content in polyamides using a DS2500 Solid Analyzer. The carboxyl end group lab value was evaluated using titration.

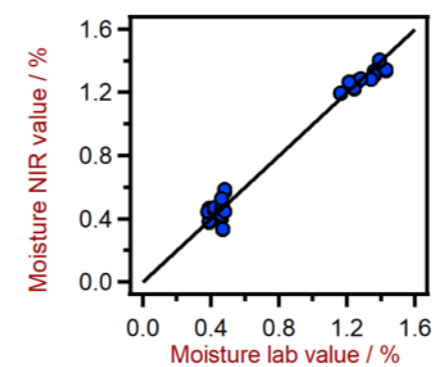
RESULT AMINE END GROUP CONTENT



Figures of Merit	Value
R ²	0.981
Standard Error of Calibration	2.5 meq/kg
Standard Error of Cross-Validation	4.1 meq/kg

Figure 5. Correlation diagram and the respective figures of merit for the prediction of amine end group content in polyamides using a DS2500 Solid Analyzer. The amine end group lab value was evaluated using titration.

RESULT MOISTURE CONTENT



Figures of Merit	Value
R ²	0.991
Standard Error of Calibration	0.041%
Standard Error of Cross-Validation	0.067%

Figure 6. Correlation diagram and the respective figures of merit for the prediction of moisture content in polyamides using a DS2500 Solid Analyzer.

CONCLUSION

This study demonstrates the feasibility of NIR spectroscopy for the analysis of some key quality parameters of polyamides. In comparison to wet

chemical methods (Table 2), the time to result is a major advantage of NIR spectroscopy, since all parameters are determined in a single measurement in less than a minute.

Table 2. Time to result overview for the different parameters.

Parameter	Procedure	Time to result
Intrinsic viscosity	Viscometry	~90 min (preparation) + ~1 min (viscometry)
Carboxyl end group	Titration	~90 min (preparation) + ~20 min (titration)
Amine end group	Titration	~90 min (preparation) + ~20 min (titration)
Moisture	KF Titration	~25 min (preparation) + ~5 min (Karl Fischer titration)

Analytes:	Intrinsic viscosity, carboxyl end groups, amine end groups, moisture
Matrix:	Polyamine
Industry:	Polymer Industry
Standards:	ASTM E1655



Quality Control of Polyols

Chemical-free determination of Hydroxyl Number according to ASTM D6342-12

Toxic and corrosive chemicals such as p-toluenesulfonyl isocyanate (TSI) and tetrabutylammonium hydroxide are used for the Hydroxyl Number analysis of polyols by titration according to ASTM D4274-16.

This application note demonstrates how the XDS RapidLiquid Analyzer operating in the visible and near-infrared spectral region (Vis-NIR) provides a cost-efficient and fast solution for the determination of the hydroxyl (OH) number of polyols. With **no sample preparation or chemicals needed**, Vis-NIR spectroscopy allows for the analysis of polyols in **less than a minute**.

EXPERIMENTAL EQUIPMENT

Polyol samples were measured with a XDS RapidLiquid Analyzer in transmission mode over the full wavelength range (400–2500 nm). Reproducible spectrum acquisition was achieved using the built-in temperature control (at 30°C) of the XDS RapidLiquid Analyzer. For convenience, disposable vials with a path length of 4 mm were used, which made cleaning of the sample vessels unnecessary. The Metrohm software package Vision Air Complete was used for all data acquisition and prediction model development.

Table 1. Hardware and software equipment overview

Equipment	Metrohm number
XDS RapidLiquid Analyzer	2.921.1410
Disposable vials, 4 mm diameter, transmission	6.7402.010
Vision Air 2.0 Complete	6.6072.208



Figure 1. XDS RapidLiquid Analyzer and a polyol sample present in a 4 mm disposable vial.

RESULT

The obtained Vis-NIR spectra (Figure 2) were used to create prediction models for quantification of the hydroxyl number in polyol samples. The quality of the prediction models was evaluated using correlation diagrams, which display the relationship between the Vis-NIR prediction and primary method values. The respective figures of merit (FOM) display the expected precision of a prediction during routine analysis.

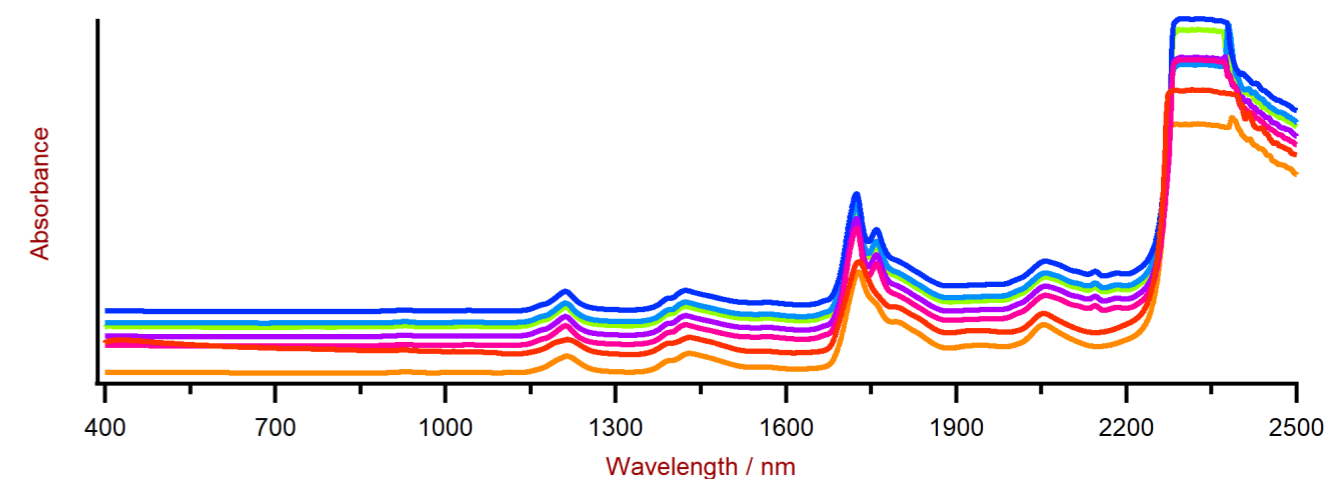
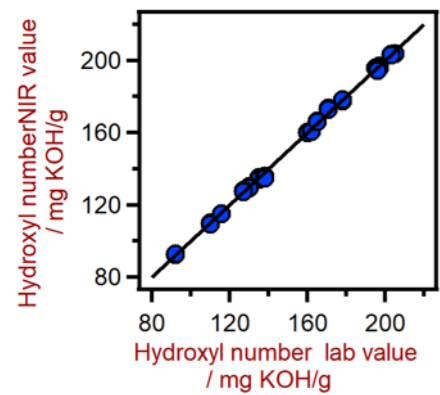


Figure 2. Selection of polyol Vis-NIR spectra obtained using a XDS RapidLiquid Analyzer and 4 mm disposable vials. For display reasons a spectra offset was applied.

RESULT HYDROXYL NUMBER



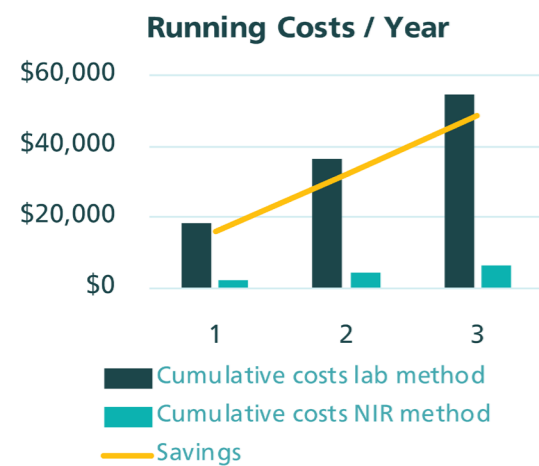
Figures of Merit	Value
R ²	0.998
Standard Error of Calibration	1.28 mg KOH /kg
Standard Error of Cross-Validation	1.42 mg KOH /kg

Figure 3. Correlation diagram and the respective figures of merit for the prediction of the hydroxyl number in polyols using a XDS RapidLiquid Analyzer. The hydroxyl number lab value was evaluated using HPLC-MS.

CONCLUSION

The following application note demonstrates the feasibility of NIR spectroscopy for the analysis of the hydroxyl number in polyols. In comparison to wet

chemical methods, running costs are significant lower when using NIR spectroscopy (Figure 3).



	Lab method	NIR method
Number of analyses (per day)	10	10
Cost of operator (per hour)	\$25	\$25
Costs of consumables and chemicals OH-Number	\$6	\$1
Time spent per analysis	5 min	1 min
Total running costs (per year)	\$18,188	\$2,063

Figure 4. Comparison of running costs for the determination of the hydroxyl number with titration and NIR spectroscopy.

Analytes: Hydroxyl Number
 Matrix: Polyol
 Industry: Chemical Industry
 Standards: ASTM D6342-12

NIR Application Note AN-NIR-035
 Version 2 – 2020-03

Boost efficiency in the QC laboratory: How NIRS helps reduce costs up to 90%



Nicolas Rühl, Ph.D. and
Alyson Lanciki, Ph.D.

Underestimation of quality control (QC) processes is one of the major factors leading to internal and external product failure, which have been reported to cause a loss of turnover between 10–30%. As a result, many different norms are put in place to support manufacturers with their QC process. However, time to result and the associated costs for chemicals can be quite excessive, leading many companies to implement near-infrared spectroscopy (NIRS) in their QC process. This paper illustrates the potential of NIRS and displays cost saving potentials up to 90%.

Quality Control with NIR Spectroscopy – A sustainable boost in efficiency

«Good quality is expensive.» One could argue that high product prices are often due to costly production processes, which result from extensive quality control (QC) and quality assurance (QA) measures. However, as a QA/QC Manager, you might disagree and refer to personal examples and scientific studies outlining the consequences of poor quality control measures. The following white paper provides a short summary about the importance of QC and QA, while illustrating action points to improve existing QC processes. Furthermore, near-infrared (NIR) spectroscopy is presented as a powerful analysis technique to increase QC efficiency while maintaining the accuracy and precision of the existing analysis method.

The importance of QC and QA

Two main failure costs are addressed and mitigated with a reasonable QC/QA framework in place:

- Avoidance of internal failure
- Avoidance of external failure

Internal failure costs are associated with internal errors (e.g. re-inspection, rework, or scrapping). External failures are related to product defects found after delivery to the customer. These are expensive and involve a significant risk because they can affect brand reputation or even induce a loss of market share. Follow-up actions such as warranties, repairs, or recalls, require a great expenditure and therefore will significantly reduce revenues.

To avoid these failures and their related costs, it is advisable to invest reasonably into prevention measures. One such activity is the continuous monitoring of used raw materials, intermediate products, and final products. More commonly, companies prefer to gamble by under-investing in this area and neglect the negative implications, which can result in a loss of turnover between 10–30%.^[1]

Aside from implementing the appropriate checks along the complete production process, companies should also challenge their existing QC processes and setups in order to discover how to further increase production efficiency. Possible approaches include:

- Reduce budget for testing and inspection
- Increase efficiency of production equipment
- Improve productivity of the operators
- Make manufacturing easier

One strategy could be to analyze each of these action points individually, in order to find any major gaps as well as to define the respective countermeasures. Alternatively, companies can also take advantage of more modern QC technologies which have the potential to address all four of these approaches directly.

Near-Infrared Spectroscopy (NIRS) is an example of a modern QC method which significantly boosts the efficiency of QC labs. In the following section, this technology and its benefits are presented and discussed.

Near-Infrared Spectroscopy (NIRS)

All spectroscopic methods determine sample properties by analyzing the specific interaction between light and matter. This interaction varies in dependence of the applied light source, and therefore the different spectroscopic technologies are defined by the applied light energy (i.e. wavelength), and by the type of interaction. With NIRS, for example, instruments detect the quantity of absorbed (absorbance spectroscopy) near-infrared light (NIR = 800–2500 nm respectively 12500–4000 cm⁻¹, see **Figure 1**) by functional groups such as -CH, -NH, -SH, or -OH.

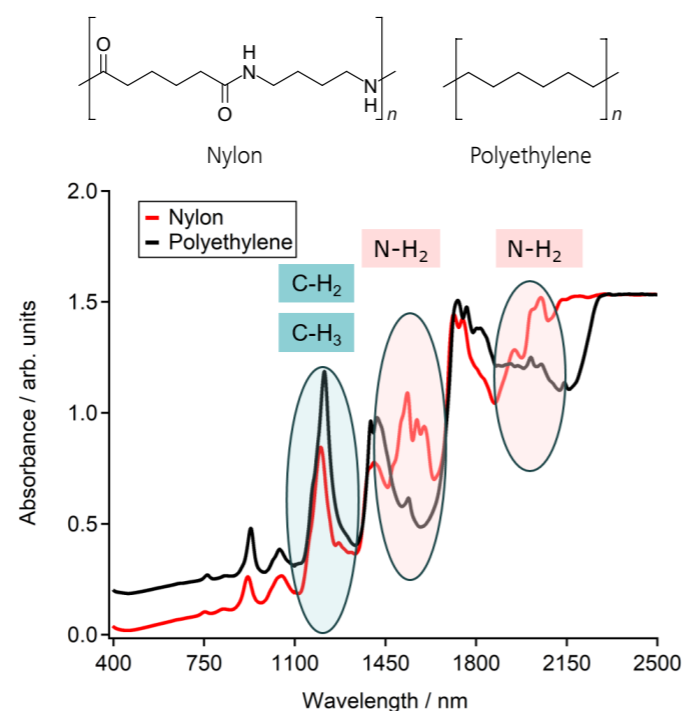


Figure 1. Comparison of spectra taken from Nylon and polyethylene in the near-infrared wavelength region. The differences seen are due to their different chemical structures – Nylon contains nitrogen functional groups whereas polyethylene does not.

Since the NIR light-matter interaction is by nature fast and non-destructive, NIRS-based analytical methods offer significant advantages over conventional approaches. Samples are analyzed as-is without time-consuming preparative steps, and remain undamaged. All NIR-sensitive information is gathered by a single measurement in less than one minute, and is displayed in the spectroscopy software as a spectrum.

The action of acquiring a quick and complete overview of information is identical to the experience of capturing the image of an object with a camera. A single picture includes all sorts of information about the object e.g. color, size, shape, position, etc. Analogous to the picture, a spectrum is a complete scan which includes numerous information about the sample (e.g. the water content, OH-Number, viscosity, or the acid number). For both the camera image and sample spectra, the only necessary action is to interpret the data, which in the case of NIRS is performed by the provided manufacturer spectroscopy software.

Currently, manufacturers of NIR instruments pay particular attention to the convenience of system operation, resulting in standardized analyzers and easily defined operating procedures. Both facets simplify the implementation of NIR spectroscopy into daily QC operations, **even across multiple locations**, requiring only minimal training of the operators.

In regards to the action points to improve QC efficiency on the previous page, it is apparent that companies which have implemented NIRS methods into their routine QC testing are able to reduce their testing budget and improve their operators' efficiency at the same time. **Table 1** and **Figure 2** present the potential return on investment (ROI) by comparing analysis costs per year between the commonly used methods of titration and viscometry versus near-infrared spectroscopy.

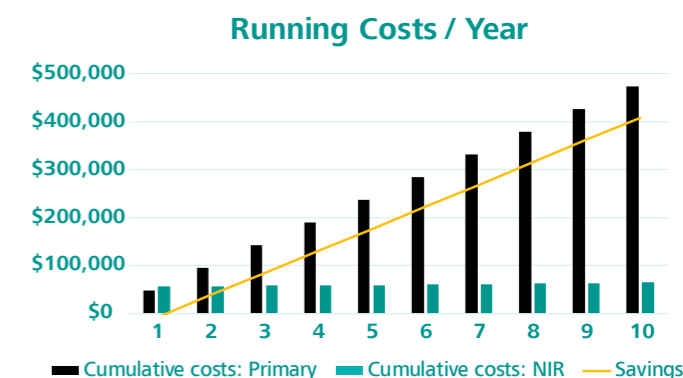


Figure 2. Possible return on investment as related to running costs when analyses are conducted with NIRS vs primary methods.

Table 1. Overview of estimated costs for the analysis of different parameters with primary methods vs NIRS. The full ROI is achieved within 11 months.

Total analyses per day	10	10
Cost of operator per hour	\$ 25	\$ 25
Cost of Analyzer	Primary Method	Near-Infrared Spectroscopy
DS2500 Analyzer	—	\$ 55,000
Total initial costs	\$ 0 ¹	\$ 55,000
Running costs consumables and/or chemicals: per analysis		
Determination of H ₂ O content (ISO 15512)	\$ 5	\$ 0
Determination of functional groups	\$ 5	\$ 0
Determination of viscosity (ISO 307)	\$ 6	\$ 0
Total costs consumables and/or chemicals: per year	\$ 35,100	\$ 0.00
Time spent per analysis (minutes)		
Determination of H ₂ O content (ISO 15512)	5.0	0.5
Determination of functional groups	5.0	0.5
Determination of viscosity (ISO 307)	15.0	0.5
Total yearly labor costs	\$ 23,438	\$ 469
Total running costs	\$ 58,538	\$ 469

¹Assumption that the instrument had previously been purchased, and therefore this cost is not included in the ROI calculation.

Application Examples

Some key parameters have already been mentioned in the previous chapter, however a complete list of possible NIRS applications would exceed the scope of this paper. Typical industries where NIRS is an established analytical QC method include:

- chemicals
- lubricants
- petrochemicals
- polymers
- paint, inks, and dyes
- pulp and paper
- pharmaceuticals
- personal care and cosmetics
- food and feed, agriculture

Chemical Industry – Polyols

Polyols, a class of organic compounds characterized by the presence of two or more hydroxyl groups, are crucial starting materials for the production of polyurethanes. Both the reaction behavior of polyols and the composition of the final product are highly dependent on the number of hydroxyl groups, which makes the analysis of this functional group so important. The reactivity of polyols also depends upon their moisture content and the acidity represented by the number of attached carboxylic acid groups.

NIRS is an established technology for the analysis of polyols (**ASTM D6342**), able to precisely determine all three parameters within 30 seconds as shown in several applications [2]. **Table 2** presents some key results from a polyol analysis utilizing NIR spectroscopy.

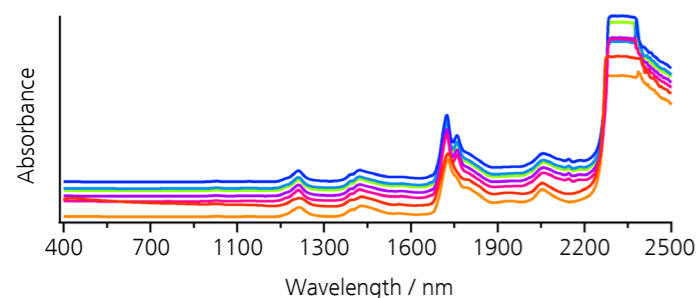


Figure 3. NIR spectra taken of polyol samples with varying OH number values.

In the following section, three different industries and application examples are described. However, it is important to note that the precision values are a function of the chosen concentration range. Therefore, selecting lower concentration ranges will most likely further enhance the precision of the results.

Table 2. Overview of typical parameters measured in the polyol industry which can also be analyzed by NIR spectroscopy.

Parameter (unit)	Range	Precision
Hydroxyl Value (mg KOH/g)	70.00–125.00	0.68
Acid Value (mg KOH/g)	0.10–8.00	0.38
Moisture content (mg/L)	75–400	52

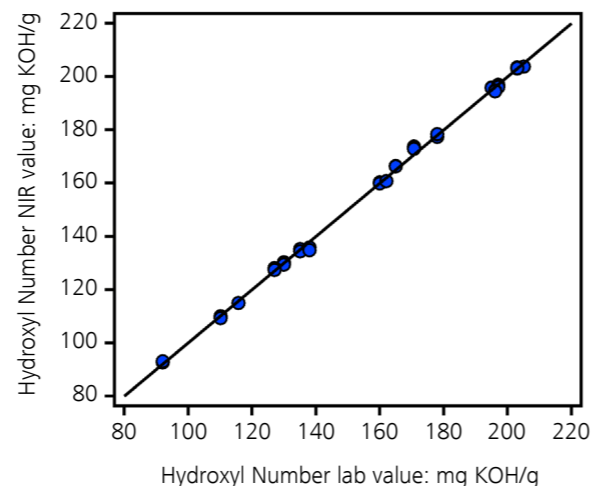


Figure 4. Correlation plot comparing NIRS to a primary laboratory method.

Polymer Industry – Polyethylene terephthalate

Polyethylene terephthalate (PET) is one of the most produced polymers worldwide, next to polyethylene and polypropylene. Raw materials for the production of PET include diethylene glycol along with either dimethyl terephthalate or terephthalic acid during transesterification and esterification reactions.

Product quality is primarily determined by the content of diethylene glycol (DEG) and isophthalic acid (which reduces the crystallinity of PET). Additionally, the intrinsic viscosity (IV) (**ASTM D4603**) and the acid number (AN) are important parameters to control in order to avoid external failures. NIRS has proven its validity as an analytical method which reliably determines these parameters. **Table 3** displays the respective concentration ranges and precision values for this application as described in the Metrohm Application Note NIR-023 [3].

Table 3. Overview of typical parameters measured in the polymer industry which can also be analyzed by NIR spectroscopy.

Parameter (unit)	Range	Precision
Diethylene glycol content (%)	1.4–2.0	0.066
Isophthalic acid content (%)	1.8–4.5	0.143
Intrinsic viscosity	0.5–0.9	0.024
Acid number	1.2–6.0	0.143

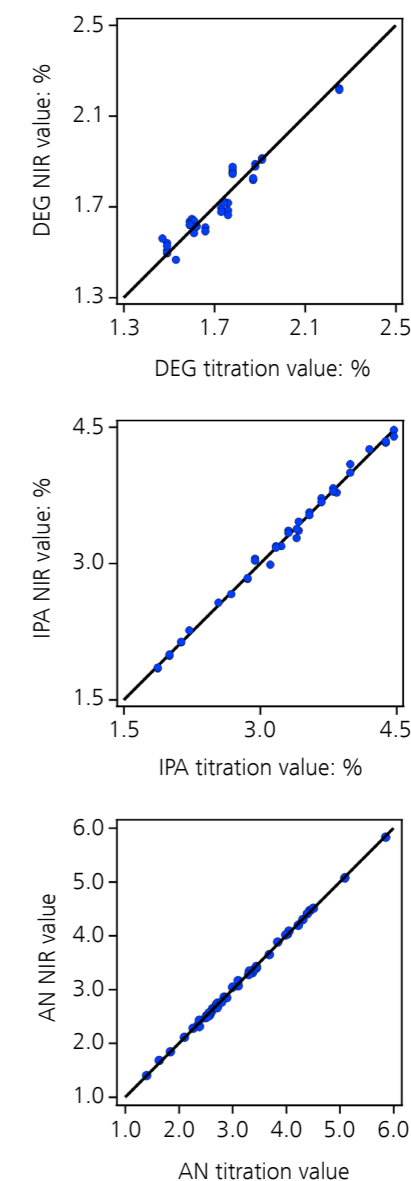


Figure 5. Correlation plots for NIRS compared to laboratory primary methods for diethylene glycol (DEG), isophthalic acid (IPA), and acid number (AN).



Petrochemical Market – Gasoline

Gasoline is one of several end products resulting from a complex production chain starting with the refinement of crude oil. This fuel product requires intensive checks on several quality parameters which need to be within specification before commercialization. These parameters, which can also be controlled by NIR analysis include the Research Octane Number (RON) and Motor Octane Number (MON), the olefins, oxygen, aromatic content, and the density.



The importance of measuring these values precisely is not just related to regulations, but this also offers manufacturers further potential to save costs. As an example, RON values exceeding the requirement will still be accepted by the market, but these products include a higher amount of lucrative long-chain organic molecules. This so-called «RON give away» (Figure 6) is estimated at approximately **0.5 RON per barrel**, resulting in **2.25 million USD/month** in lost revenue for a production of 100,000 barrels per day.

Ready-to-use NIRS systems are available for monitoring several gasoline parameters, which cover varied ranges and their respective precisions, shown in Table 4. Additionally, the manufacturers of NIRS analyzers usually offer application support to extend these ranges or improve upon the precision.

Table 4. Overview of typical parameters measured in the petrochemical industry which can also be analyzed by NIR spectroscopy.

Parameter (unit)	Range	Precision
RON	85.00–94.00	0.68
MON	81.00–100.00	0.53
Olefins (%)	1.0–25.0	1.3
Oxygen (%)	0.200–2.000	0.045
Aromatics (%)	20.0–45.0	1.1
Density (g/cm ³)	0.7400–0.7600	0.0024

Summary

At first glance, investment into quality control might increase product costs. However, this reduces costs related to external and internal failures, which are of higher magnitude and have the potential to reduce up to 30% of the turnover.

Besides enforcing a reasonable quality control program, the efficiency of the QC and QA department is required to produce materials cost-effectively. One way to achieve this is to implement modern, easy to use, fast QC methods. NIRS is an established methodology used across different industries. This technique combines these requirements and provides significant potential to reduce costs and increase operator efficiency.

References

- [1] Why Improving Quality Leads to Lower Manufacturing Costs, QualityInspection.org. (accessed October 30, 2019). <https://qualityinspection.org/improving-quality-cost-china/>
- [2] Metrohm Application Note **NIR-035** Hydroxyl number in liquid polyols using Vis-NIR spectroscopy [AN-NIR-035](#)
- [3] Metrohm Application Note **NIR-023** Diethylene glycol, isophthalic acid, intrinsic viscosity, and acid number in PET granulate by NIRS [AN-NIR-023](#)

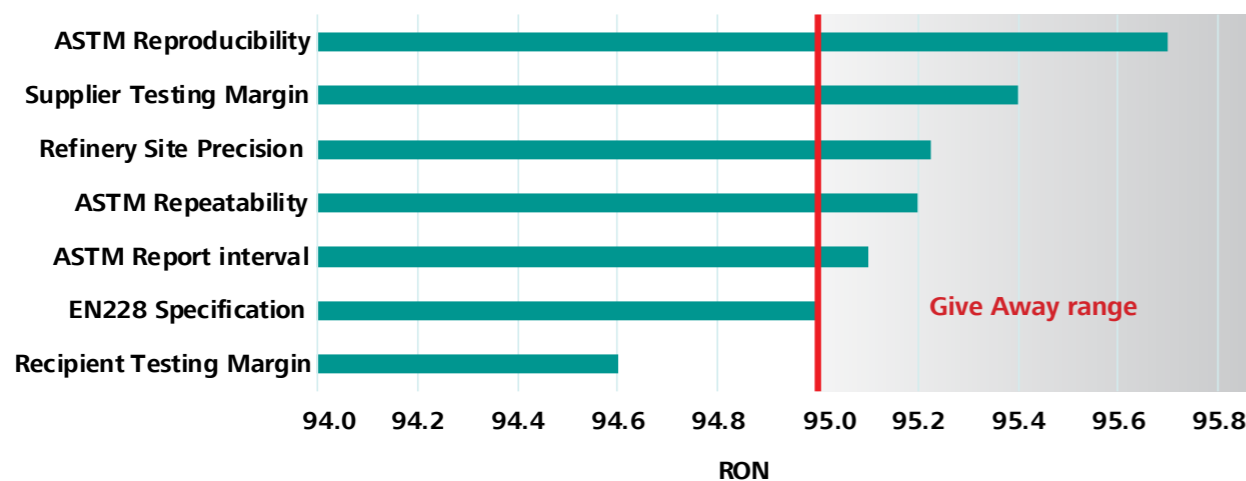


Figure 6. Overview of typical RON give aways in relation to different methods.

Data Integrity with NIR-Spectroscopy Software



Nicolas Rühl

Data Integrity is currently a hot topic issue that has created much attention and has raised concern within companies working in regulated environments. This White Paper explains some of the key terms used in the context of Data Integrity and outlines how the requirements of Data Integrity can be understood and implemented.



Introduction

Recent news about various Data Integrity violations revealed by governing bodies has created much attention and has raised concern within companies operating active in regulated environments. Figure 1 shows the increase in violations of data integrity aspects during cGMP (current good manufacturing practice) inspections. (1)

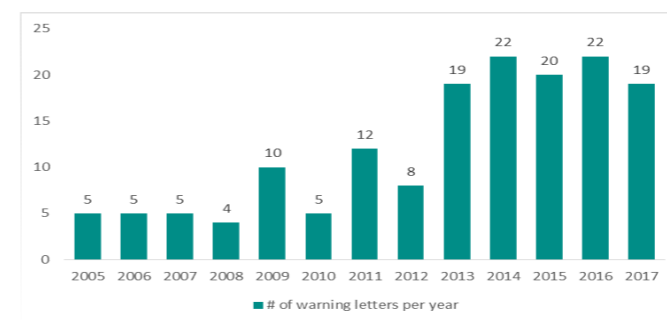


Figure 1. Number of data integrity violations over the last years.

To help understand the topic Data Integrity and its requirements, this White Paper provides an overview of important terms used in this context and presents examples of software functionalities which help to fulfill requirements stipulated in the FDA guidelines for data integrity. (2)

Data Integrity Terms – An explanation

ALCOA/ALCOA+

Data integrity includes several aspects which are summarized under the acronym ALCOA and ALCOA+. ALCOA stands for the requirements attributable, legible, contemporaneous, original, and accurate. This set of requirements has been recently extended by the aspects complete, consistent, enduring, and available (ALCOA +). A detailed explanation of these requirements with examples can be found in the chapter The ALCOA Principle.

Data and Metadata

The FDA distinguishes in their Data Integrity guideline between “data” and “metadata”. Data is understood as a collection of facts, which can, for example, be a number, a list of measurements, or a record. Metadata, or contextual data, on the other hand, provides additional information describing data, for example, by whom and when a measurement was done. For Data Integrity and more specifically for the requirements of transparency, consistency, and reproducibility, both data types are always required (see figure 2).

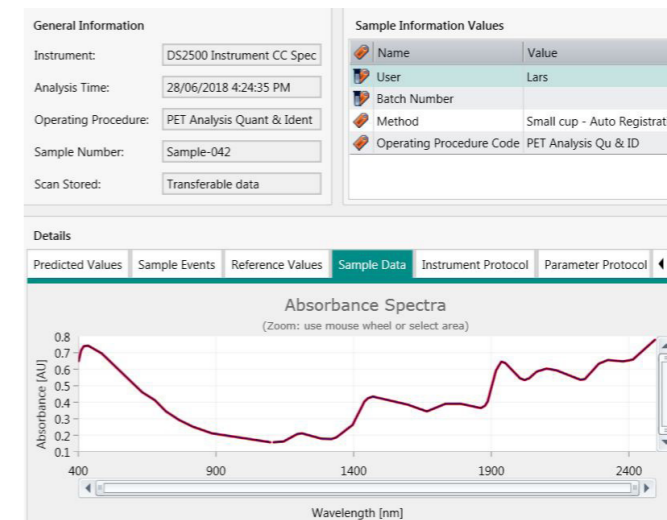


Figure 2. Display of metadata in Vision Air for a single measurement. Time stamps, user names, operating procedure type, to name only a few, are displayed together with the collected spectrum and the predicted results.

Dynamic and static data

Apart from the distinction between data and metadata, data can be classified as being dynamic or static. Static data includes all non-changeable data, such as records on paper or stored as PDF. Electronic records, on the other hand, where user have the possibility to make changes, are defined as dynamic. While the latter offers users convenience, it also involves a risk to lose transparency. This risk needs to be accounted for, e.g., by means of automatic history tracking.

Figure 3 shows a typical example of how dynamic data can be tracked. Signing events (signing on different levels, adding comments, or withdrawing signatures) are recorded automatically in the Vision Air software.

Signature	Timestamp	User ID	Name	Reason	Comment
Withdrawn	7/3/2018 1:36:56 PM	admin	Max Maximus	Rejected	Certificate for used standard expired
Level 2	7/3/2018 1:36:00 PM	nru	Nicolas Rühl	Reviewed	
Level 1	7/3/2018 1:35:17 PM	admin	Max Maximus	Instrument ready to use	Instrument test conducted according to SOP
Configuration - Level 2	7/3/2018 1:21:30 PM	nru	Nicolas Rühl	Approved	
Configuration - Level 1	7/3/2018 1:21:22 PM	admin	Max Maximus	Approved	

Figure 3. Display of changes for dynamic data. All signing and withdrawing steps are clearly documented, allowing users to track the individual steps performed.

The ALCOA Principle

The ALCOA and ALCOA+ requirements are the basis to achieve data integrity. All these requirements have a significant overlap with requirements stated in the FDA 21 CFR Part 11 regulation. Therefore, when trying to achieve Data Integrity, it is advisable to use software which has been developed in accordance with 21 CFR Part 11 requirements to simplify the effort. However, it is important to highlight that similar to achieving compliance with the 21 CFR Part 11 guideline, software functionalities do only cover parts of these requirements, more precisely technical ones. That's the reason why compliant-ready software can only act as a solid base to achieve Data Integrity. To achieve Data Integrity process, aspects must also be defined within the company, which is typically done by implementing standard operating procedures.

In the following chapters, each aspect is first explained briefly and then a practical example based on Metrohm's Vision Air software is presented.

Attributable – When did who do what?

To conform with Data Integrity requirements, workflows need to be traceable. As mentioned in the previous chapter, a combination of both data and metadata is required. The requirement of attributability focuses on the availability of metadata, specifically the user ID and the time stamp for each measurement.

Figure 4 shows the typical sample registration information field created for each measurement in Vision Air. Each measurement follows a predefined operating procedure, which provides guidance to the operator. The time stamp and user information by whom and when a measurement was performed is tracked. The user is identified by his unique user ID and a user name. For additional information, user-defined fields can be added. In this example, an input field for a batch number was created.

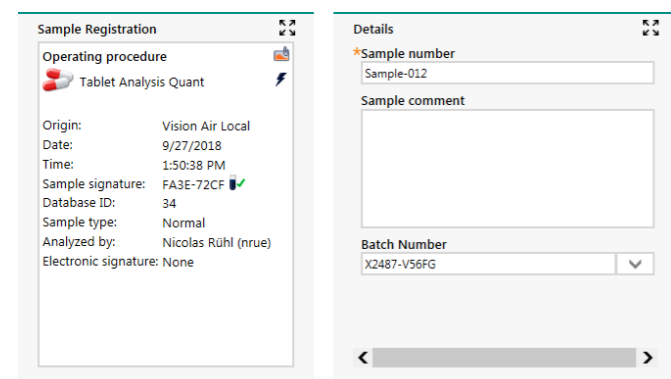


Figure 4. Sample registration window during routine analysis in Vision Air. Both automatically created and user-entered metadata are available for each measurement.

Legible – Do data remain readable through the complete lifecycle?

The requirement of legibility states that data and metadata be readable and permanent. While this may sound trivial, the implementation can be challenging, especially with regard to long-term readability. A common approach for this requirement is to offer the possibility to print or to export data into frequently used formats.

Vision Air provides export options for reports (PDF, XML, and CSV). Furthermore, the Vision Air automatic backup scheduler offers users a convenient way to back up the entire database, which can be reimported at any time (see Figure 5). Both features guarantee long-term readability.

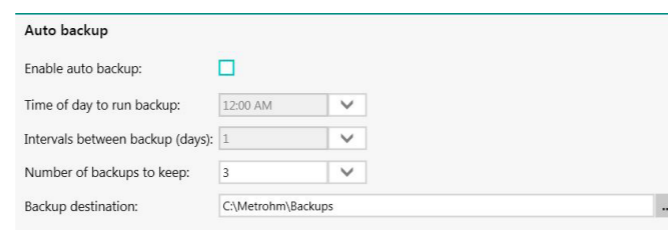


Figure 5. Automatic backup screen scheduler in Vision Air. Vision Air allows users to define an automatic backup procedure to ensure long-term readability.

Contemporaneous – Are records created at the time of the activity?

The paper-based documentation approach, which was common in the past, enabled back-dated entering of data. This approach always involves a significant risk of unprecise and false documentation, since information can be forgotten or misremembered. The nowadays more established form of electronic documentation eliminates this risk by creating records ideally at the time an activity takes place.

In Vision Air, each measurement is instantly stored in the SQL database. Successful storage is clearly displayed with icons (see figure 6). In comparison to a file-based system, the storage location and the data structure is set automatically, which guarantees full functionality of the system.

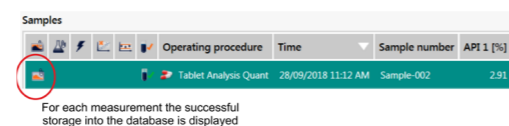


Figure 6. Visual display of successful storage of data. In the sample history view in Vision Air, an icon displays the successful storage of data in the SQL database.

Original – Is this the first recorded observation or a verified, true copy?

Result values collected during analyses are typically dynamic data sets, thus allowing post- or reprocessing activities. In NIR spectroscopy, post-processing is more common than reprocessing, which is a typical activity performed, for example, for titration or ion chromatography data sets. Typical post-processing operation of data in NIR spectroscopy are slope/bias correction or general post-calculation. For the sake of transparency, each of these calculations and the individual results must be clearly displayed.

In Vision Air, users have the possibility to display both the unprocessed (raw) result and the processed result. If configured, post-processing is done automatically during result calculation, thus avoiding human errors or manipulations. Figure 7 shows a typical detailed result display in Vision Air, where the raw, unprocessed result and the post-processed result from a slope/bias adaptation is clearly displayed for the parameter moisture.

Entity	Intrinsic Viscosity	Moisture
SubSample 1	2.74	2.79
Raw Result	2.74	1.99
Reported Result	2.74	2.79
Min	2.738	2.786
Max	2.738	2.786

Raw Result = Unprocessed
Reported Result = Processed Result
e.g. modified Slope/Bias

Figure 7. Detail result display. In the detail view in Vision Air, the unprocessed and the post-processed result (e.g., a slope and bias correction) are displayed for each measurement.

Accurate – Is data stored correctly and are modifications clearly documented?

Alteration of data, if allowed, e.g., of dynamic data, has to be documented transparently. For configuration changes of the instrument, extensive review functionalities, typically a two-level signing function as recommended in the 21 CFR Part 11 regulation, should be in place to ensure and help with accurate documentation.

Vision Air Pharma, which was developed to fulfil the requirements of the FDA 21 CFR Part 11 regulation, includes a two-level signing system for every configuration change (see figure 8). Successful application of a configuration change is displayed using unambiguous icons, and each configuration change is listed in a table for later review. Comments can be entered for each modification made to increase further transparency.

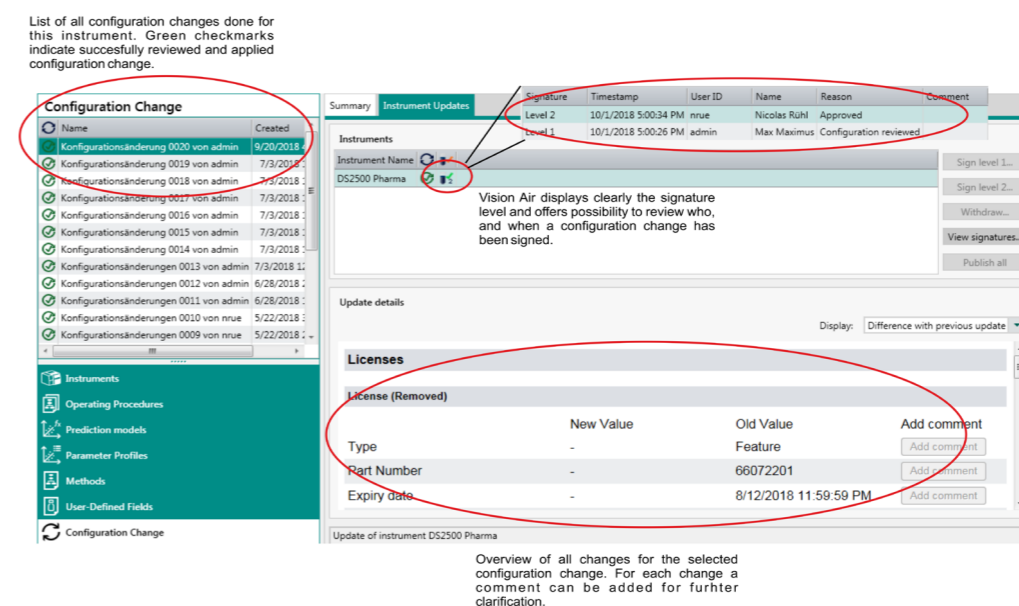


Figure 8. Configuration change viewer in Vision Air. The configuration change viewer in Vision Air allows users to track all changes of the system in a transparent manner.

The ALCOA + extension

ALCOA+ extends the requirements to include aspects such as completeness, consistency, and availability of data:

Complete – Is all relevant data properly stored?

With the change to electronic documentation, assessing whether data has been properly stored becomes more difficult. For both kinds of storage (file-based as well as a data-based), the software support users by showing clearly that data storage was successful.

The SQL database which is used in Vision Air for data storage has the advantage to provide a higher level of data security as opposed to a file-based concept. The risk of corrupted data sets or unauthorized data manipulations can be significantly reduced by using a database system rather than a file-based system. In the Vision Air software, each measurement is linked with a unique signature (see figure 9) indicating that data is not only correctly stored within the database but has also not been modified.

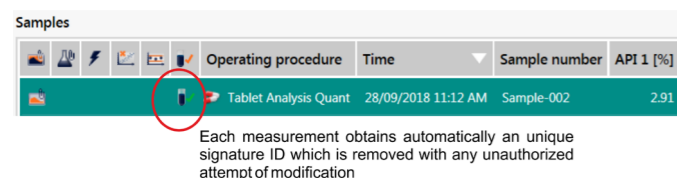


Figure 9. Visual feedback of correct storage of data in the database. The icon highlighted with a red circle indicates a correct hash signature.

Consistent – Can the operation workflow be reconstructed?

The above mentioned requirements all seek to make sure workflows are transparent. However, not only from the point of view of transparency, but also from the point of view of efficiency, workflows should be consistent and easily reconstructible.

Workflows in Vision Air can be easily defined by using so-called operating procedures guiding operators during measurement. Each operating procedure consists of a set of prediction models and an element called method, which defines exactly how measurements are to be conducted (see figure 10).



Figure 10. Structure of operating procedures in Vision Air. An operating procedure defining how a measurement is done consists of prediction models and a method which specifies different measurement parameters.

A method can, for example, specify the sample temperature for a measurement (see figure 11), which input fields are accessible, and which input fields are mandatory to be filled.

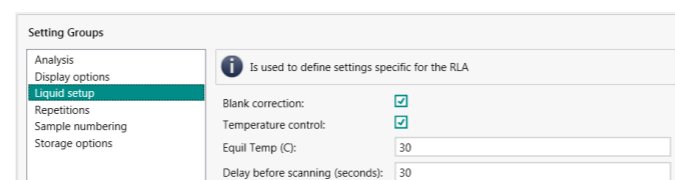


Figure 11. Method setting options for liquid analysis. In the settings for a method, different measurement parameters can be set. For example, the temperature of the sample vessel for liquid analysis.

Enduring – Does stored data remain available longtime? Available – Is data accessible / readable / printable?

The final two aspects mentioned in the FDA Data Integrity guideline are enduring and available. Enduring and available further highlights the importance of longtime availability of stored data and the possibility to access and read data in common ways.

Both aspects are covered by the previously mentioned SQL database storage approach and the availability of audit trails (see figure 12), backup functionalities, and automatic print functions. In the Vision Air audit trail, all relevant activities can be easily reviewed using the integrated filter features.

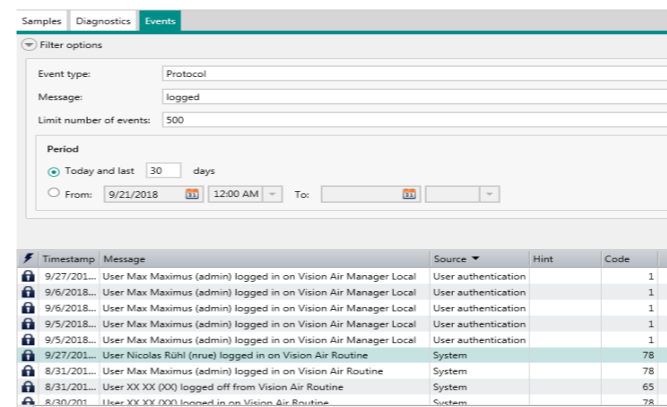


Figure 12. Audit trail view for login events. In Vision Air, different filter settings can be set to find events easily, for example, all events which refer to a login or logout.

Summary of important software functionalities for Data Integrity

The previous chapter discussed many different software functionalities. In general, it can be said that one of the most important software functions to achieve and maintain operation transparency are audit trails. Audit trails allow for the reconstruction of operations performed by clearly displaying by whom, when, and why actions were taken. Besides automatically generated information, such as user ID and time stamps, functions such as comment fields in combination with preselected reasons of action should be available. Besides transparency, data safety is an important aspect of data integrity. This includes mainly data storage and manipulation control. Increased data security can be achieved by following a database approach rather than file-based approaches, where files, for example, can be more easily deleted or modified. Databases furthermore allow for easier tracking of data manipulation using unique signatures for each collected data.

Literature:

- (1) http://www.nsf.org/newsroom_pdf/pb_data_integrity_closer_look.pdf (accessed November 30, 2018)
- (2) <https://www.fda.gov/downloads/drugs/guidances/ucm495891.pdf> (accessed November 30, 2018)

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