Application Note

Raw Material Identification

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Application of Spatially Offset Raman Spectroscopy to In-Container Testing of Raw Materials for PIC/S GMP Annex 8 Using the Agilent RapID Raman System

This is a translated excerpt of an original article published in *Pharm Tech Japan*, **2015**[1]. The original article was written by authors at Astellas Pharma Tech Co., Ltd., Japan.

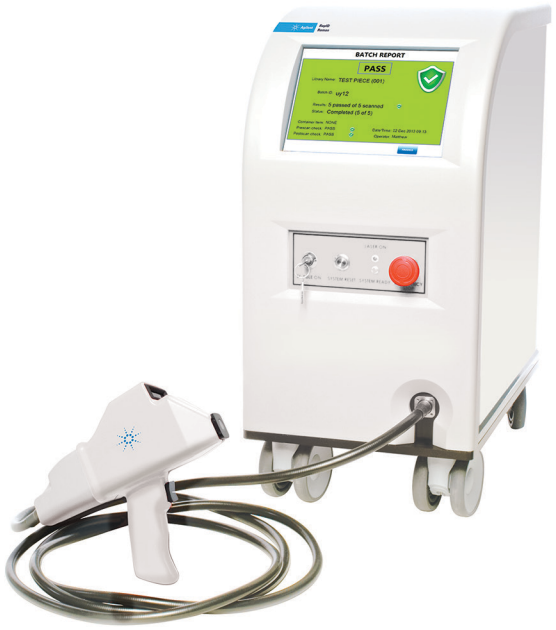
Abstract

Since Japan joined PIC/S in July 2014[2], Astellas Pharma Tech Co., Ltd. has investigated how to guarantee effective identification of packaged raw materials, as stipulated in EU GMP Annex 8. In a 2013 publication[3], Astellas presented the results from real-world tests using a fixed Raman spectrometer (Raman RXN2 1000) and a portable Raman spectrometer (TruScan RM). Following this, further investigations were carried out into PIC/S GMP Annex 8 compliance using a spatially offset Raman spectrometer (Agilent RapID). The results, summarized here, showed that the instrument was capable of detecting materials inside both a paper sack and a nontransparent polyvinyl sack—something that the existing Raman spectrometers failed to do. This makes it possible to complete acceptance testing, while economizing manpower. It also reduces the risk of foreign material or microbial contamination at the point of sampling to zero.

Introduction

There are two types of raw material samples that are tested before release to manufacturing. One is a sample intended for testing various quality attributes, for example, purity, collected from several packages using a statistical selection method. The intention of this testing is to assess the overall quality of the entire lot. The other type of sample is individually taken from every container, with the purpose of guaranteeing identity (through testing), as stipulated by Annex 8. Using the original testing scheme, the overall process is complicated and resource-intensive. Unopened packages are sent from the warehouse, brought into the sampling room, opened, sampled, resealed, then returned to the warehouse. The greatest benefit in using the Agilent RapID Raman system is that it is unnecessary to open packages to collect samples, and tests can be carried out on-site, in the warehouse.

For packages that are only tested for identification purposes, it is possible to take an approach where there is no invasive sampling. This would improve the workflow, eliminate the need to transport heavy goods, and reduce the risk of microbial and foreign material contamination to zero.



Agilent RapID system.

Raw material identity verification through a multilayer paper sack.

Experimental

At Astellas Pharma Tech Co. Ltd, Japan, we decided to compare a real-world application of the new and old testing schemes based on the Annex 8 approach[1]. We chose lactose monohydrate, one of our main production materials used in the majority of our factories, and calculated the production costs of acceptance testing using the Japanese Pharmacopeia testing methods (IR absorption spectrometry, potassium bromide disk method, hereafter the IR method). We then compared it with the production costs of implementing the RapID test.

There were 200 units per one lot in paper sack packages intended only for identification testing. In the IR method, it was necessary to sample all 200 containers, and test each sample individually. The QC department had to prepare individual labels upon receipt of each container, open the container, remove a sample from the packaging, and finally, reseal the container in preparation for storage. Additionally, the logistics team had to move the sacks to and from the warehouse.

Results and Discussion

Using RapID not only eliminates the need for this extended IR process, but also significantly decreases the amount of time needed to carry out the tests themselves (Table 1), reducing manpower costs by over 90 %. While the IR method for testing lactose takes a comparatively short amount of time, the benefits of using RapID are even more impressive when considering the lengthier testing process required for other raw materials.

Table 1. Comparing time taken (work-hours) for IR and Agilent RapID tests for ID verification of 200 sacks of lactose.

Department	Action	IR	Agilent RapID
QC	Preparation of sampling container labels	0.5	0
Logistics	Delivery from the warehouse	0.5	0
QC	Breaking the seal (and visual inspection)	1.5	0
QC	Sampling	1.0	0
QC	Resealing	10.0	0
Logistics	Return to the warehouse	0.5	0.5
QC	Confirmation test	33.5	3.5
Total		47.5	4.0

Table 2. Combination of packaging form and capability of raw material measurement by Agilent RapID.

Department	Package	Color	Successful spectrum
Lactose	Kraft sack	White	Y
Mannitol	Kraft sack	Brown	Y
Maltose	Kraft sack	Brown	Y
Magnesium stearate	Kraft sack	Brown	Y
Corn starch	Kraft sack	Brown	Y
Cross – carmelose calcium	Polyethylene sack	None	Y
Hypromellose	Polyethylene sack	None	Y

Conclusions

While bringing acceptance testing of raw materials in line with Annex 8, there is an ongoing discussion around increased production costs and the increased risk of foreign material and microbial contamination when opening raw material containers. Most of these issues have been eliminated using an Agilent RapID Raman system. The breadth of application of RapID to raw materials packaged in nontransparent polyvinyl and paper packaging is noteworthy (see Table 2).

The quality of a product's raw materials is representative of the quality of the product itself, and is, therefore, very important. As a company, we intend to continue our investigations to ensure that best practice is upheld in every respect of our acceptance testing to guarantee quality, effectiveness, and in accordance with (PIC/S) GMP compliance.

References

1. Kawakubo, S.; *et al. Pharm Tech Japan* **2015**, *Vol. 31, No. 12*, 71–80.
2. https://picscheme.org/layout/document.php?id=167
3. Inoue, H.; *et al. Pharm Tech Japan* **2013**, *Vol. 29, No. 6*, 105.

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