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INDATECH

Ensuring Compliance with the Pharmaceutical Standards (USP/PhEur): Full Compatibility of Our INDATECH Ready Software

Introduction

At Indatech, we are committed to supplying you with data management software compliant with the pharmaceutical industry's strictest standards. Our software complies with the FDA's 21 CFR Part 11 regulation, as well as the USP 856, 857 and 858 and PhEur 2.2.40, 2.2.25 and 2.2.48 pharmaceutical standards.

The USP *(United States Pharmacopeia)* and PhEur *(Pharmacopée Européenne)* standards are essential references in the pharmaceutical industry and other health-related sectors. They define criteria and requirements designed to guarantee the quality, safety, effectiveness and purity of the drugs, health products, food supplements and other items used in healthcare. Companies in the pharmaceutical sector must comply with these standards to obtain regulatory approval and meet the requirements of the health authorities and consumers.

The crucial requirements of the USP and PhEur standards include the need for qualification, and particularly operational qualification (OQ) and performance qualification (PQ). PQ is performed by means of Routine System Verification (RSV). This RSV procedure aims to ensure that the instrument maintains its performance levels in accordance with the established specifications over time. The RSV guarantees that the instrument remains precise and reliable, which is essential in the pharmaceutical sector where the precision of the analyses plays a critical role in terms of the safety and effectiveness of health products. Fulfillment of these requirements remains crucial to comply with these regulatory standards and guarantee the quality of pharmaceutical products.

Our INDATECH Ready software

Our INDATECH Ready software offers a comprehensive solution to meet these instrument qualification requirements, and particularly OQ and PQ. It is important to note that our software proposes OQ modules which are applied during installation and maintenance work. All these modules are theoretically applicable as a matter of routine in the context of RSV. However, we advise our customers to apply at least the following tests (see Table 1) regularly in the context of their PQ strategy.

Table 1: RSV modules available for each spectroscopic technology

Asuryan (UV-Vis)	SAM-Spec (NIR)	Viserion (Raman)
Reference	Dark	Wavelength Accuracy
Wavelength Accuracy	Reference	Photometric Precision
Wavelength Precision	Wavelength Accuracy	
Photometric Accuracy	Photometric Accuracy	
Photometric Precision		
Stray Light		

The modules specifically integrated in our software simplify and automate the RSV process.

They provide advanced functions for continuous monitoring of the instruments' performance, thus ensuring that our equipment remains in compliance with the USP/PhEur standards.

Measure up

Example of RSV: Raman "Wavelength Accuracy" Verification

The "Wavelength Accuracy" test is a spectrophotometric analytical procedure designed to assess the instrument's precision concerning the wavelength at which it performs measurements.

The "Wavelength Accuracy" module of our INDATECH Ready software lets you generate a reference sample for comparison with your routine measurements. In this example, in accordance with the pharmacopeia standards, we measured an appropriate high-purity product, cyclohexane, and selected 5 characteristic peaks for the product in the Raman spectral range from 250 to 3200 cm^{-1}. Finally, taking into account the resolution of our Viserion Raman spectrometer, we established acceptation limits at ± 3 cm^{-1} for each peak. Using the RSV module, we then checked the accuracy of the wavelengths. The results are shown in Figure 1.

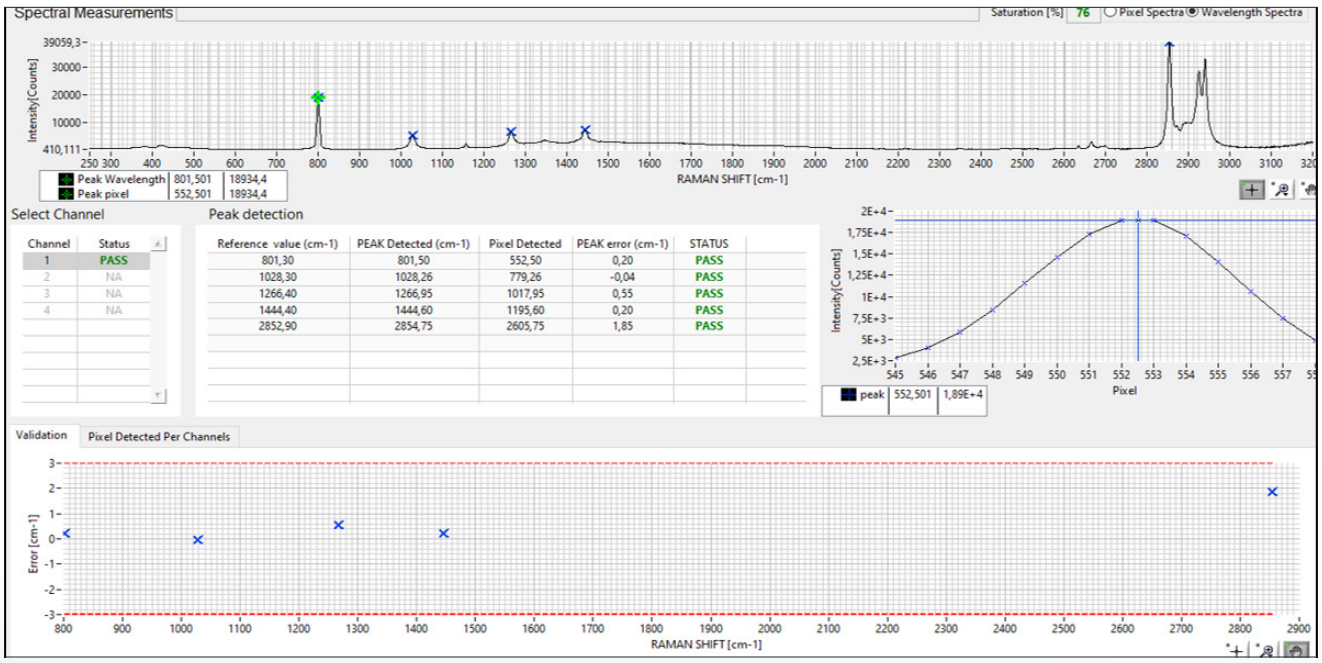


Figure 1: Results of a "Wavelength Accuracy" RSV test for Viserion

The difference between the peak observed and the peak certified is indicated. At the bottom, the error is plotted as a function of the Raman shift. The red lines indicate the tolerance limits set by the user. If the error for each peak is within these limits, a "PASS" result is indicated. If one of the peaks observed shows an error greater than the tolerance limits, a "FAIL" result will be indicated for the whole test.

Example of RSV: NIR "Dark+Reference" Verification

The "Dark+Reference" test is used to monitor the condition of the system and guarantee high-precision measurements. By combining the "Dark" test and "Reference" test, the NIR spectrometer can be maintained in optimum condition. The "Dark" test monitors the system's level of background noise and checks that there is no stray light. The "Reference" test can be used to check the signal level obtained on a reference sample used routinely to calculate the absorbance. This guarantees that the NIR measurements are reliable and reproducible.

The "Dark+Reference" module in our INDATECH Ready software lets you generate a reference sample for comparison with your routine measurements. In this example, we measured a NIST-certified 99% reflectance standard and defined acceptance limits of ± 5% in the NIR spectral range from 900 to 1650 nm. Using the "Dark+Reference" module, we then checked the "Dark" and the "Reference". The results are shown in Figure 2.

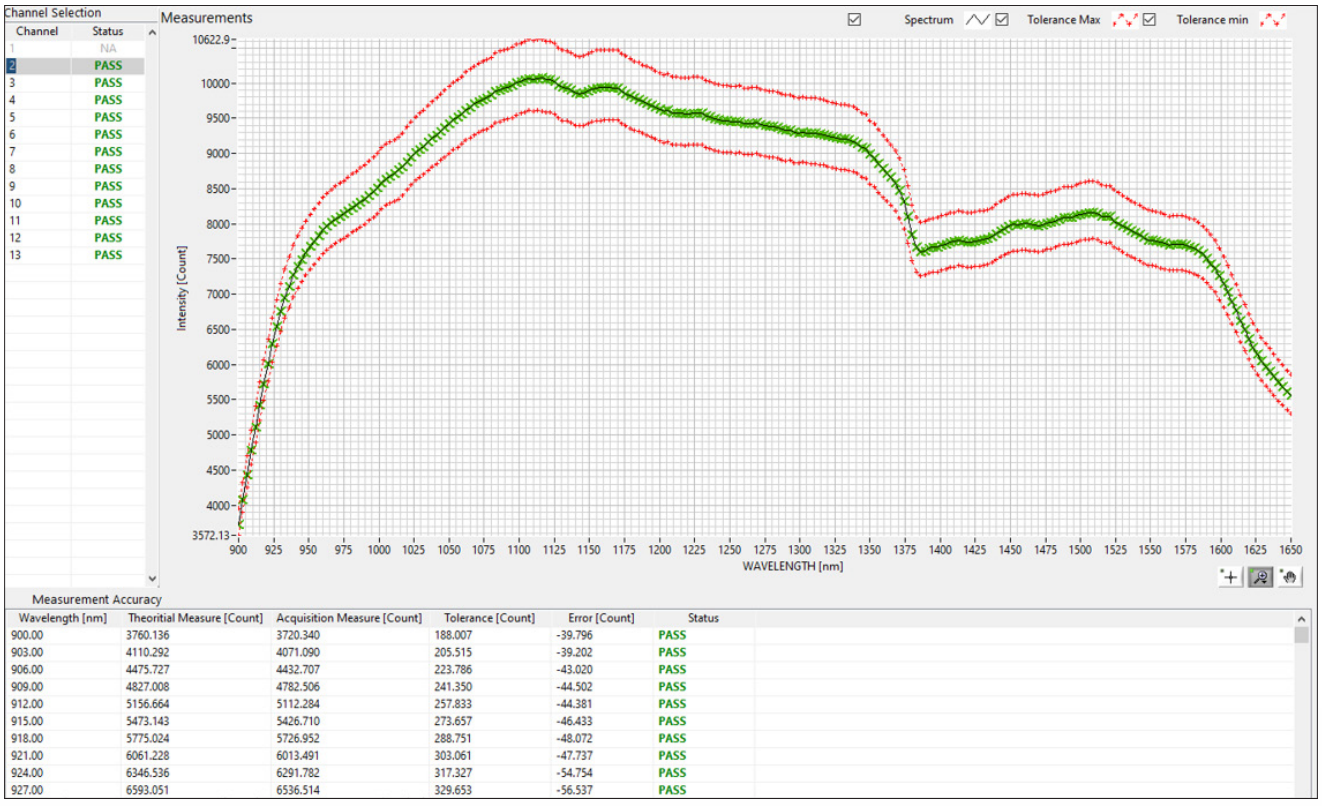


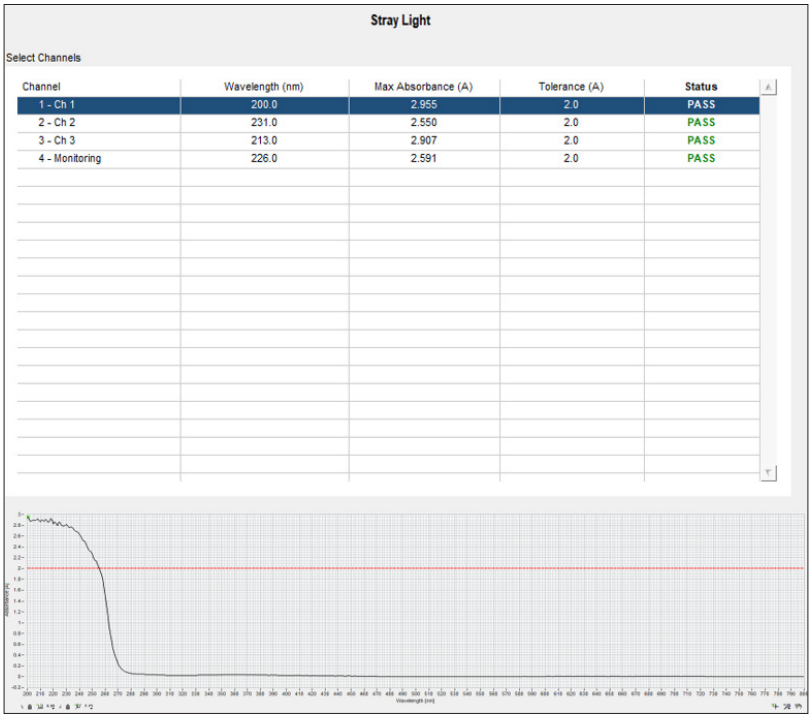
Figure 2: Results of a "Dark+Reference" RSV test
The 'Channel' column shows the different measuring channels of our SAM-Spec multipoint NIR spectrometer.

The spectral measurements are displayed in Intensity (Counts). The red lines indicate the tolerance limits of +/- 5% in relation to the spectrum of reference. If the reference sample measured and the 'Dark' measurement are within these tolerance limits, a "PASS" result is generated. However, if a single pixel on one of the channels lies outside the tolerance limits, the result will be "FAIL".

Example of RSV: UV-Vis "Stray Light" Verification

The "Stray Light" test is an essential procedure designed to assess the effect of stray light in UV-Visible spectrophotometric. Stray light is the unwanted light which enters the spectrometer's optical path and interferes with the measurement. This may cause inaccuracies in the spectra recorded. An appropriate stray light test helps to identify this unwanted light, thus avoiding erroneous results.

The "Stray Light" module in our INDATECH Ready software lets you generate a reference sample to compare with your routine measurements. In this example, we took a measurement on a certified reference sample (CRM) provided by Hellma and composed of sodium iodide in pure water. Pure water was used as the reference for the absorbance calculation. Then, in compliance with the pharmacopeia standards, we set an acceptance limit at 2.0 absorbance units (AU) in the spectral range from 210 to 259 nm. Using the RSV module, we then performed a stray light test. The results are shown in Figure 3.



Stray Light

Select Channels

Channel	Wavelength (nm)	Max Absorbance (A)	Tolerance (A)	Status
1 - Ch 1	200.0	2.955	2.0	PASS
2 - Ch 2	231.0	2.550	2.0	PASS
3 - Ch 3	213.0	2.907	2.0	PASS
4 - Monitoring	226.0	2.591	2.0	PASS

Figure 3: Results of a "Stray Light" RSV test.
The "Channel" column shows the different measuring channels of our Asuryan multichannel UV/Vis spectrometer.

The maximum absorbance of the sodium iodide CRM sample is indicated for each channel. The red line indicates the acceptance limit set at 2 AU. If the maximum absorbance value at 210-259 nm for all the channels is greater than the predefined acceptance limit, a "PASS" result is announced. However, if the maximum absorbance value for one of the channels is lower than this limit, the result will be "FAIL".

▪ Automation of RSV

In addition, our software offers the possibility of automating the RSV process, which can be carried out either directly in the software interface or via a PLC, thus offering precious guidance for users. Users are free to define the automated RSV test sequence and apply it by following the step-by-step instructions displayed in the RSV interface (see Figure 4)

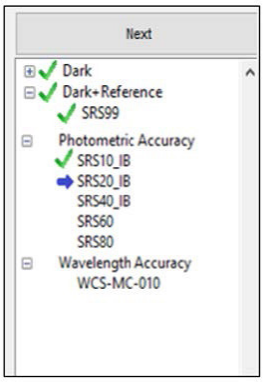
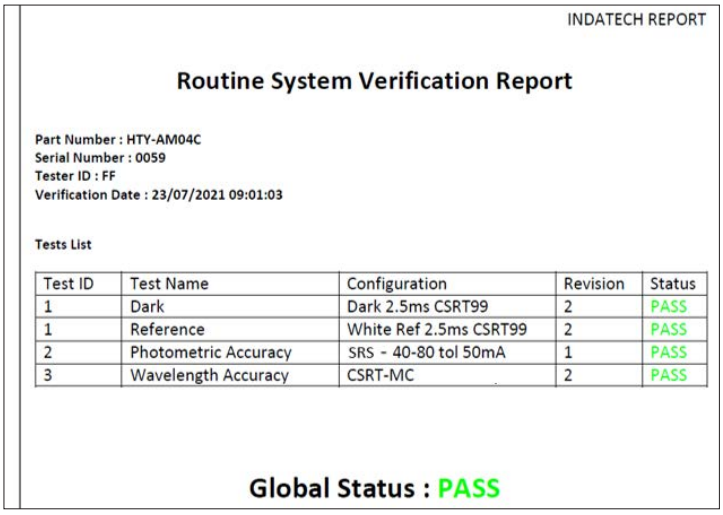


Figure 4: The interface of the automatic RSV performed with the SAM-Spec NIR spectrometer.

A report containing the RSV results is generated and saved automatically.

Figure 5 shows an example of a report generated when performing an automatic RSV on our SAM-Spec system. This report includes the global status of each RSV test performed and the details of the numerical results obtained for each test (not presented here for reasons of concision).



INDATECH REPORT

Routine System Verification Report

Part Number : HTY-AM04C
Serial Number : 0059
Tester ID : FF
Verification Date : 23/07/2021 09:01:03

Tests List

Test ID	Test Name	Configuration	Revision	Status
1	Dark	Dark 2.5ms CSRT99	2	PASS
1	Reference	White Ref 2.5ms CSRT99	2	PASS
2	Photometric Accuracy	SRS - 40-80 tol 50mA	1	PASS
3	Wavelength Accuracy	CSRT-MC	2	PASS

Global Status : PASS

Figure 5: Report generated in PDF format to present the results of the automated NIR RSV process.

In the System Status tab of the INDATECH Ready software, a status indicator is displayed when the RSV is a "PASS". This status remains active during the period of validity which is fully adjustable to meet users' specific needs.

▪ The advantages of the INDATECH Ready software

- Execution of the automated RSV routines corresponding to the standards in the USP and PhEur pharmacopeias
- Total compliance with the CFR21 part 11 data integrity standards
- Compatibility with various communication protocols such as OPC-UA and TCP-IP
- Easy integration of chemometric predictive models (Eigenvector, Sartorius)

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