Sampling Guidelines for Handheld Raman Measurements; What You Need To Know

By: Enrique Lozano Diz and Katherine Bakeev

In recent years, Raman spectroscopy has seen increased adoption as the technique of choice for the rapid identification of materials; especially for raw material identification in the pharmaceutical industry, identification of controlled substances and explosives for security applications, polymer material identification for packaging and plastics recycling, and mineral and gemstone identification and authentication. This is a clear indication that there is demand for rapid methods for identification of materials in industry and security inspection. Material testing in the field (understood as anywhere out of the traditional laboratory) is continuing to grow in response to issues of substandard raw materials, product adulteration, and counterfeit ingredients, especially in the pharmaceutical industry where regulations require the testing of all raw materials before use.

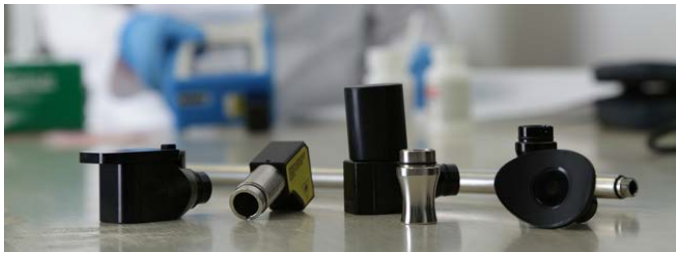
The growing implementation of Raman as an identification tool in the market can be attributed to the increased availability of portable and handheld Raman instrumentation and the ease of use of Raman technology.[1] Raman spectra can be collected without any sample preparation, directly through a transparent container and provide rich characteristic chemical information of the material. Raman analysis of incoming goods in the warehouse and dispensing areas has proven to be an extremely cost effective and highly traceable procedure to qualify and validate the transit of materials, without the need to have samples sent to an analytical laboratory. As a result, more and more global facilities are expanding their Raman analysis capabilities with portable and handheld Raman devices. Additionally, the capability to take a powerful material characterization tool such as a Raman spectrometer anywhere in the field is expanding the capabilities of researchers to be more productive and efficient when running samples on the go, such as in mineralogy, art restoration, safety in chemicals plants, first responders and firefighters and many other fields.

When it comes to rapid material identification, there is a large variety of sampling requirements that are specific to each industry, factory or even team within a company. There is also a numersous sample forms that need to be tested, so it is necessary to ensure flexibility in measuring samples for the best data with minimal sample preparation and handling. Historically, representative samples have been taken from the shipping container and placed into another sample container for transport to a laboratory for testing by one or more tests to confirm the identity. To increase the ability to measure all incoming materials, rather than a representative sample, it makes more sense to bring the analysis to the sample in the receiving area. A handheld Raman spectrometer provides the ability to sample a material directly in its original package, or to take a small sample for testing in or close to the receiving area. Each company has specific requirements for how to acquire data and the level of sample manipulation that is acceptable, with the goal of ensuring the highest quality materials are received

with a verified identity, in the most cost effective manner. Therefore, it is necessary to have techniques that provide a high return on investment (ROI) without introducing complexity to the incoming material inspection and receiving process. Handheld Raman spectroscopy has proven to bring great value to industry in this regard.[2]

One of the main factors that has an impact on Raman data reproducibility and accuracy of results is how and where the Raman data are obtained. As a reminder, Raman signal can penetrate through transparent and opaque materials and provide a reading of the content of the container. This means that Raman signal is independent of where the data is acquired, and users should expect the results of chemical identification to be accurate with minimal contribution of the packaging. So whether the sample is inside a glass bottle, inside a plastic bag or measured directly, the measurement will be the same and the packaging itself will not interfere. Most parameters of operation for handheld and/or portable Raman devices are defined by the manufacturer based on the customer's requirements, but the point of analysis remains at the discrimination of the user.

Due to the large number of sampling possibilities and variety of specific needs, there is a challenge for Raman manufacturers to provide a single suitable solution since it is not possible to offer a sole tool or accessory to be optimal for all samples. An additional point of consideration is whether or not the operator is experienced in Raman spectroscopy, and how to assure an optimal Raman signal and the best possible data reproducibility is achieved. Easily exchangeable accessories with self-explanatory names such as "bottle adaptor" that can be easily attached (and not require the operator to understand when to use such an accessory) to the handheld instrument, increase the versatility of the Raman analytical tool and provide a means to get the best data for different sample types. This translates to a much higher confidence on the results obtained with a handheld or portable device in different conditions (glass vial, plastic bag, pill/tablet, etc.)



Another factor that manufacturers must consider with Raman units that will be operated in the field is environmental light; and B&W Tek has made a strong effort to analyze and correct this factor. Since room light can interfere with Raman spectral data, the development of accessories must be such to minimize infiltration of light during the measurement, regardless of the sample form or shape. B&W Tek accessories minimize environmental light that can interfere with the measurement, and B&W Tek assures all spectra are compensated from background light (mostly environmental).

Acquisition time in portable Raman units is an important factor of consideration; it should ideally be as short as possible (seconds rather than tens of seconds) since the operator needs to stand still in order to acquire the data from a single point, which is not always easy or possible. B&W Tek's unique

temperature stabilized technology in the NanoRam handheld Raman spectrometer system automatically sets up the best acquisition time for each sample and optimizes spectral data handling to assure maximum data reproducibility.

At B&W Tek, we have developed a number of accessories to be used with our NanoRam® products to satisfy the majority of the most common applications in the material identification and verification market segment; each one optimized for a specific type of sampling. The most general of these is the **Point and Shoot Accessory** which can be used for general contact sampling, or through transparent packaging. A Raman signal will be acquired approximately 1mm below the contact surface. This is ideal for plastic bags, including drum liners and direct measurement of materials. It is the most common and versatile of all accessories. Simply press the sample against the accessory and hold it in contact until the end of the data acquisition.

An extremely useful accessory for contact sampling of liquids is the **Immersion Probe** which consists of a long, chemically-resistant body 316SS with a sapphire window that can be used to take direct measurements in large or small containers. (Note: for cleaning procedures in controlled environments, this can be treated as a stainless-steel needle).[3] With a probe length of 36cm (12in), it can be inserted into sample containers such as drums or barrels, allowing for measurements at more than one sample depth without the need to remove materials. The probe can be used in combination with a disposable plastic sleeve molded to snugly fit the probe so that it can be used with little need to clean it between measurements, and to avoid cross contamination of samples. The immersion probe can further minimize the need for sampling by allowing for *in situ* analysis of liquids and/or solids; thus providing an effective way to more rapidly evaluate a large number of samples with minimal sample handling.

Another type of contact accessory is the **Bottle Adaptor** designed to take measurements of samples inside glass or plastic bottles, such as solvent bottles. It is designed to snugly fit against the rounded bottle surface, reducing ingress of light and the potential risk of side reflections for the operator, while at the same time optimizing the data acquisition by reading the liquid inside the bottle. The focal point (where the Raman signal is most detectable) is approximately 5-6mm from the contact surface, so Raman signal is obtained from the inside of the bottle (liquid) and not from the container itself, or too far inside the liquid (which would dramatically reduce the Raman signal). Using a handheld Raman spectrometer with a bottle attachment allows for nondestructive testing without the need to even open the packaging, hence reducing sampling time as well as any possibility of sample contamination. For bottles that are especially thick (such as 2.5l Winchester type brown solvent bottles commonly found in research laboratories), i.e. those with thickness higher than 5mm, B&W Tek has a long-working distance shaft that operates at 10mm from the lens. This allows for the unit to focus beyond the glass thickness. This shaft is compatible with almost all other accessories for Raman, which makes the possible combinations extremely versatile.

Liquid samples are often placed in glass vials since they are simple to work with, inexpensive, inert, and require a minimal amount of sample. Vials can be sealed and stored for future analysis or used for storage of retained samples. A specially designed **Vial Holder** can be used with disposable 15 mm glass vials, and has a cover that blocks ambient light so that this does not interfere with the measurement. The adaptor assures a reproducible positioning of the vial, avoiding operator errors and enhancing data reproducibility. The focal point of the measurement is a few millimeters from the vial wall, providing a spectrum of the material inside the container and minimizing glass contribution (clear or brown).

For hands-free measurement of samples on a surface, the **Right Angle Adaptor** is an accessory that facilitates measurements at a 90° angle, allowing the NanoRam to be placed on a surface (such as a lab bench) and the measurement to be made without the need for holding the sample or the unit during the course of the analysis. Samples can be in transparent sample bags or measured directly. The data are obtained approximately 1mm below the contact

surface, which assures minimum contribution of the container itself and maximizes the Raman signature of the sample.

For testing and identification of solid dosage forms, a **Tablet Holder** is available, giving a larger spot size than the **Point and Shoot Adaptor**, thus a more representative measurement on the sample surface (over few millimeters, instead of hundreds of microns). The tablet holder provides reproducible positioning of a pill or tablet and is covered; both features are key for data reproducibility. This type of accessory is ideal for measurements based on chemometrics, such as those used for robust, rapid identification methods with results reported as the p-value.[4]

When customers are running samples in the field, we always recommend contemplating the location in which they want to measure the material. B&W Tek provides a set of simple but effective tools to allow you to obtain the best information for various analysis environments. To analyze a plastic container and its content, it is possible to identify the plastic of the container itself with the **Point and Shoot Adaptor** and to identify the content by simply changing the shaft and the same accessories or using the bottle adaptor without the need to change the shaft. These options are very simple but extremely effective.

The versatility of having specialized sample accessories enhances the utility of handheld Raman spectroscopy for all sample types without having to compromise data quality with a "one size fits all" approach. The sample accessories are readily interchangeable without the need for any tools. Portability of Raman spectroscopy is essential for its application at the point of material and sample receipt and is a key advantage of this instrumentation along with its nondestructive nature and the high information content of Raman spectra, allowing for rapid sample identification.

References:

1. D. Yang and R. J. Thomas, "The Benefits of a High-Performance, Handheld Raman Spectrometer for the Rapid Identification of Pharmaceutical Raw Materials", American Pharmaceutical Review, December 6, 2012. http://www.americanpharmaceuticalreview.com/Featured-Articles/126738-The-Benefits-of-a-High-Performance-Handheld-Raman-Spectrometer-for-the-Rapid- Identification-of-Pharmaceutical-Raw-Materials/

2. E. Lozano Diz and R. J. Thomas, "Portable Raman for Raw Material QC: What's the ROI?", Pharmaceutical Manufacturing, January, 2013. http://www.pharmamanufacturing.com/articles/2013/006.html?page=1

3. Radhakrishna S Tirumalai, Ph.D., <1072> "Disinfectants and Antiseptics", Pharmacopeial Forum: Volume No.30(6) http://www.drugfuture.com/Pharmacopoeia/usp32/pub/data/v32270/usp32nf27s0_c1072.html

4. Katherine A. Bakeev and Robert V. Chimenti, "Pros and cons of using correlation versus multivariate algorithms for material identification via handheld spectroscopy", European Pharmaceutical Review online White Paper, July 15, 2013. http://www.europeanpharmaceuticalreview.com/19813/whitepapers/material- identification-using-handheld-spectroscopy/

A version of this work was originally published by European Pharmaceutical Review online September 1, 2014: https://www.europeanpharmaceuticalreview.com/whitepaper/26479/sampling-guidelines-handheld-raman-measurements-need-know/#.VA9m-PldWSp

