

Raw Material Identity Verification in Sterile Manufacturing Using the Agilent RapID Raman System



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Abstract

Avoiding contamination in the manufacture of parenteral, intravenous, and other sterile products is essential. However, verifying the identity of incoming materials typically involves opening the packaging and exposing both the contents and the operator. The Agilent RapID Raman system verifies material identity through unopened nontransparent containers. This Application Note highlights the ability of the RapID system to analyze materials typically used in sterile manufacturing without compromising the container's seal.

Introduction

For raw materials received at pharmaceutical manufacturing plants, identity testing is both mandatory and highly resource intensive. Often, the materials must be stored in quarantine before being opened in a sampling booth, tested or sampled and then resealed. Avoiding this expensive and time-consuming process used to be impossible for most incoming goods testing, until the launch of the Agilent RapID noninvasive materials verification system.

The RapID system enables material verification through unopened sacks, tubs, bottles, FIBCs, and plastic barrels—in fact, most nontransparent or colored materials such as paper, plastic, glass, and multilayer sacks. When supplied as powders or liquids in opaque containers, spectroscopic identification is often impossible without exposing the contents. The RapID system speeds up testing by enabling identity verification in the warehouse without using containment facilities. Another benefit is that the container remains sealed, avoiding contamination of the product. For incoming raw materials testing, this means that it is not necessary to sample the containers, making 100 % inspection cost-effective.

Preventing contamination is particularly important in injectable and intravenous product manufacture as the costs of downtime and lost production can be significant. By using Agilent spatially offset Raman spectroscopy (SORS)¹ technology the container can remain closed and still verify the content's identity reliably.



Agilent RapID Raman system.

Experimental

Several typically used parenteral ingredients were analyzed with the RapID system through the original unopened packaging.

Results and Discussion

The data shown are the SORS model spectra obtained for the material used for identity verification. For routine identity testing using RapID, the spectra are not displayed, but a pass/fail is used based on a correlation with the model spectrum. The verification can be performed in an office or in a warehouse, and does not require sterile or laboratory conditions.

Liquid Materials

Liquids such as phenol, benzyl alcohol, and *m*-cresol are commonly used in parenterals manufacture. They are chemically similar, and are typically supplied in 1 or 2-L brown glass bottles. These small containers mean that the number of bottles received annually is often very high—potentially thousands per year. Figure 1A shows the spectra obtained through brown glass bottles in 5–7 seconds. They are correctly verified in 100 % of the validation and test measurements.

Other liquid excipients such as ethanol, glycerol, and 1,2-propanediol may be supplied in plastic barrels. These materials are difficult or impossible to analyze spectroscopically by near infrared (NIR) or conventional handheld Raman instruments. Figure 1B shows the spectra obtained through opaque plastic barrels.

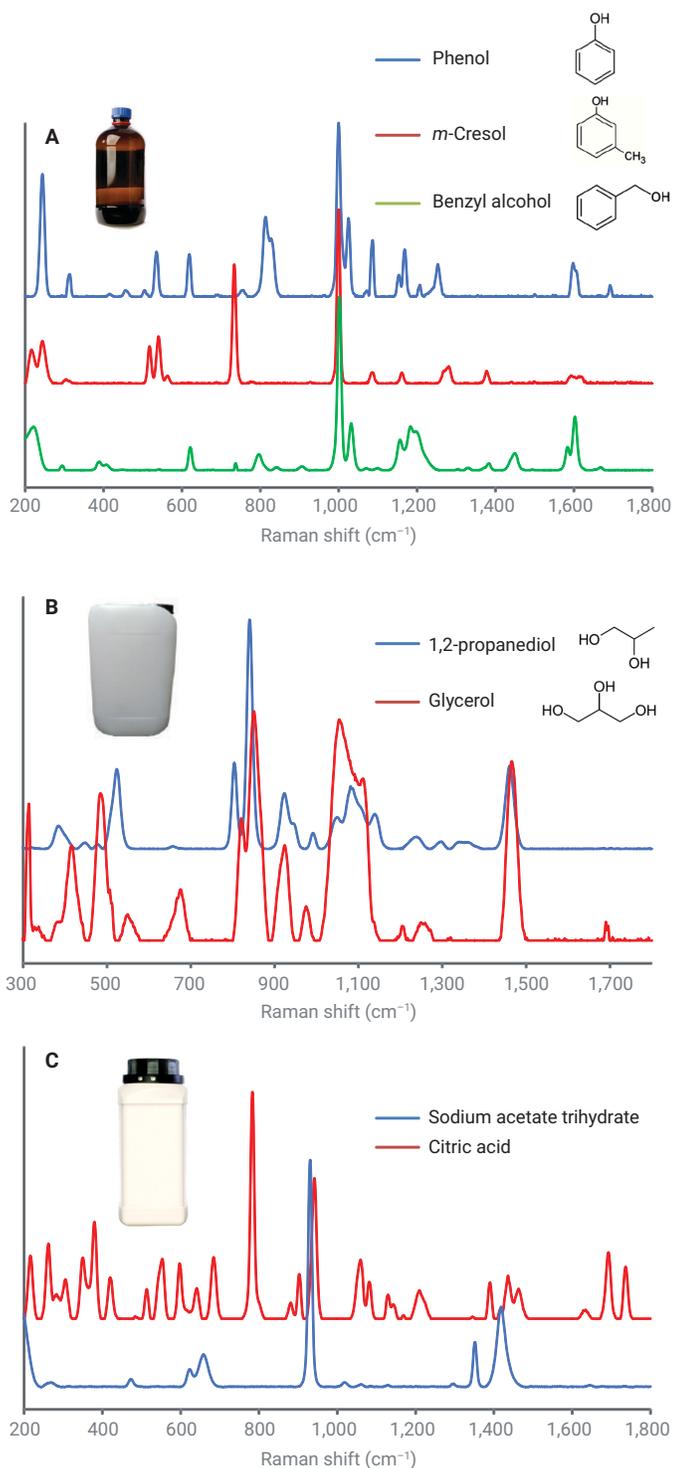


Figure 1. SORS spectra of common materials through their containers. Y-axes are normalized. In 1A and 1B, the materials may be supplied in similar containers, and are chemically similar.

Solid Materials

Salts are often used in injectable products. Monatomic ionic compounds do not have a Raman spectrum unless they are chemically bound with water, so sodium chloride (NaCl) cannot be detected by conventional Raman spectroscopy. However, magnesium chloride hexahydrate ($\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$) and calcium chloride dihydrate ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$) can be identified through unopened paper and plastic sacks. Generally, solids can be measured through plastic/paper sacks (for example, citric acid) and HDPE bottles (for example, sodium acetate trihydrate), as shown in Figure 1C.



Figure 2. Verification through a nontransparent plastic sack.

Table 1. Solid materials identified through their container using an Agilent RapID system.

Material	Container	Agilent RapID analysis time
Phenol, benzyl alcohol, <i>m</i> -cresol	Brown glass bottle	5–7 seconds
Citric acid, $\text{MgCl}_2 \cdot \text{H}_2\text{O}$, $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$	Plastic/paper sacks	10–15 seconds
Propane-ols, ethanol	Plastic barrel	10–15 seconds
Sodium acetate trihydrate	HDPE bottle	10–15 seconds
Acetic acid	Plastic bottle	10 seconds

Conclusions

The Agilent Rapid Raman system successfully and quickly verifies the identity of many commonly used materials without compromising the container's seal, preserving sterility. Analysis times are fast, and verification is robust and repeatable through a wide range of different packaging types.

Reference

1. Non-invasive identification of incoming raw pharmaceutical materials using Spatially Offset Raman Spectroscopy, *JPBA* **2013**, 76, 65–69.

www.agilent.com/chem/raman

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