Application Note
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Identifying Raw Materials Directly Through Paper Sacks

Using a hand held Vaya Raman spectrometer to reduce the time associated with identifying materials

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Introduction

Papers sacks are often used as primary or secondary containers for raw materials employed in the manufacturing of pharmaceutical products. Their enduring popularity continues, as they can easily be disposed of or be recycled to minimize the impact on the environment. They are also the most cost-effective way to package and ship high-volume raw materials. Excipients like lactose monohydrate, mannitol, microcrystalline cellulose, and sucrose are often supplied to pharmaceutical manufacturers in multilayer paper sacks.

The Agilent Vaya Raman system is a handheld spectrometer capable of identifying raw materials through transparent and opaque containers to simplify and accelerate the receipt of raw materials in GMP environments.

This application note highlights how the Vaya instrument can be used for the identification of raw materials through paper sacks in a pharmaceutical warehouse.

Magnesium stearate, microcrystalline cellulose (MCC), mannitol, sucrose, and lactose monohydrate are commodities often used as fillers or excipients for oral solid dosage. These materials are typically received in paper sacks for easy handling and discarding.

At receipt and before use, these excipients must have their identities verified in compliance with regulatory requirements.

On arrival, the excipients in paper sacks are unloaded from the truck and moved to a quarantine area in the warehouse. Following a visual inspection, up to 100% of the received paper sacks are moved to a sampling booth where they are opened and sampled. Next, the samples are analyzed either directly in the booth with a handheld Raman or NIR system, or they are sent to a QC lab for analysis with FTIR or wet chemistry methods. Once sampled/analyzed, the paper sacks are sealed and moved back to the quarantine area to await approval for release to production stock. This process is time and resource intensive and can take days to complete (see Table 1).

Table 1. Time required for FTIR and conventional handheld Raman tests for identity verification of 200 paper sacks of lactose monohydrate.

		Process Hours with:	
Department/Task		**FTIR Performed in the Lab**	**Conventional Raman Handheld in the Sampling Booth**
QC	Preparation of sampling container labels	0.5	0.5
Warehouse	Movement of containers from quarantine area to sampling booth	0.5	0.5
QC	Paper sack opening	1.5	1.5
QC	Sampling	1	1
QC	Paper sack resealing	10	10
Warehouse	Movement of containers from sampling booth to quarantine	0.5	0.5
QC	Confirmation test	33.5 (counting waiting time)	1.7
Total		47.5 hours (Booth cleanup not included)	14.7 hours (Booth cleanup not included)

Figure 1. Using a Vaya Raman instrument to identify contents through a multilayer paper sack.

Verifying through paper sacks

The Vaya instrument uses spatially offset Raman spectroscopy (SORS), a unique Agilent solution, to verify the identity of raw materials through unopened nontransparent containers like paper sacks. Testing can be performed directly in a quarantine area.

SORS uses a pharmacopeia method— using the chemically-specific fingerprint to identify a raw material inside the container. Using the property of photon propagation inside diffusively scattering media, SORS generates a container-free Raman spectrum of the raw material to enable verification against a known reference.

Experimental

To demonstrate the performance of the Vaya instrument, SORS spectra of a variety of excipients were acquired through paper sacks and compared against their respective references acquired through thin polyethylene liners. The excipients magnesium stearate, microcrystalline cellulose, sucrose, and mannitol were used. All products were supplied by Sigma-Aldrich UK. SORS spectra were acquired for each material in two types of sacks: a three-layer paper bag (one white outer layer, two brown inner layers with a polyethylene liner) from DFE Pharma, Goch, Germany and a two-layer brown paper bag with a polyethylene liner from Meggle Group, Wasserburg, Germany. Scan time for each SORS spectrum was recorded. Reference spectra were acquired in conventional back-scattering mode by measuring a thin polyethylene liner. This reference spectrum was then subtracted from the sample spectrum to eliminate any container contribution to the reference spectra.

Results and discussion

SORS can identify materials through paper bags

Figure 1 shows how the "polyethylene plastic liner" (i.e., reference) spectra can be easily overlaid with their corresponding "through paper bag" or SORS spectra for all excipients in both paper sacks. By producing a content spectrum free of container interferences, the Vaya instrument can easily verify the identity of a raw material through multilayer paper bags.

Vaya can identify large batches in hours rather than days

Table 2 lists the scan and process times for the verification test performed for each excipient. The Vaya instrument can verify identity through multilayer paper sacks in 90 seconds or less. Using this approach in quarantine reduces the identity verification process time by a factor of >3 when compared with conventional Raman handheld systems in a warehouse and by a factor of >9 for FTIR in a QC lab. Time-consuming steps like paper sacks sealing, sampling booth cleanup, and container handling are eliminated.

Using the Vaya instrument for excipient analysis in paper sacks enables warehouses to shorten their material identity verification process and release materials the day they are received.

Figure 2. Sucrose and mannitol through a DFE sack, MCC and lactose monohydrate through a Meggle sack. SORS spectra overlaid with sucrose, mannitol, MCC, and lactose monohydrate Raman spectra through a polyethylene liner.

Table 2. Typical scan time for each raw material in Meggle and DFE paper sacks, with process hours in comparison to process hours by FTIR or conventional Raman.

				Time Reduction Factor in Comparison with:*	
Excipients	**Typical Scan Time**	**Containers**	**Total Hours**	**Conventional Raman devices**	**FTIR in QC**
Lactose monohydrate	1 min 20 s	DFE bag	4.4	× 3.5	× 10.7
Lactose monohydrate	1 min	Meggle bag	3.3	× 4.7	× 14.3
MCC	1 min 20 s	DFE bag	4.4	×.3.5	× 10.7
MCC	1 min 30 s	Meggle bag	5.0	× 3.1	× 9.5
Sucrose	45 s	DFE bag	2.5	× 6.3	× 19.0
Sucrose	30 s	Meggle bag	1.7	× 9.4	× 28.5
Mannitol	40 s	DFE bag	2.2	× 7.1	× 21.4
Mannitol	35 s	Meggle bag	1.9	× 8.1	× 24.4

** Time reduction factor is calculated by assuming that total hours for the identification process are independent of which raw material is being measured with conventional Raman devices and FTIR. The total time for identifying lactose monohydrate (from Table 1) has been used as the basis for these calculations..*

Vaya can identify material directly in quarantine and bypass the sampling room

Using a Vaya instrument, the integrity of the paper sacks is preserved during the analysis. Materials can be identified outside the sampling booth. The approach also eliminates the need for costly consumables like disposable booth garbs and sampling utensils such as vials and thieves. The Vaya instrument enables QC to identify raw materials at the lowest cost possible.

Conclusions

The Vaya Raman system can accelerate the receipt of raw materials by enabling identity verification through transparent and nontransparent containers in the quarantine area. By avoiding opening paper sacks, Vaya can reduce the time taken for receipt of large volume excipients to a matter of hours rather than days, reducing the cost of testing.

References

1. EU GMP Annex 8: Sampling of Starting and Packaging Materials
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