

Techniques for ~~developing~~ Developing Raw Material Libraries

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Part 1: Sampling and Scanning

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For many years ~~now, the~~ pharmaceutical and related industries have ~~utilized~~ used near-infrared spectroscopy (NIRS) as a means to identify raw materials as they are ~~being~~ received by a manufacturing facility. ~~This is because the~~ The NIRS technique is highly specific for many of the organic compounds used in the formulation of tablets, capsules, crèmes, ~~and suspensions, etc...~~ T.

The development of portable and smaller instrumentation has ~~allowed~~ helped many organizations ~~to~~ become much more mobile with the use of the method, ~~to the point~~ where by point of receipt/point-of-receipt/storage analysis is possible. This technical note is the first of a two-part series that ~~introduces~~ discusses the critical issues behind ~~sampling of materials~~ material sampling. In particular, it addresses collecting ~~leading to the collection of~~ the most representative spectral measurements possible, ~~that leads to~~ enabling developing and deploying a ~~the most~~ robust identification library ~~development and deployment~~.

Background

The use of infrared radiation as a means to identify organic structures ~~can be~~ is attributed to Coblenz [1] ~~and it has been a~~ widely-used method ~~widely used~~ in recent decades, mainly because ~~of the improvement of~~ improved instrumentation and computer power. ~~Near Infrared~~ Near-infrared radiation offers many practical advantages over mid-infrared spectroscopy for raw material identification, ~~mainly due to e,~~ including ease ~~ase~~ of sampling and robustness of instrumentation. It is also a complimentary method to Raman ~~Spectroscopy~~ spectroscopy, and both methods should be used in tandem to solve the myriad problems that both technologies cannot solve individually. The pioneering work of Plugge and Van Der Vlies [2] opened up the many opportunities we now see for the use of NIRS in the pharmaceutical industry, particularly Raw Material Identification in raw material identification (RMID).

Where to Start? ~~.....~~ Be Smart!

Just because you have 1000 different ~~Raw Materials~~ raw materials in your retention store doesn't mean you have to make a library of them all at once. Plan your development based on the 80:20 rule, ~~i.e.:~~ what are the 20% of materials that come in 80% of the time. ~~!?~~ Identifying these ~~is easy~~ ~~then to find the~~ materials first that will provide the most benefits up front in terms of quality assessment and efficiency.

Remember: ~~Remember that~~ NIRS is typically not capable of assessing ~~cannot assess~~ the identity of inorganic salts and other inorganics based on the lack of -CH, -OH and -NH bands associated with organic compounds. Be careful and discerning in this regard.

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Make a list of all ~~of the~~ incoming raw materials ~~incoming to the facility~~ and assess the history of the materials for past failures or deviations. Also, look for materials that don't come in as frequently as the ~~higher~~ higher-volume materials, but require lengthy and tedious laboratory analyses, ~~—~~ for example, ~~Magnesium Stearate~~ magnesium stearate where the stearate ~~which~~ requires a detailed and lengthy identification procedure ~~to identify the stearate~~. ~~For materials~~ Identifying materials that

come in only once or twice a year, ~~these~~ will not typically give you the benefits upfront, so schedule those materials for second- or even ~~third~~ third-phase library developments.

The general process is to gain some form of self-assessment status with the regulator in your region by submitting the development and ~~Standard Operating Procedures~~ standard operating procedures (SOPs) for the method based on the materials most commonly delivered. In this way, you gain the benefits of the method ~~are being gained~~ as soon as possible.

Sampling: The Major Stumbling Block

The correct way to sample ~~has been a~~ is a debated and somewhat confusing topic ~~that has caused so much debate and confusion~~ in the NIRS world. As an identification tool, NIRS can be trained for most sampling applications, but there ~~are still remains two major schools of thought regarding main approaches to~~ sampling:

1. Physical sampling from containers and scanning the material in glass vials-
2. Using handheld instruments or ~~fibres~~ fiber optic probes to measure in the container or through the packaging material-

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Years of experience ~~has~~ have shown that physical sampling and scanning through glass vials is the best way of developing robust libraries, but is the least ~~favourable~~ convenient method for in terms of "convenience" to the operator. In a perfect world, direct scanning through packaging materials or directly into the container would be the best options, ~~however,~~ However, there are a few things that must be kept in mind of which two important aspects are ~~described below~~:

1. Many materials come in sealed, non-transparent containers or paper bags ~~of which through~~ which NIRS cannot scan ~~through~~. Although spatially offset Raman spectroscopy (SORS) has been suggested as an alternative, the physical state of the material in the bag cannot be ascertained visually and SORS is not useful for the types of the packaging used for most active pharmaceutical ingredients (APIs) ~~come delivered in~~.
2. Regulations ~~are now requiring~~ increasingly require 100% inspection systems ~~to be used and the need for collecting~~ the need for collecting retention samples is still a requirement, therefore, physical sampling is unavoidable.

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For these reasons, the use of glass vials is a highly versatile methodology, particularly for traceability, ~~i.e. where, for example,~~ the sample measured is the one ~~that is~~ kept in retention. By physically sampling, the materials state can be assessed and the packing of the material into the vial can be controlled, minimizing any measurement differences between samples. The major benefit of the glass vial approach is that it enables predicting material conformity and even processability ~~predictions can be made, thus taking~~ This takes NIRS from an RMID tool to a process analytical technology (PAT) tool.

This requires some innovative thinking from companies looking to get the most out of ~~the investment made into~~ their investments in the NIRS technique. Some companies ~~are performing~~ perform sub-sampling at the warehouse using a handheld system such as the MicroNIR™-MicroNIR™ OnSite ~~for verification of~~ to verify material ID on delivery ~~and then~~ they then implement ~~implementing~~ a 100% approach in the dispensary, where every material is scanned and an ID and Conformity ~~conformity~~ test is applied, just before the material is used. This is in line with cGMPs for

the 21st Century [3] where a scientific, risk-based approach to quality is encouraged. In this regard, NIRS provides many advantages over other instrumental techniques, and in many situations—its applications are not only confined to RMID.

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Another advantage of the glass-glass-vial method is that the infinite depth of penetration of material can be determined such that consistent spectra are collected each time. It is easy to fill a vial with various levels of a material and use a backing material of known spectral characteristics to work out where the features of this material are removed and when only the material of interest is being scanned. This provides an easy and clear way to validate sampling practices and write them into SOP's.

MicroNIR™ for RMID and Much More Other Applications

The Viavi MicroNIR™ Pro 1700 is Viavi Solutions' a general-purpose NIRS analyzer for addressing the that addresses many challenges the industry faces by utilizing using smarter systems of quality assurance and control. This system can be fitted with a glass-glass-vial holder, a sapphire contact sampling window, or a transmission stage for the many types of material that exist. The MicroNIR Pro spectrometer, like all Viavi spectrometers, can be qualified to USP 1119 and the verification status can be checked on a regular basis.

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The optional transmission stage is useful for measuring liquid raw materials and avoids the use of scattering agents such as Titanium Dioxide titanium dioxide (TiO₂) for taking measurements of measuring liquids in diffuse reflectance (otherwise, infinite absorption effects can cause unwanted spectral anomalies).

The MicroNIR™ OnSite is Viavi Solutions' mobile spectrometer is designed for point-point-of-manufacture analysis. The ruggedized design and IP65 rating allows MicroNIR OnSite to be used enables use in typical manufacturing environments without the need of special enclosures or housings for stability. Using a purpose-purpose-built software application for tablets and other mobile devices, sample scanning and analysis is an easy and validated process. MicroNIR™ OnSite can also be used with the standard MicroNIR™ Pro software platform for greater ease of method development in an office environment.

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MicroNIR MicroNIR OnSite can be used as a direct contact measurement system, or it can be fitted with accessories for measuring glass vials or measuring liquids in transmission mode. The MicroNIR™ OnSite spectrometer, like Like all Viavi spectrometers, it can be qualified to USP 1119 and the verification status can be checked on a regular basis.

The MicroNIR™ Advantage for RMID

There are many systems on the market for RMID and when a new or even experienced user wants to evaluate a system for use in their facility, the information overload may lead to "analysis paralysis." The MicroNIR™ family of portable NIR spectrometers can help take the guesswork out of this decision by providing:

- 1. A system that can be qualified to pharmaceutical regulations-
- 2. The spectral range and resolution adequate for RMID and ~~Conformity~~conformity-
- 3. Method development and software deployment systems that are tightly integrated-
- 4. Robustness ensured through no moving parts and smart design-
- 5. All the sampling features of more expensive systems in a fraction of the size and cost-

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MicroNIR™MicroNIR is also supported by and endorsed by many of the world's leading experts in NIRS. All systems come with a complete product lifecycle documentation and Viavi Solutions can also provide ~~Installation and Operational Qualification~~ installation and operational qualification (IQ/OQ) documentation for those companies looking to take advantage of the recommendations of the GAMP©5 guidance.

Part 2 of this technical note evaluates the chemometric methods used for library development. These methods are only useful if the principles of good and robust sampling outlined in this technical note are followed.

If you require For more information regarding better sampling and method development, please contact Viavi Solutions at viavisolutions.com.



Figure 1- MicroNIR Pro spectrometer and the home page of software

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Figure 2:- MicroNIR Pro with a glass vial accessory-

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Figure 3- MicroNIR OnSite

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Figure 4- MicroNIR OnSite shown attached to a tablet computer showing a large applicator on the left, convenient when pressing against soft materials such as the case would be when measuring materials inside a plastic bag; the middle component in the middle is an encapsulated white reference standard.

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Figure 5- MicroNIR Pro attached to a transmission stage-

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References

- [1] Coblenz, W. W., "Investigation of Infrared Spectra, Part I" Carnegie Institution, Washington D.C., 1905.
- [2] Plugge W, and van der Vlies C., "The use of near infrared spectroscopy in the quality control laboratory of the pharmaceutical industry". *J Pharm Biomed Anal.* 1992 Oct-Dec;10(10-12):797-803.
- [3] US FDA, "Pharmaceutical cGMPs for the 21st century – A risk based approach, final report", 2004. <http://www.fda.gov/drugs/developmentapprovalprocess/manufacturing/questionsandanswer/soncurrentgoodmanufacturingpracticescgmppfordrugs/ucm137175.htm> accessed 8th March, 2016.

About the Author



Brad Swarbrick is the owner of Quality by Design Consultancy, an Australian company that services a number of industries in Oceania, SE Asia, and Japan, particularly supporting pharmaceutical applications of [Chemometrics](#)~~chemometrics~~, PAT, and QbD when applied to spectroscopic and process data.

Brad has over 20 years of experience in the application of [Chemometrics](#)~~chemometrics~~ and design of experiments (DoE) methodology in a wide range of industries, including agriculture, petrochemical and pharmaceuticals. Until recently, Brad was the chief operating officer of CAMO Software, a ~~world~~ world-leading provider of the [Chemometrics](#)~~chemometrics~~ software package The Unscrambler where he successfully brought a number of new software developments and large projects to commercial reality. Prior to CAMO Software, Brad worked in the pioneering Pfizer Process Analytical Technology (PAT) group, developed the entire NIR program for Sigma (now Aspen) pharmaceuticals, and worked as a GMP consultant for one of SE Asia's largest pharmaceutical consultancy groups.

Brad has a unique combination of technical and business skills that have allowed him achieve the many business objectives that his clients are now enjoying. Brad is a globally recognized expert trainer in

chemometrics and design of experiment methodology and has many years of expertise in near-infrared (NIR) spectroscopy and process analytical technology (PAT). Brad is the current section editor of pharmaceuticals, for the *Journal of Near Infrared Spectroscopy*, has written a number of textbook chapters on NIR and ~~Chemometrics~~*chemometrics*, in particular, Brad wrote the popular short book, *"Multivariate Analysis for Dummies"*.

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Brad has a ~~Bachelor of Science~~*B.S.* degree, ~~majoring in Chemistry~~ *chemistry*, and has a post-graduate degree in ~~Chemometrics~~ *chemometrics*, and is currently ~~doing working on earning~~ *doing working on earning* his Ph.D. ~~degree~~ *degree* in ~~Biospectroscopy and Advanced Chemometrics~~ *biospectroscopy and advanced chemometrics* at the University of Sydney's Vibrational Spectroscopy Core Facility.