White Paper

Agilent
Trusted Answers

Vaya Raw Materials Verification System: Compliance with USP <1120>, USP <858>, USP<1858> and EP 2.2.48

Introduction

Purpose

The purpose of this document is to allow users of the Agilent Vaya Raman instrument to determine how the system meets the relevant Raman spectroscopy guidance of the United States Pharmacopeia (USP) <1120>, <858> and <1858> and European Pharmacopoeia (EP) 2.2.48. In addition, areas where standard operating procedures are needed to achieve full compliance are identified. This assessment is made with the latest release of the Vaya software.

Scope

The scope of this assessment is for a Vaya instrument installed, by a qualified Agilent representative, following standard procedures and used in a manner recommended by Agilent (see the Agilent Vaya Raman Raw Material Identity Verification System User's Guide for details).

Related documents

The Agilent Vaya Raman Raw Material Identity Verification System User's Guide is related to this assessment. The guidance from USP <1120>, USP <858>, USP<1858> and EP 2.2.48 overlaps significantly and so has been collated under common sections for clarity. Where there is ambiguity, the following guidance

has been consulted, but in any case, the qualification of the assessment of each criterion is provided. The result of the assessment of each criterion are recorded as “Yes” (met), “No” (not met), or “N/A” (Not Applicable). Each "No" or "N/A" response requires a clarification in the Response column.

System overview

The Agilent Vaya instrument is used for non-invasive identification/verification of chemicals and raw materials, both solids and liquids, in non-metallic (e.g., plastic, glass and paper) containers without opening the package and exposure to the environment including operators.

Definitions and Acronyms

Acronym	Detail
FAT	Factory Acceptance Testing performed during manufacturing
ASTM	American Society for Testing and Materials
ASTM E1840	Standard Guide for Raman Shift Standards for Spectrometer Calibration
HgAr	Mercury Argon Light
NIST	National Institute of Standards and Technology
IQOQPQ	Installation Qualification Operational Qualification Performance Qualification
SORS	Spatially Offset Raman Spectroscopy
PTFE	Polytetrafluoroethylene

USP and EP requirements

The column headed "USP and EP specification" are from the USP and EP requirements listed in the "References" section. The column headed "Response" details how the software or the customer meet the specification.

Table 1. USP and EP requirements

USP and EP specification	Response	Met
Calibration		
X-axis (Wavenumber)		
Could use an emission lamp.	A Mercury-Argon (HgAr) lamp is used to calibrate the x-axis.	Yes
Must have an x-axis calibration procedure that can be performed by the user.	X-axis calibration can be performed by an Agilent service representative.	Yes
Should calibrate using multiple atomic emission lines.	Multiple argon emission lines and the only available major mercury emission line in the Vaya spectrometer range are used for calibration.	Yes
Must perform a system calibration before laser calibration.	System calibration is performed independently of laser calibration.	Yes
Laser wavelength		
Must confirm laser wavelength.	The laser wavelength is supplied with a certificate of conformance from the manufacturer.	Yes
Should use a suitable Raman shift standard, e.g., ASTM E1840-96 or other suitable material.	Polystyrene is used for the supplied test piece. Band locations taken from ASTM E1840.	Yes
Should use low-pressure arc lamp emission in addition to shift standard.	Testing uses a HgAr lamp (see X-axis (Wavenumber)).	Yes
External calibration devices reproduce exactly the optical path taken by the scattered radiation.	Polystyrene is an external standard and therefore is superior to using an internal standard.	Yes
The primary wavelength X-axis calibration should be performed, as per vendor procedures, just prior to measuring the laser wavelength.	X-axis calibration is performed independently of laser calibration, and system calibration is performed prior to measuring the laser wavelength.	Yes
For external calibration[1], the Raman shift standard should be placed at the sample location.	Calibration performed using the supplied polystyrene test piece, which is scanned at the sample location.	Yes
The peak center of a strong, well resolved band in the spectral region of interest should be evaluated.	The strongest peak in the polystyrene spectrum is evaluated (1001.4 cm^{-1}), through use of the supplied polystyrene test piece.	Yes
The peak center could be assessed manually or automatically with a suitable, valid, peak picking algorithm.	The peak center is assessed automatically using a Gaussian fit peak fitting algorithm.	Yes
Laser wavelength should be adjusted by software or manually.	Laser wavelength cannot be adjusted by the user and is locked by design. Internal standard correction automatically takes into account any laser wavelength variation.	Yes
Y-axis (Intensity)		
A broad-band emission source should be used.	**Not applicable.** Method B is used.	N/A
Method A procedure should be: • Measure light source at sample location with laser off. • Calculate ratio of measured response to true response and create a correction file. • Correction file applied to spectra acquired with the instrument.	**Not applicable**.	N/A

1 External calibration devices exactly reproduce the optical path taken by the scattered radiation

Table 1. USP and EP requirements, continued

USP and EP specification	Response	Met
Calibration, continued		
Should provide user with documentation of lamp calibration and source validity (lifetime).	**Not applicable.** NIST SRM 2246 document is provided.	N/A
Method B procedure should be: • Measure reference spectrum at sample location with laser on. • Calculate ratio of the measured response to the true response and create a correction file. • Correction file applied to spectra acquired with the instrument.	A NIST SRM 2246 green glass is used to calibrate the Y-Axis/ intensity.	Yes
External calibration		
External standards should be employed if the optical path is modified (e.g., components are replaced).	System will be calibrated after repair/extensive service.	Yes
Qualification and verification of Raman instruments		
Periodic operation qualification		
Performance verification should be performed on a more frequent basis than operation qualification.	The system check is performed using the supplied test piece as required by the user's organization SOP. System Check performs a zero, offset and SORS measurements of the test piece and requirements are checked on all three spectra. PQ can be performed as often as required by the user's organization SOP. Note: PQ is the system check.	Yes
Performance verification should assess the quality of fit to an initial scan performed during instrument qualification.	The system check is performed using the supplied polystyrene test piece as required by the local procedure. System Check performs a SORS measurement of the test piece. Quality of fit is assessed by peak position and area changes from nominal values set during calibration and confirmed during FAT and IQ.	Yes
History of performance verification could be recorded and available for viewing to assess long-term stability.	All PQ system checks performed on the instruments are recorded and made available to users for long term stability analysis.	Yes
Frequency of testing		
Instrument qualification should be performed at designated intervals or following a repair or significant optical reconfiguration.	Operation qualification (OQ) service is available. Instrument qualification is performed after repair. If the user's organization performs the OQ service, they are responsible for all required documentation.	Yes
Instrument operation qualification		
Check wavelength and photometric precisions against acceptance limits.	Wavelengths and photometric precisions are checked during system check against published limits.	Yes
Performance qualification		
Check wavelength precision, intensity-scale precision and sensitivity within specified limits.	Wavelength precision and intensity-scale precision data are acquired during PQ and checked against the data that was collected during qualification and specified limits.	Yes
Quantitative measurements of an external performance verification standard to check wavelength (x-axis + laser) and photometric (intensity) precision.	Polystyrene peak positions (x-axis) and peak area (intensity) are quantitatively checked during PQ against qualification levels.	Yes
Wavelength precision		
A single spectrum of Raman shift standard should be collected and used for a period equal to that used in the photometric consistency test for the wavelength precision.	The two tests for x and y axis are synchronous.	Yes
Peaks across the range should be used to calculate precision.	The PQ supplied system check using PTFE/Polystyrene involves multiple peaks across the entire spectral range.	Yes
Current peak positions should be matched to those collected during instrument qualification.	Polystyrene peak positions (x-axis) and peak area (intensity) are quantitatively checked during PQ against Instrument Qualification results.	Yes
Should have a standard deviation < ± 0.3 cm^{-1} (adjustable depending on application). (EP tolerances for wavenumber shifts are ± 2 to 3 cm^{-1} for non-laboratory based instrument and dependant on peak).	The application is non-laboratory hence USP limit is adjusted to EP non-laboratory limit for wavenumber shifts tolerances. Operational validity range is therefore set as < ± 1.5cm^{-1} for all peaks.	Yes
Photometric consistency		
Peak areas calculated. Largest is set to 1, and others normalized to this.	Absolute peak areas are calculated and normalized to largest.	Yes

Table 1. USP and EP requirements, continued		
USP and EP specification	**Response**	**Met**
Qualification and verification of Raman instruments, continued		
Photometric consistency, continued		
Should: Peak areas should not vary more than 10% (adjustable depending on application). (EP ± 10 % variation in band intensity).	Absolute peak areas are checked for variance against the previous qualification at a limit of ± 10%.	Yes
Spectral resolution. For identity tests, a tolerance of maximum 15 cm^{-1} is prescribed, unless otherwise prescribed in a monograph.	On average < 14 cm^{-1} (measured according to ASTM E2529 / EP 2.2.48).	Yes
Laser Power Output Precision and Accuracy (Applicable to the Vaya instrument as it is using internal laser power meter)		
Set laser on representative output.	Laser power is set to representative output by setting previously determined drive voltage and the calibrated internal power meter confirms representative output.	Yes
Output should be measured and checked against output measured at instrument qualification.	The output is measured during FAT and testing is the system specified power and an external meter is used to calibrate the internal meter. The laser power output is set during manufacturing and checked during FAT.	Yes
Should not vary by more than 25% compared to qualified level – Should service if variation is greater than this.	Laser power is monitored through the system check using the internal power meter. If the Laser power varies by more than ± 25% of the initial qualified level, the system check receives a FAIL result.	Yes
The accuracy of values generated from internal power meter compared to calibrated external laser power meter at an interval of not more than 12 months.	The internal power meter is compared to a calibrated external power meter and recalibrated (if necessary) during the operation qualification service (typically annually).	Yes
If not possible to use external power meter, then supplier recommends a procedure for the above during service visit.	Same as directly above.	N/A

Conclusion

This document details the collective Raman spectroscopy requirements of USP and EP. No gaps were identified. Therefore the features and tools available when using the Vaya system support testing to meet the USP and EP requirements.

Document references

Listed below are:

- Parent documents, higher level, that direct this document (P);
- Business documents, outside the CAG/LSG quality system but within the Agilent organization, that supplement this document (B);
- Sibling documents, same level, that supplement this document (S);
- Child documents driven by this document (C).

Document #	Title	P/B/S/C
G6915-90000	Vaya User Manual	S

Records

Unique records generated by this process are maintained according to the requirements of AQ24.3 Control of Agilent QMS Quality Records and the Agilent General Retention Schedule.

Document control information

This is a controlled document. Versions of this document prior to its import into the Document Management System are considered draft versions.

Filename:	**PLRM-CUD24 Vaya Raw Materials Verification System USP (1120) EP 2.2.48 compliance**
Document Owner:	Product Management
Document Number:	G6915-90013
Document Title:	Vaya Raw Materials Verification System USP (1120) EP 2.2.48 compliance

References

Document Name and Number
European Pharmacopeia 2.2.48
United States Pharmacopeia 1120 & 858 & 1858

www.agilent.com/chem

DE.7404398148

Printed in the USA, December 2022
G6915-90013, Rev. 4.0

Agilent
Trusted Answers