

Identifying Raw Materials Inside Containers Using a Handheld Raman Spectrometer

Reducing the cost of quality with the Agilent Vaya Raman system

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Overview

With profit margins in the pharmaceutical industry under ever increasing pressure, manufacturing groups are incentivized to achieve First Time Quality (FTQ) and reduce costs.

The identification of raw materials, a current Good Manufacturing Practice (cGMP) mandated process (1, 2), is typically resource- and time-intensive and therefore an excellent target for improvements and cost-out efforts.

The Agilent Vaya Raman system is a handheld spectrometer capable of identifying raw materials through transparent and opaque containers. This white paper discusses some of the benefits of deploying a Vaya system in a pharmaceutical warehouse, to simplify and accelerate the ID verification of raw materials at receipt.

To address ever-growing pharmaceutical supply chain challenges and maintain quality standards, regulatory bodies mandate the verification of raw materials before use in production. Up to 100% of all received raw material containers must be checked for identity.

For solid raw materials packaged in paper sacks, tubs, FIBC/ big bags, paper sacks, tubes, bottles, and barrels, ID verification is a multistep process. It starts by unloading raw materials from the truck and moving them to the quarantine area. There, after visual inspection, a proportion of all the containers (up to 100%) are moved to a sampling room. In the booth, after garbing up, an operator opens the container or secondary, outer packaging. The raw material is then verified directly through the transparent primary package using a conventional hand held Raman spectrometer. If this is not possible, the material is sampled to be analyzed using a Raman device, or sent to a QC lab for mid-IR/ NIR analysis.

For most QC labs, this protocol is time- and resource-intensive and therefore not cost effective. It is also not scalable or flexible enough to absorb increases in testing or new combinations of raw materials/ containers.

SORS

Spatially offset Raman spectroscopy (SORS) is a unique solution from Agilent Technologies that enables the verification of raw materials through containers. SORS improves the depth of penetration of conventional Raman spectroscopy. By leveraging the property of photon propagation inside diffusively scattering media and separating the laser illumination area from the light collection area, SORS can acquire a raw material-rich spectrum. A container-rich signal can be collected when the laser illumination and light collection areas coincide. The scaled subtraction of the container-rich spectrum from the raw material-rich spectrum yields a container-free raw material spectrum. This can be used for identifying pharmaceutical APIs and excipients directly through transparent or opaque containers. Raw materials can be identified without sampling or opening secondary, outer containers. SORS works with opaque packaging like paper sacks, FIBCs/ big bags, polyethylene tubs, drums and other containers.

The Agilent Vaya Raman system

The Vaya is a handheld SORS-based spectrometer from Agilent. The Vaya is the fastest handheld identity verification solution available. For example, it can verify lactose monohydrate in a three-layer paper bag in 80 seconds. Citric acid in a white HDPE bottle can be identified in 15 seconds with no sampling and no mess. It drastically simplifies the identification process by enabling almost instantaneous screening of incoming containers on arrival. The Vaya system can verify the identity of raw materials in quarantine with a single operator. Unnecessary movement of containers, sampling booth clean up, sampling consumables, and PPE for testing personnel are all reduced.

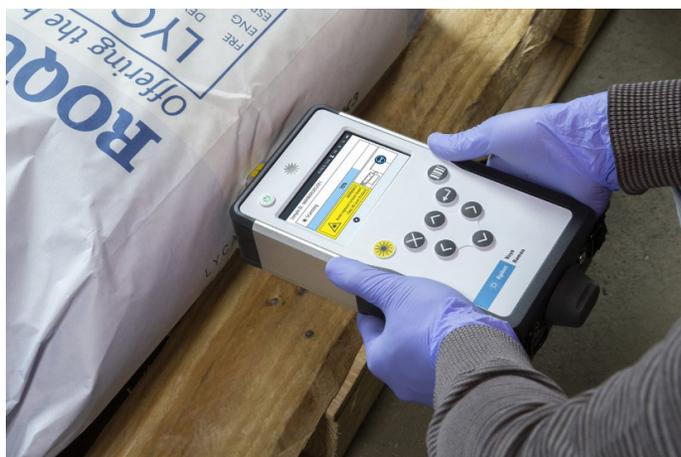


Figure 1. Vaya identifies raw materials through multilayer paper sacks.

Cost comparison between handheld Raman systems and Vaya

A small case study easily demonstrates the power of the Vaya system and how pharmaceutical manufacturers can benefit from true raw material identification at receipt.

In this study (see Table 1), a time/cost analysis comparing the Vaya system with a conventional handheld Raman system was carried out. The analysis was based on a medium-sized pharmaceutical organization receiving 150 consignments per month of raw materials, representing a total of 1200 samples per month (eight containers verified per consignment). Table 1 compares performing raw material identification tests using a Raman handheld device to performing the same tests using a Vaya system. In the warehouse, as per this company's materials receiving procedure, any ID tests requiring the opening of the container are performed in a sampling booth. When the ID test can be performed through the container with no container opening (using the Vaya), the analysis is conducted in the quarantine area. Only the staff hours are included in this study.

Table 1. Comparative cost study for identifying 1200 samples per month using a Vaya system versus a conventional handheld Raman system.

Task	Process Hours with		
	Vaya		Conventional Raman
	In quarantine	In booth	In booth
Number of samples ¹	720	480	1200
Container movements (15 min per raw material consignment moved to/from sampling booth)	0 min	900 min	2250 min
Container handling (1.2 min per container - opening, resealing, labeling)	0 min	576 min	1440 min
Scan time (Vaya in quarantine 0.75 min /Vaya in booth 0.45 min/ Conventional Raman 0.55 min per sample) ²	540 min	216 min	660 min
Sampling room (50 min prep and clean-up time per raw material consignment)	0 min	3000 min	7500 min
Total time per year in hours	1,047 Hours ²		2,370 Hours
Total cost per year ⁴	\$36,808		\$83,320
Cost-per-sample	\$2.5		\$5.80

Bypassing the sampling booth and decreasing container handling and movements lowers the cost-per-sample and the ID process time by 50% over a one year period. Using the Vaya system, daily arrivals of raw materials are easily manageable as testing only takes 35 min per consignment in this scenario. All received consignments can be mixed with production stock in less than 5 hours, in comparison to ~10 hours with a conventional handheld Raman solution. With a Vaya, raw materials can be made available for production on the same day they are received.

Increasing your throughput capability without increasing your costs

Regulatory requirements change, as do quality and testing needs. A Vaya system future proofs the identification protocol by keeping costs low even with high sample volumes. If the quality department requires an ID test on all containers (100% ID) to meet regulatory requirements in countries like Japan or Korea, costs would go up from \$36 K/year to \$74 K/year⁵ with a Vaya. If a conventional Raman system was being used, the costs would rise from \$83 K/year to \$142 K/year. A Vaya can achieve 100% ID at a cost lower than that for $\sqrt{N}+1$ testing performed with conventional Raman. If regulators require increased testing, a Vaya allows you to develop higher throughput testing without any additional equipment or people.

Increasing your throughput capability without increasing your costs

A Vaya can have a positive impact on less obvious expenses too. Using a Vaya in a warehouse helps decrease the stock levels needed to meet production requirements. Reduced stock means lower inventory carrying costs. Savings will depend on how frequently the inventory is used during the year and its cost. A simple reduction of 5% can translate to >\$5 K/year for an inventory stock worth \$0.75 M⁶ and immediate first year savings of >\$35 K.

Sampling booth expenses can also be reduced. In the booth, an operator is required to use a disposable garment at a cost of ~\$10 each., face mask ~\$0.2 each., disposable sampling utensil ~\$1.5 each⁷. These required items can quickly add up to a saving >\$10 k/ year. Use of other disposable items like cleaning accessories is also reduced with a Vaya.

By verifying ID directly through the container, a Vaya system helps preserve inert packaging conditions and maintain the expiration date of raw materials. For air sensitive materials like polysorbates, it means that materials can be fully used before the expiration date instead of being discarded. This alone can easily translate into savings >\$100 per tested container.



Figure 2. A Vaya verifies the identity of acetic acid in an opaque plastic carboy container.

¹Assumption: Vaya works through non-transparent containers, and this is assumed to be 60% of all incoming materials. For containers that do not work with Vaya, the ID is performed with Vaya in a booth, container opened through the plastic liner.

²Scan times derived from an average time to run weakly and strongly raman active raw materials through liners and non transparent containers.

³Sum of time for analysis performed in quarantine and in booth for Vaya.

⁴Operator annual salary: \$45K with 1.5 overhead multiplier.

⁵Assumption: The sampling booth is large enough to accommodate 40 containers. If not, additional container movements would need to be added.

⁶With a 15-20% inventory carrying cost.

⁷List prices.

Vaya return on investment

The study calculated a return on investment (ROI) when transitioning to a Vaya system over a four year period from a different handheld Raman solution. For the ROI calculation, deployment costs of the Vaya system, including preparation, method development/validation, were factored into the start-up costs. Over a four-year period, for an initial investment including method development/validation and startup costs of ~\$115 K in the first year, a Vaya had a net value of ~\$114 K or a 61% ROI⁸. If a Vaya system is purchased to address a transition to 100% ID, the ROI almost doubles to 107% with a net value of \$191 K. The Vaya system is therefore an effective investment to reduce the cost of raw material identification and address increased testing volumes without increasing costs.

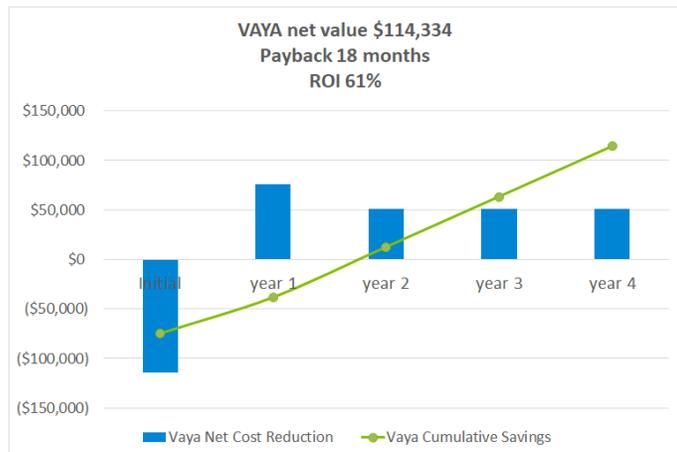


Figure 3. Return on investment when transitioning to a Vaya system from a conventional Raman handheld solution over a four year period.

Conclusion

With a Vaya system, it becomes possible to inspect and identify raw materials immediately at receipt. No container handling, no container opening required, and no compromise to sterility. By simplifying the ID process, a Vaya offers a cost-effective alternative to current conventional Raman based solutions. Using a Vaya makes the identification test easily scalable to meet 100% ID requirements and production demands. It also future-proofs your ID protocol against regulatory changes or more stringent quality requirements. Without sampling, you can test more materials for the same cost, or perform multipoint surveys of your raw material containers.

References

1. Title 21 Code of Federal Regulations, part 2.11.84.
2. EU GMP Annex 8: Sampling of Starting and Packaging Materials

⁸Net present value (NPV) applied for the calculation of the ROI.

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