ROBUSTNESS OF THE ASSURx® G7 HANDHELD RAMAN ANALYZER

APPLICATION NOTE RAMAN-010 (A4)

Contents

Abstract

Handheld Raman Analyzers are commonly used in pharmaceutical manufacturing processes to inspect and verify incoming raw materials. While there can be a wide variety of material suppliers and a vast array of packaging materials that can be used to contain the raw materials, it is important that a Handheld Raman Analyzer used for raw material verification, be able to make a verification analysis, in light of these varying conditions.

This application note describes the robustness of the ASSURx G7 analyzer to be able to positively verify raw materials, from a variety of lots, grain sizes and different suppliers. This application note will also demonstrate the ASSURx G7 analyzer's robustness with various packaging materials and container wall thicknesses. The ASSURx G7 analyzer will show that materials added to its library using one packaging material, can be used to accurately verify the material in a variety of different packaging materials and container wall thicknesses. The high robustness of the ASSURx G7 analyzer ensures raw materials can be correctly verified, whether they are from different suppliers, or in different packaging.

Introduction

It is important for a Handheld Raman Analyzer to be able to create a custom library of raw materials it intends to verify, and be assured that the methods in this library can correctly verify this material whether it comes from different lots, suppliers, or is contained in different packaging. When a Raman analyzer can correctly verify materials under these varying conditions, it is said to be highly robust.

Robustness can be measured by the Raman analyzer's propensity to give false negatives (i.e. to not verify the material positively, when it should). An analyzer with high robustness, will produce no/low false positives. An analyzer with low robustness, will produce high false positives.

In this application note, the ASSURx G7 analyzer robustness to material supplier, packaging material and container-wall thickness will be determined.

Methods and Results

Experiment 1: Robustness to Material Supplier, Grain-Size and Lot Differences

Method:

In the first experiment, eleven different sugars (sucrose samples) were obtained from unique manufacturers and distributors. All the sugar samples were sucrose: $C_6H_{12}O_6$. One of the sucrose samples, 365 Powdered Sugar, was first scanned into the ASSURx analyzer library. Then this method, based on the 365 Powdered Sugar sample, was run against each of the remaining different sucrose samples to determine if the ASSURx analyzer could correctly verify the other sugars. Each sugar was verified three separate times.

Figure 1. Sugar (sucrose) samples

Results:

A table of the Hit Quality Index (HQI) scores for each of the different sugars run is presented in Figure 2. An HQI of 0 indicates no match, and an HQI score of 1 is considered a perfect match. An HQI score >0.8 is considered a passing material match. The results show that despite the different sucrose samples having different suppliers, lots and grain sizes, they could still all be verified as sucrose using the Library entry created using 365 Powdered Sugar.

Sample	HQI 1	HQI 2	HQI 3
365 Cane Sugar	0.980	0.984	0.974
Caster Sugar	0.986	0.987	0.987
C&H Baker's Sugar	0.983	0.989	0.980
Great Value Pure Sugar	0.986	0.982	0.982
C&H Pure Cane Sugar	0.974	0.982	0.967
Essential Everyday Granulated Sugar	0.963	0.947	0.950
Crystal Sugar Granulated	0.980	0.988	0.986
Crystal Sugar Granulated	0.986	0.968	0.974
365 Organic Cane Sugar	0.932	0.950	0.934
Trader Joe's Organic Sugar	0.957	0.953	0.948
365 Powdered Sugar	0.979	0.977	0.975

Figure 2. HQI Results from analyzing sucrose samples

The ASSURx G7 analyzer's demonstrated it was highly robustness using one sample method, to correctly verify different material supplier, different lots, and different grain sizes. This robustness with one library entry is beneficial in method development to reduce the time it takes to create a custom material library.

Experiment 2: Robustness to Packaging Materials

Method:

In this second experiment, methanol (MeOH) is used in various packaging materials to determine the robustness of the ASSURx G7 to be able to verify materials measured in one container material, and verified in another. The experiment measured methanol samples in: 1) clear glass vials, 2) Amber glass vial, 3) high-density polyethylene vial, 4) brown-colored, thick-glass bottle, and 5) clear, thick-glass bottle. The library scan was made using methanol in a clear glass vial.

Results:

Figure 3 below shows the HQI scores when running the MeOH method from the clear glass vial, on methanol samples in the various different packaging materials. The results show that the ASSURx analyzer could correctly verify (HQI >0.8) the methanol using the method created with the clear glass vial, for all the other methanol packaging materials shown. For the HDPE, brown bottle, and thick glass bottle, these required a longer working distance lens accessory that is provided with the ASSURx G7 analyzer. But again, the ASSURx G7 analyzer is robust to various packaging materials.

Container	MeOH HQI	Comments
Clear vial	0.958	Vial accessory
Amber vial	0.958	Vial accessory
HDPE	0.951	Long working distance lens, with light shielding
Brown bottle	0.954	Long working distance lens, with light shielding
Thick glass bottle	0.956	Long working distance lens, with light shielding

Figure 3. HQI scores when running the MeOH method

The ASSURx G7 analyzer's demonstrated it was highly robustness using one sample method, to correctly verify the material in different packaging. This robustness with one library entry for various packaging materials is beneficial in method development to reduce the time it takes to create a custom material library, and instills confidence that variations in package material will not adversely affect the ASSURx G7 analyzer's ability to make a correct material verification.

Experiment 3: Robustness to Different Packaging Thicknesses

Method:

In this third experiment, the effect of increasing package thickness on the ASSURx G7 analyzer's ability to correctly verify materials is investigated. Acetaminophen powder is used as the sample. Progressively more sheets of transparent Low-Density Polyethylene (LDPE) are added between the ASSURx G7 analyzer and the sample, and the HQI score is recorded as a function of package material thickness.

Results:

Figure 4 below shows the effect of the LDPE thickness on the ASSURx G7 analyzer's HQI score, for two different sampling lenses tested: 1) Surface/Contact Lens (Red), and 2) Long focal length lens (blue). For the Surface/Contact Lens, after four layers of LDPE (~2 mm thickness, since each layer is approximately 0.5 mm thick), it can be seen that the HQI scores falls below 0.9, and after about six layers (~3 mm), the material verification fails (HQI <0.8).

For the Long Focal Length Lens, it can be seen that the HQI scores fall below 0.9 after 12 layers (~6 mm), showing that the long focal length lens is good for thicker packaging materials.

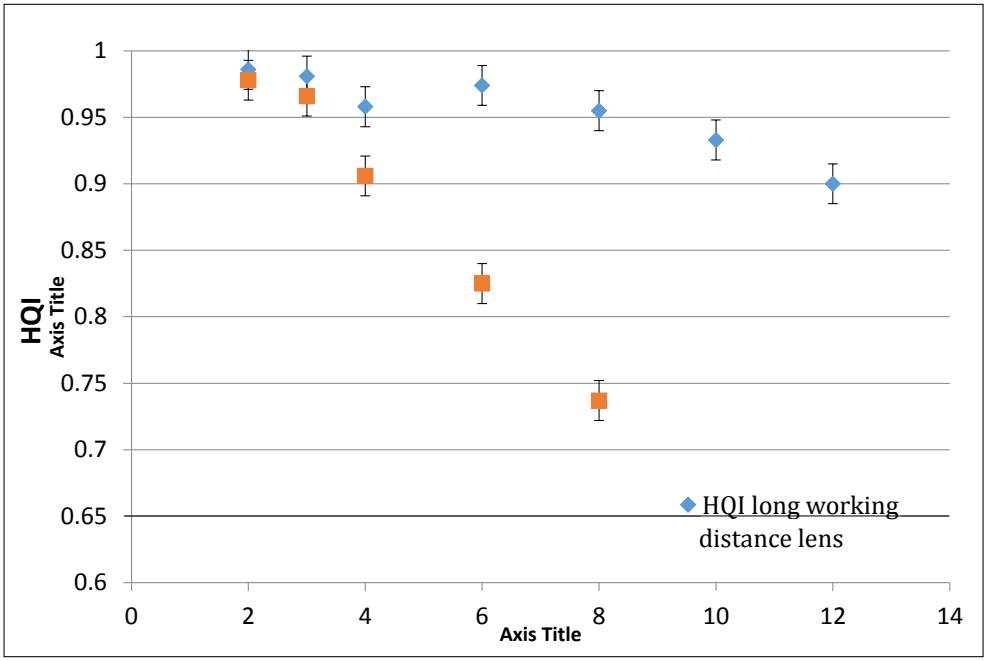

Figure 4. LDPE plastic layers between sample and lens

The results show that the Surface Contact lens is good for transparent packaging material up to ~2 to 3 mm thick, while the Long Focal Length Lens is good for making measurements through packaging material ~6+ mm thick.

While it is necessary to change sampling tips to suit the material packaging thickness, the ASSURx G7 analyzer demonstrated it can be used to accurately verify material through thick and thin packaging materials.

Conclusions

This application note showed that the ASSURx G7 analyzer is a robust handheld Raman analyzer for the verification of materials. A single ASSURx G7 analyzer method was shown to work with different material suppliers, lots and grain sizes. A single ASSURx G7 analyzer method was shown to work with different packaging materials, from plastics, to glass, to colored packaging. With various sampling tips that can focus the Raman measurement to either a shallow (0-2 mm) or deep (0-6 mm) range, the ASSURx G7 analyzer can measure through thin and thick packaging. As a result of the high robustness of the ASSURx G7 analyzer, QC professionals can be assured their material verification measurements are going to be accurate. Furthermore, with the high robustness of single ASSURx analyzer methods, library development time can be minimized.

TSI Incorporated – Visit our website www.tsi.com for more information.

USA	**Tel:** +1 800 874 2811	**India**	**Tel:** +91 80 67877200
UK	**Tel:** +44 149 4 459200	**China**	**Tel:** +86 10 8219 7688
France	**Tel:** +33 1 41 19 21 99	**Singapore**	**Tel:** +65 6595 6388
Germany	**Tel:** +49 241 523030		

RAMAN-010 Rev. A (9/25/2018) A4 Printed in U.S.A.