Application Note

Biopharmaceuticals

# Rapid Testing of Solvents Through Amber Bottles using an Agilent Vaya Handheld Raman Spectrometer

## Raw material identification using Vaya with spatially offset Raman spectroscopy (SORS) technology


**Authors**

Aveline Neo and
Christopher Welsby
Agilent Technologies, Inc.

## Abstract

The Agilent Handheld Vaya Raman spectrometer is a pharmaceutical analysis system that can be used to perform material verification of a range of chemical solvents through amber bottles. Using spatially offset Raman spectroscopy (SORS) technology, Vaya can perform through-barrier identification tests and produce easily interpretable "pass/fail" results on the screen of the handheld device. The solvents tested in this study are commonly used in the synthesis of some biopharmaceuticals or during analytical testing of the quality attributes of biologics throughout the production process. Data are provided that demonstrate how the Vaya Raman can be used for rapid verification testing of raw materials in a warehouse, without the need to open any bottles.

## Introduction

Biopharmaceuticals are biotherapeutics that are typically produced using biotechnology rather than extracted directly from a non-engineered biological source. They encompass a large collection of different products from recombinant proteins and nucleic acids (DNA, RNA, or antisense oligonucleotides) to monoclonal antibodies (mAbs). To produce these types of biologics, a cell is used as a production plant and, so, during purification of the cell, proteins from the host cells are co-purified.

During the manufacturing processes of biologics, product impurities or host-cell proteins as well as protein aggregation are some of the critical quality attributes that are monitored. Organic solvents such as methanol, ethanol, isopropanol, acetonitrile, and toluene are often used during synthesis of biologics or analytical testing of the quality attributes throughout the manufacturing processes. As quality starts with the raw materials and process reagents, variability in raw materials or contamination of reagents can impact on the characteristics and quality of the final drug products.

Raw material identification (RMID) is an analytical qualitative test that is used to identify or verify the identity of a chemical entity used for drug product manufacturing processes. Currently, this test can be performed in a warehouse or a quality control (QC) lab, and a qualitative pass/fail outcome is usually acceptable.

According to ICH requirements for raw materials[1], biopharmaceutical manufacturers must carry out raw materials identification before use. Raman spectroscopy is widely used in the industry as it provides identity verification of raw materials directly, without the need to open sample bottles or containers.

In this study, an Agilent Vaya Raman spectrometer with SORS technology (Figure 1) was used for the verification and differentiation of solvents in amber bottles. The solvents are often used during the analytical analysis of biologics such as mAb and for the synthesis of oligonucleotides. Vaya can perform a qualitative test of the solvents directly through amber bottles within a few seconds. The noninvasive method allows an operator to receive, test, and release large batches of raw materials quickly and conveniently.


**Figure 1.** The Agilent Vaya Raman handheld spectrometer with SORS technology being used to identify materials/solvents through an amber bottle.

## Experimental

Methanol, ethanol, isopropanol, acetonitrile, and toluene in amber glass bottles were bought from Sigma-Aldrich. To demonstrate the identification (ID) of the solvents using the Vaya Raman, an ID verification method was developed for each solvent. The methods were developed using the method development wizard and standard settings (specific to amber glass containers) accessible from the handheld spectrometer. Apart from information on the container type, which is provided by the operator, the Vaya system automatically sets all the other acquisition parameters.

A performance qualification test was performed before acquisition of the SORS spectra. Each ID verification method was used to generate the spectral data presented in this application note. No additional data processing was performed beyond the automated baseline correction that is part of the normal analysis protocol for the Vaya. All measurements were performed in normal ambient light conditions.

## Results and discussion

Raman spectra for the five solvents in amber bottles are shown in Figure 2. Distinct spectra were observed for each solvent.

- Methanol has a very strong band at 1,033 $cm^{-1}$, which corresponds to C-O stretching, and another distinctive peak at 1,464 $cm^{-1}$ that corresponds to $CH_3$ d-deformation.[2]
- The ethanol spectrum has one strong band at 886 $cm^{-1}$, which is assigned to C-C stretching, and two small bands at 1,050 and 1,098 $cm^{-1}$, which are assigned to C-O stretching and $CH_3$ rocking, respectively.[2,3]
- Isopropanol has a strong band at 820 $cm^{-1}$ due to the C-C-O band. Two other smaller bands at 954 and 1,454 $cm^{-1}$ represent C-O stretching and $CH_3$ bending, respectively.[4,5]
- Acetonitrile has a strong band at 921 $cm^{-1}$, which is indicative of the C-C skeletal vibration mode.[6]
- Toluene has two distinct bands at 1,001 and 1,032 $cm^{-1}$, corresponding to ring stretching.[7]

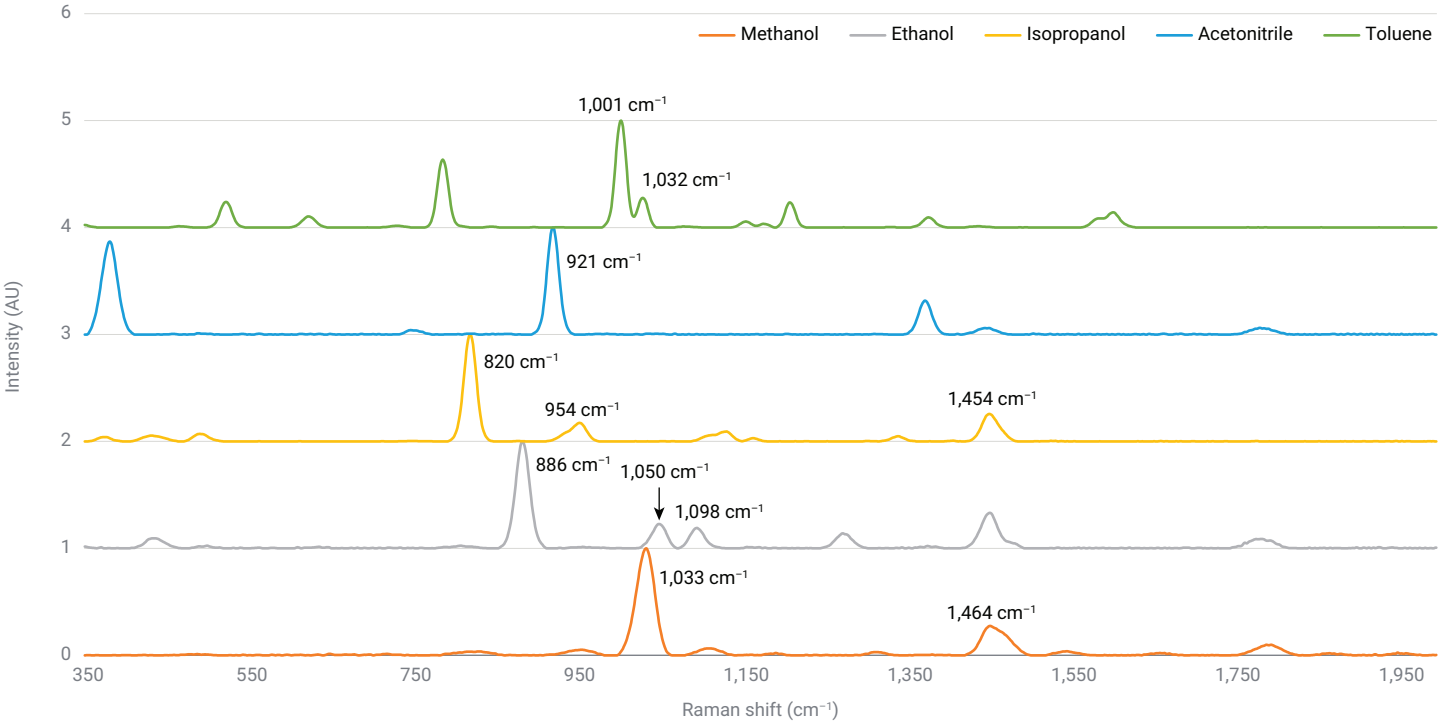


**Figure 2.** Agilent Vaya Raman SORS spectra of methanol, ethanol, isopropanol, acetonitrile, and toluene. These solvents are often used during the analytical analysis of mAbs or synthesis of oligonucleotides.

### Evaluation of the ID test methods

An ID test was conducted for each of the solvents in an amber bottle using the ID verification method developed for each analyte. Figure 3 shows a challenge matrix that represents graphically how an ID test differentiates and verifies the identity of the different solvents.

A viable challenge matrix will show a high pass rate along the matrix diagonal (as shown in Figure 3), which indicates that the method correctly recognizes its corresponding material. Off the diagonal, the challenge matrix should display only pass score rates of below 0.1 to indicate that the method rejected the incorrect analytes.

For all the solvents tested, the Vaya Raman SORS spectrometer showed excellent selectivity, and correctly identified each of the analytes.

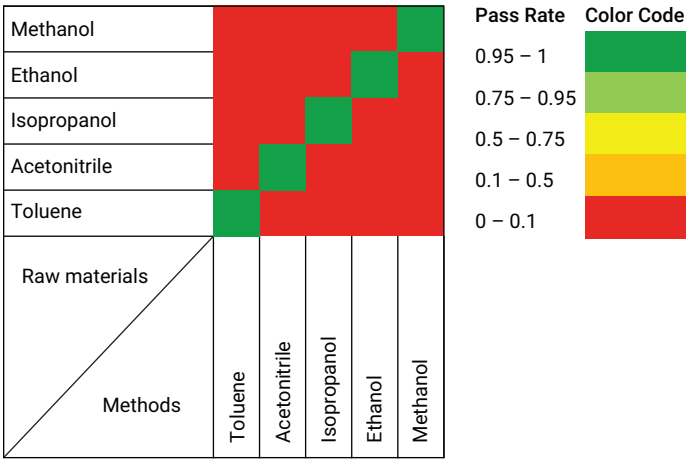


**Figure 3.** Identification of methanol, ethanol, isopropanol, acetonitrile, and toluene using a SORS challenge matrix.

## Conclusion

An Agilent Vaya Handheld Raman spectrometer with SORS was used for the selective identification of solvents that are commonly used in biopharmaceutical processes. This technique allowed the direct measurement of the solvents in amber glass bottles. There was no need to open the bottles for sampling, avoiding the possibility of sample contamination and speeding up the analysis.

Sufficiently good quality spectra were obtained for each solvent through the amber bottles in less than 35 seconds. The spectra were then used to successfully differentiate each solvent from other solvents in the same material class.

With fast analysis times and the ability to measure materials directly through amber bottles, the handheld Vaya Raman is ideally suited for ID testing of large quantities of biopharmaceutical raw materials.

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