Application Note

Raw Material Identification

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Raw Material Identity Verification in Biopharmaceutical Production Using the Agilent RapID Raman System

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Abstract

Biological compounds derived from living cells offer exciting possibilities for treatment of a growing number of medical conditions. Most biologically derived proteins cannot be terminally sterilized and must be produced under aseptic conditions. This Application Note describes the use of spatially offset Raman spectroscopy (SORS) and the Agilent RapID Raman system for verifying common starting materials in biological production without compromising sterility.

Introduction

The last decade has seen a growing shift from traditional, small molecule active pharmaceutical ingredients to large molecules derived from living cells, such as monoclonal antibodies (mAb) and proteins. Growth in biological production, currently around 10 % per year, is being driven by the exhaustion of small molecule targets for new therapies. Biopharmaceutical manufacturing must be aseptic, and requires a large range of starting materials, including growth media, solvents, denaturants, buffering agents, and preservatives. Typically supplied as a bulk dry powder, growth media are proprietary blends of carbohydrates, amino acids, vitamins, minerals, and buffers. Opening the container for raw materials testing exposes the media to atmospheric moisture and, potentially, microbial contamination, which could affect yields, potency, and safety.

Experimental

Raman spectroscopy can be an excellent method to differentiate between complex mixtures. However, conventional Raman systems are limited to measuring powders in clear bags or glass vials, requiring containers to be opened and sampled for many materials. The Agilent RapID system uses spatially offset Raman spectroscopy (SORS) to acquire a Raman spectrum through the container for quick and noncontaminating ID verification (Figure 1 and Table 1).

Table 1. Example materials and containers with typical analysis time for identification through the container.

Material class	Example materials	Containers	ID Time
Tween	Polysorbate 20, 40, 60, and 80	Amber glass	20 s
Buffers	HEPES, MOPS, CAPS, Tris	White HDPE, Tyvek	10 s
Media blends	Dulbecco's Modified Eagle's Medium	White HDPE, Tyvek	10 s
Carbohydrates	Mannitol, dextrose, maltose, sorbitol	HDPE sacks	10 s

Figure 1. RapID verification system identifying a material through a plastic container.

Results and Discussion

Figure 2 shows the SORS spectra of two chemically similar media blends acquired through a white HDPE bottle. The blends differ only in their proportions and type of amino acids present, but the RapID system can differentiate them easily.

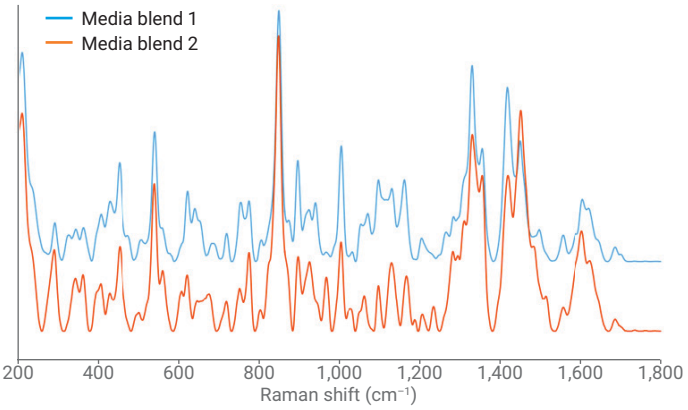

Figure 2. Similar media blends, differentiated through an unopened white HDPE container.

Environmentally sensitive materials

If a sample is opened for identity verification and cannot be used immediately, its shelf life may be affected. Polysorbates (Tween) may react with atmospheric oxygen and lead to the formation of peroxides, which could lower product yield. Polysorbates 20 and 80 are used universally throughout the manufacture of mAbs, antibody drug conjugates (ADCs), and vaccines as a surfactant to prevent protein aggregation, and are typically supplied in amber glass bottles under nitrogen. Figure 3 shows comparison SORS spectra from polysorbate 20 and 80 acquired through unopened amber glass bottles. The spectra are easily differentiated, preventing misidentification.

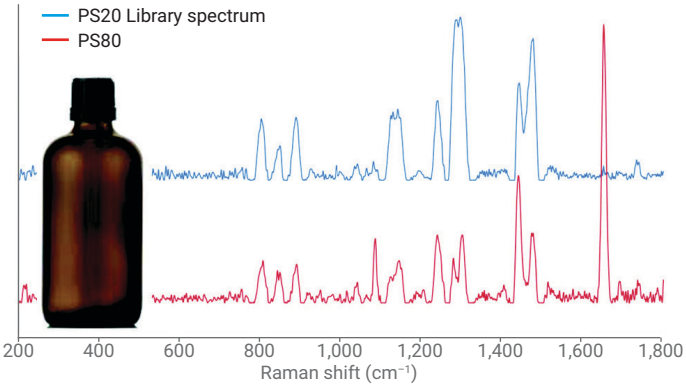

Figure 3. SORS spectra of Tween 20 and 80 through unopened brown glass containers. The samples are stored under nitrogen for stability.

Buffering agents

There are a wide variety of buffering agents, including organic compounds such as HEPES, MOPS, and CAPS. *Tris*(2-amino-2-hydroxymethyl-propane-1,3-diol, THAM, tromethamine) is commonly supplied in large volumes in Tyvek sacks or in white HDPE tubs for small volumes. Identification of the form (acid or salt) is important due to their different effects on buffering. However, opening the container could expose the contents to microbial contamination. Tyvek (woven HDPE fibers) has a strong Raman spectrum, preventing identity verification of the contents by conventional Raman systems. Requiring only 10 seconds per container, the RapID system is able to acquire and differentiate pure Tris base and HCl irrespective of the opaque containers in which they are supplied (Figure 4).

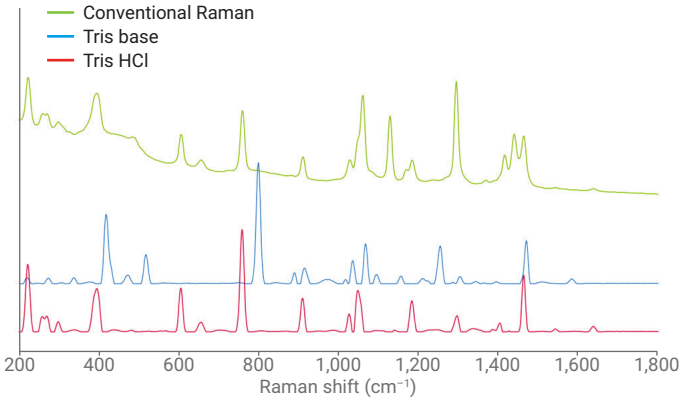

Figure 4. Comparison of conventional Raman of Tris HCl in a white Tyvek sack and SORS spectra of Tris variants.

Conclusions

The Agilent RapID Raman raw material identity verification system can quickly identify a range of biopharmaceutical starting materials through unopened containers. With no sampling step for raw materials, quality control can avoid shelf-life and storage issues, and reduce potential contamination risks.

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