White Paper

Agilent
Trusted Answers

Pharmaceutical Analysis using FTIR: Compliance with European, US, Indian, and Japanese Pharmacopoeia

Meeting the requirements of global pharmacopoeia with the Agilent Cary 630 FTIR

Introduction

Fourier transform infrared (FTIR) spectroscopy is a commonly used technique in the pharmaceutical industry. FTIR spectroscopy is often used for quality assurance / quality control (QA/QC) of pharmaceutical substances and material identification.

The Agilent Cary 630 FTIR spectrometer incorporates ease-of-use, reliability, and flexible sampling accessories in a highly compact system with class-leading performance. Designed to meet the requirements of a regulated pharmaceutical environment, it is ideal for routine measurements such as analyzing, characterizing, and verifying raw materials and ingredients.

The Cary 630 FTIR spectrometer has a modular design. This design allows the instrument to be reconfigured with permanently aligned sample modules for the different samples and applications. Modules are simply attached to the front of the Cary 630 FTIR engines, available with either KBr or ZnSe optics, and can be exchanged in seconds.

Several pharmacopeias describe how FTIR spectrometer performance is verified to demonstrate suitability for the intended operational range of analysis.

This white paper demonstrates how Agilent Cary 630 FTIR instruments (with KBr and ZnSe optics) can be verified as meeting the performance requirements of the European, US, Indian, and Japanese Pharmacopoeia. Where applicable, the instruments were verified for transmission and ATR measurement mode as specified in the respective pharmacopeia.

The following sampling modules can be used for transmission measurement mode tests:

- Cary 630 Transmission Module (used in this white paper)
- Cary 630 DialPath Modules
- Cary 630 TumbIIR Module

The following sampling modules can be used for ATR measurement mode tests:

- Cary 630 Diamond ATR Module (used in this white paper)
- Cary 630 ZnSe ATR Module
- Cary 630 Ge ATR Module

Control of instrument performance

Control of instrument performance is a critical aspect in qualifying the instrument suitability for the intended analysis to be performed. Spectral resolution and wavenumber accuracy are the performance parameters that are described in most pharmacopeia, sometimes using slightly diverging terminology. These parameters are checked using suitable reference materials.

All Pharmacopeias referenced here recommend the use of a NIST SRM 1921b traceable polystyrene film of approximately 35 µm thickness (available from Agilent: p/n: 925-0128).

Spectral resolution

Passing the spectral resolution test confirms the resolving power of the system. This parameter is measured to ensure that closely observed bands can be resolved.

Wavenumber accuracy

Passing the wavenumber accuracy test ensures that the wavenumber axis of the collected IR spectrum is accurate within acceptable limits across the intended operational range. The test is usually done by recording the spectrum of a suitable reference material. The wavenumbers of maximum response are then compared with the known band positions of the standard, as given in the respective pharmacopeia.

Further pharmacopeia-specific performance requirements will be discussed in the respective sections.

Instrument performance check using MicroLab software

The Agilent MicroLab software suite is easy-to-use software that is provided with all Cary 630 FTIR spectrometers. Step-by-step guidance using instructive pictures and an intuitive software design allow easy navigation through the entire workflow.

The MicroLab software suite consists of four workflow-focused software applications:

- MicroLab PC: Method-driven software to collect and analyze data using predefined methods
- MicroLab Light: Software for offline review and analysis of FTIR data
- MicroLab OQ: Automated Operational Qualification (OQ) software. Can be used to routinely verify instrument performance
- MicroLab Quant: Software for the development and verification of quantification models

MicroLab Pharma is an optional software package for the Cary 630 FTIR. The software supports users in regulated environments, providing tools to help achieve compliance with electronic record regulations such as 21 CFR Part 11 and EU Annex 11.

The following section describes how MicroLab OQ and MicroLab PC can be used verify the Cary 630 FTIR instrument performance.

Instrument performance check using MicroLab OQ software

MicroLab OQ allows users to easily perform spectral resolution and wavenumber accuracy tests (called “Laser Frequency Calibration Check” and “Spectral Resolution Check” in MicroLab OQ). In addition, the software can be used to perform signal-to-noise and stability tests, which are not part of the international pharmacopeias’ requirements. MicroLab OQ has an intuitive pictorial interface, which guides the user through the qualification process (Figure 1) as follows:

1. Select the Cary 630 FTIR modules to be verified. The software automatically recognizes the module attached to the engine.
2. An automatic diagnostic system check examines the health condition of the instrument.
3. The list of available tests is displayed. Select the tests to be performed and adjust the settings if required.
4. The software navigates the user through the entire test procedure with step-by-step guidance using instructive pictures.

MicroLab OQ software generates a PDF report showing the diagnostic values, the test results, and the specifications for the tests and pass/fail criteria for future reference (Figure 2).

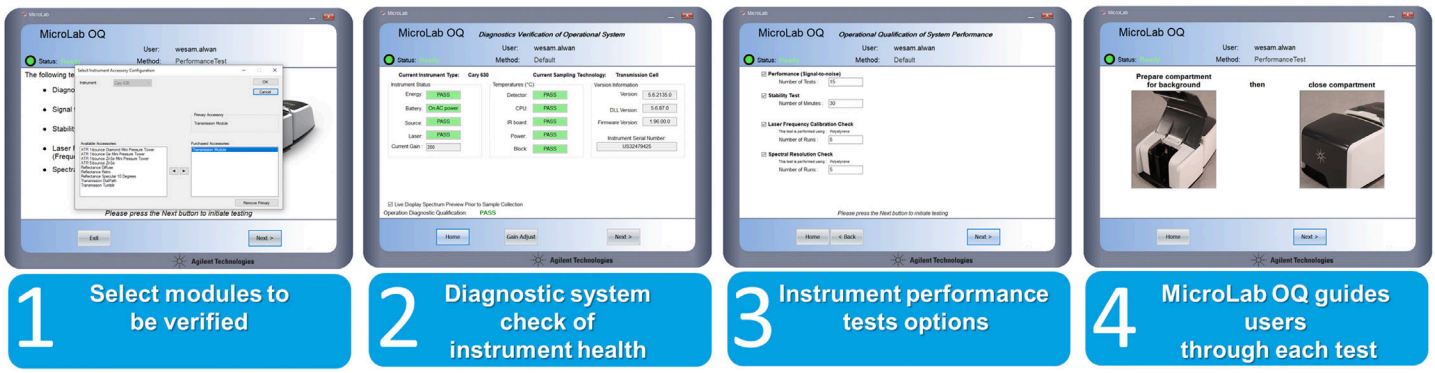
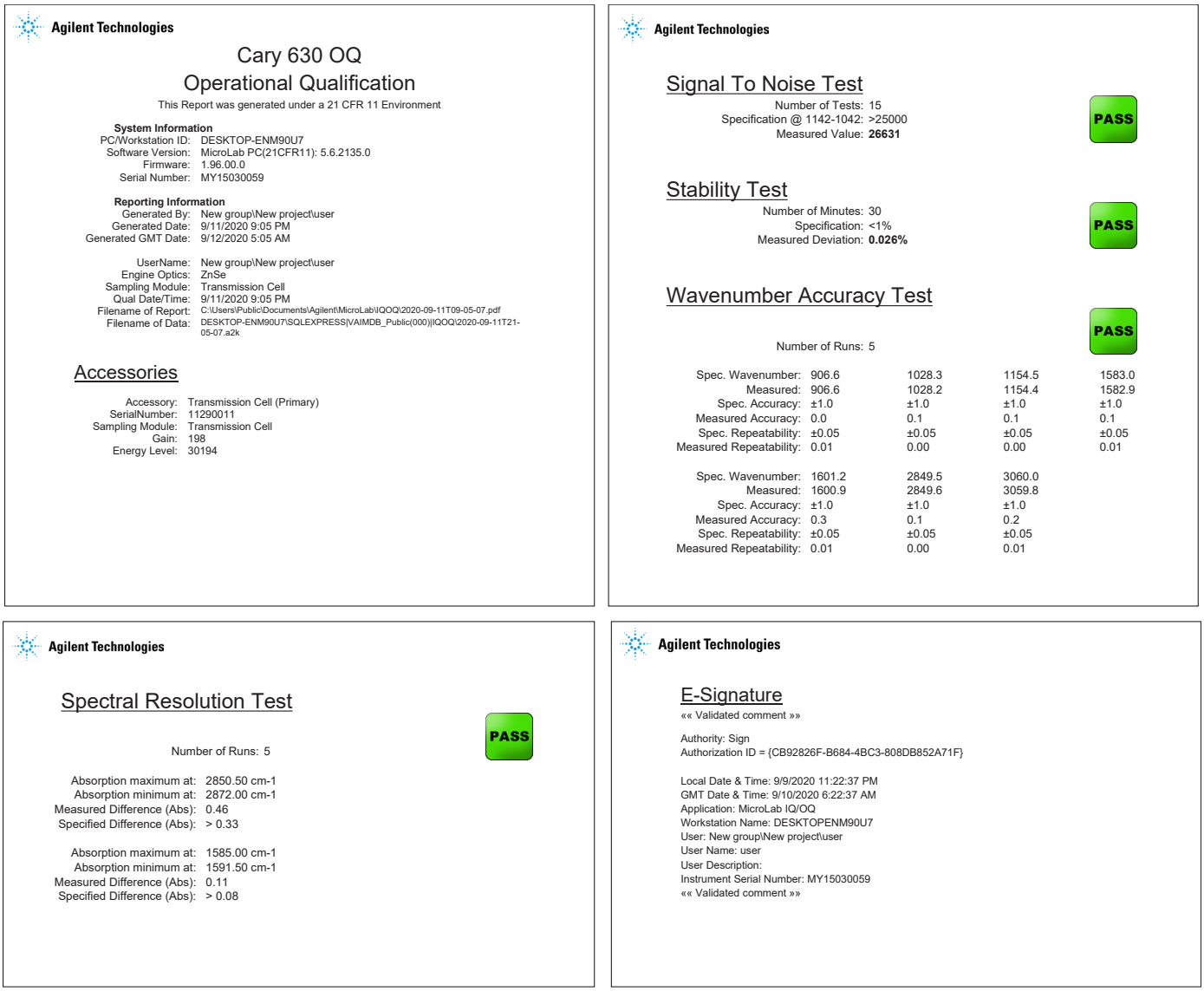


Figure 1. MicroLab OQ software guides users to perform instrument qualification through simple and easy steps.



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Cary 630 OQ
Operational Qualification

This Report was generated under a 21 CFR 11 Environment

System Information
PC/Workstation ID: DESKTOP-ENM90U7
Software Version: MicroLab PC(21CFR11): 5.6.2135.0
Firmware: 1.96.00.0
Serial Number: MY15030059

Reporting Information
Generated By: New group\New project\user
Generated Date: 9/11/2020 9:05 PM
Generated GMT Date: 9/12/2020 5:05 AM

UserName: New group\New project\user
Engine Optics: ZnSe
Sampling Module: Transmission Cell
Qual Date/Time: 9/11/2020 9:05 PM
Filename of Report: C:\Users\Public\Documents\Agilent\MicroLab\IQOQ\2020-09-11T09-05-07.pdf
Filename of Data: DESKTOP-ENM90U7\SQLEXPRESS|VAIMDB_Public(000)|IQOQ\2020-09-11T21-05-07.a2k

Accessories

Accessory: Transmission Cell (Primary)
SerialNumber: 11290011
Sampling Module: Transmission Cell
Gain: 198
Energy Level: 30194

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Signal To Noise Test

Number of Tests: 15
Specification @ 1142-1042: >25000
Measured Value: **26631**

PASS

Stability Test

Number of Minutes: 30
Specification: <1%
Measured Deviation: **0.026%**

PASS

Wavenumber Accuracy Test

Number of Runs: 5

PASS

Spec. Wavenumber:	906.6	1028.3	1154.5	1583.0
Measured:	906.6	1028.2	1154.4	1582.9
Spec. Accuracy:	±1.0	±1.0	±1.0	±1.0
Measured Accuracy:	0.0	0.1	0.1	0.1
Spec. Repeatability:	±0.05	±0.05	±0.05	±0.05
Measured Repeatability:	0.01	0.00	0.00	0.01

Spec. Wavenumber:	1601.2	2849.5	3060.0
Measured:	1600.9	2849.6	3059.8
Spec. Accuracy:	±1.0	±1.0	±1.0
Measured Accuracy:	0.3	0.1	0.2
Spec. Repeatability:	±0.05	±0.05	±0.05
Measured Repeatability:	0.01	0.00	0.01

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Spectral Resolution Test

Number of Runs: 5

PASS

Absorption maximum at: 2850.50 cm-1
Absorption minimum at: 2872.00 cm-1
Measured Difference (Abs): 0.46
Specified Difference (Abs): > 0.33

Absorption maximum at: 1585.00 cm-1
Absorption minimum at: 1591.50 cm-1
Measured Difference (Abs): 0.11
Specified Difference (Abs): > 0.08

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E-Signature

«« Validated comment »»

Authority: Sign
Authorization ID = {CB92826F-B684-4BC3-808DB852A71F}

Local Date & Time: 9/9/2020 11:22:37 PM
GMT Date & Time: 9/10/2020 6:22:37 AM
Application: MicroLab IQ/OQ
Workstation Name: DESKTOPENM90U7
User: New group\New project\user
User Name: user
User Description:
Instrument Serial Number: MY15030059
«« Validated comment »»

Figure 2. Operational Qualification (OQ) report generated using MicroLab OQ under MicroLab Pharma. Results are reported with all test parameters along with easy to ready pass/fail results.

Instrument performance check using MicroLab PC

MicroLab OQ software may not cover some pharmacopeia tests and limits. When this is the case, MicroLab PC can be used to verify the instrument performance. MicroLab PC is a method-driven software that uses the same picture-guidance as MicroLab OQ to help users through all steps of the analysis.

A selection of widely applicable methods for wavenumber accuracy and spectral resolution are preinstalled with the MicroLab software. These methods can be used as is or customized to verify instrument performance according to the global pharmacopeia requirements.

A color-coded result view, and automatic PDF report (fully customizable) generation are provided at the completion of each test (Figure 3). The result screen can be customized as required (Figure 4).

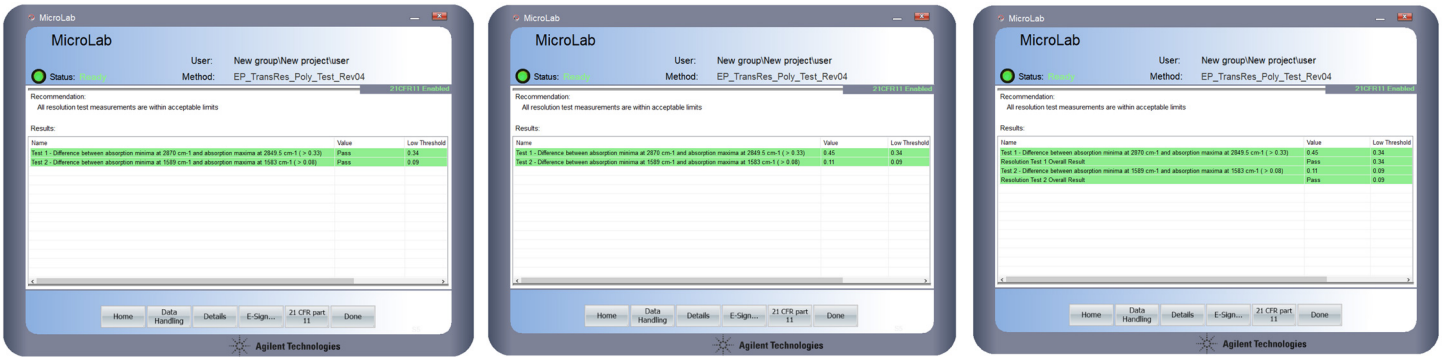


Figure 3. Examples of customized spectral resolution test methods following Ph. Eur. The method can be customized to show (A) a pass/fail indication along with the tolerance limits for the test, (B) a combination of both result values along with the tolerance limits for the test, or alternatively, (C) a combination of both pass/fail indication and result values along with the tolerance limits for the test. Color-coding (green), indicates a pass value.

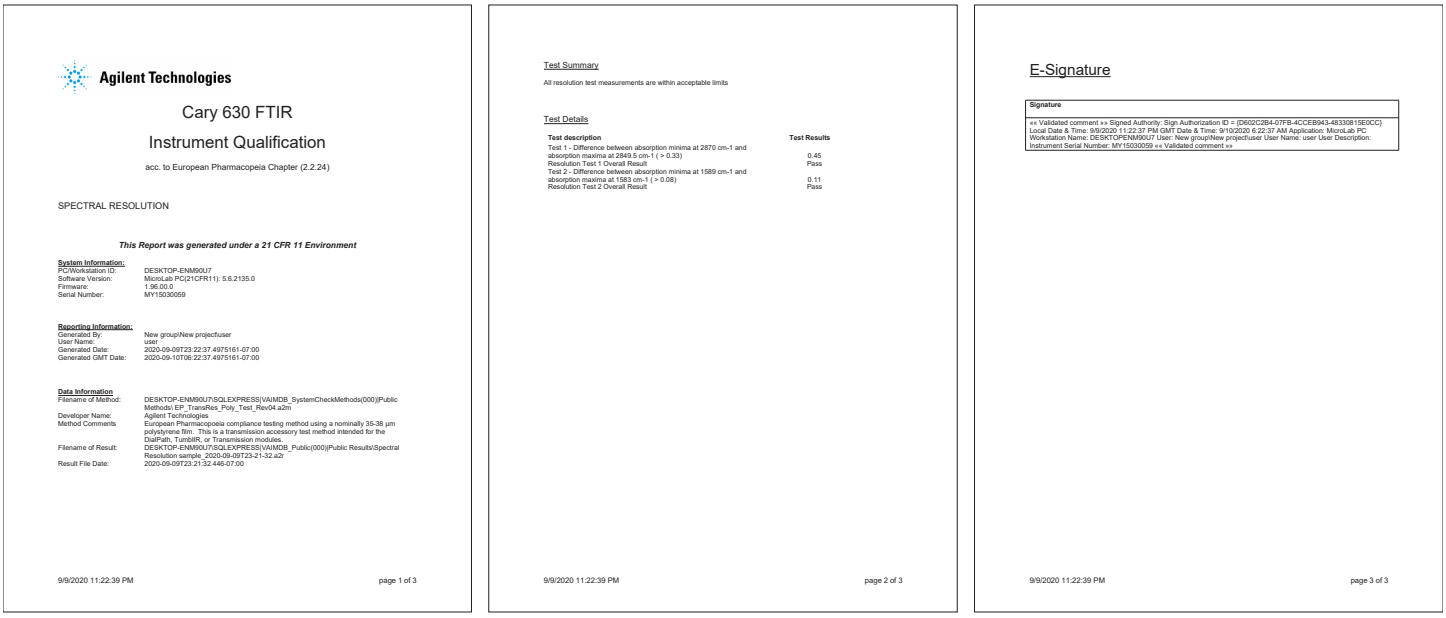


Figure 4. A PDF report is automatically generated following the completion of a test. The report is fully customizable to report the relevant information and test details. The shown report has been created from the method example C in Figure 3.

European Pharmacopeia (Ph. Eur.)

Requirements for IR spectrometer performance are outlined in Chapter (2.2.24) of the Ph. Eur. The chapter describes the performance parameters that must be verified to qualify the Cary 630 FTIR spectrometers. These parameters are *Wavenumber Scale* (equivalent to wavenumber accuracy) and *Spectral Resolution*. Chapter 2.2.24 specifies the test procedure for transmission and ATR measurement mode. The MicroLab OQ software can be used to evaluate the performance of Cary 630 FTIR spectrometers (in transmission and ATR measurement mode) in accordance to the Ph. Eur. requirements (number of runs set to "1" for both tests).

Transmission measurement mode

Passing the "Laser Frequency Calibration Check" (= *Wavenumber Scale*) and the "Spectral Resolution Check" in the MicroLab OQ software indicates that the instrument is performing to Ph. Eur. specifications. Table 1 shows the test parameters, their limits for transmission measurement mode as well as the test outcome for two Cary 630 FTIR instruments. Figure 5 shows the automatically created PDF report for the Cary 630 FTIR with ZnSe optics. Extra bands are tested under the "Laser Frequency Calibration Check" that are not required by the Ph. Eur.

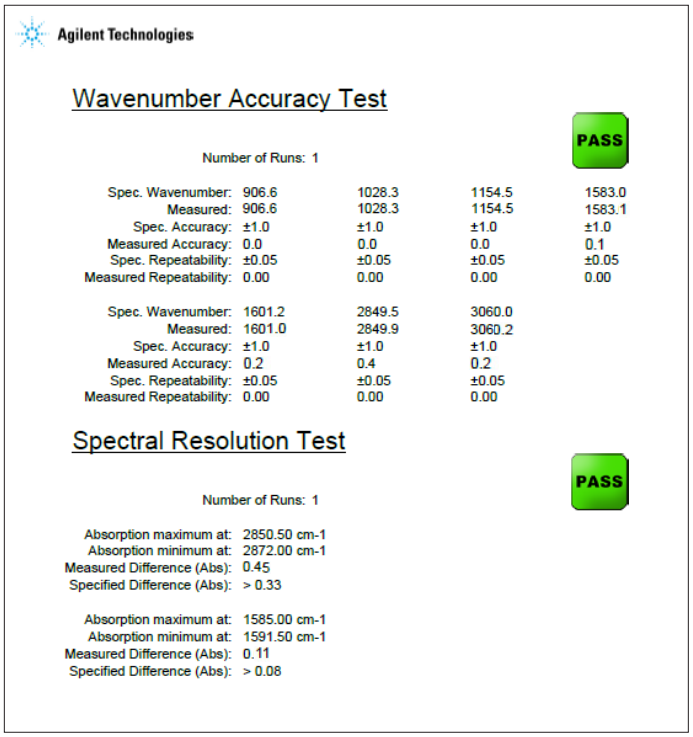


Figure 5. Extract from the Operational Qualification (OQ) report generated by MicroLab OQ. It verifies that the Cary 630 FTIR with ZnSe optics operated in transmission measurement mode met the Ph. Eur. requirements. Results are reported with all test parameters along with easy to ready pass/fail results.

Table 1. Ph. Eur. system verification test descriptions and test limits as well as the test outcome for the two tested Cary 630 FTIR instruments in transmission measurement mode.

		Results	
Test description and limits		Cary 630 with KBr optics	Cary 630 with ZnSe optics
Wavenumber Scale			
Position of band maxima of polystyrene film			
906.6 cm^{-1} 1028.3 cm^{-1} 1601.2 cm^{-1} 3060.0 cm^{-1}	±1.0 cm^{-1}	✓	✓
Spectral Resolution			
Difference between the absorbance values at:			
the absorption minimum at 2870 cm^{-1} and the absorption maximum at 2849.5 cm^{-1}.	>0.33	✓	✓
the absorption minimum at 1589 cm^{-1} and the absorption maximum at 1583 cm^{-1}.	>0.33		
Overall Verification Result		Pass	Pass

Table 2. Ph. Eur. system verification test descriptions and test limits as well as the test outcome for the two tested Cary 630 FTIR instruments in ATR measurement mode.

		Results	
Test description and limits		Cary 630 with KBr optics	Cary 630 with ZnSe optics
Wavenumber Scale			
Position of band maxima of polystyrene film			
906.1 cm^{-1} 1027.7 cm^{-1} 1601.0 cm^{-1} 3059.7 cm^{-1}	±1.0 cm^{-1}	✓	✓
*Spectral Resolution**			
Ratio between absorbance value at:			
absorption maximum at ~2850 cm-1 and absorbance value at 2870.0 cm^{-1}	≥1.15	✓	✓
absorption maximum at ~1601.0 cm-1 and absorbance value at 1589.0 cm^{-1}	≥1.30		
	Overall Verification Result	Pass	Pass

ATR measurement mode

The *Wavenumber Scale* test for ATR measurement modes uses the same methodology as for transmission measurement mode with band maxima as specified in Table 2. The Ph. Eur. does not define the *Spectral Resolution* requirements for IR spectrometers operating in ATR measurement mode.

Instead, in the section "*Spectral Resolution*", the Ph. Eur. states that:

- appropriate assessment criteria must be defined for the control of *Spectral Resolution* in ATR mode, and
- this assessment needs to be made in accordance with the specifications of the instrument.

To verify *Spectral Resolution* of Cary 630 FTIR spectrometers operating in ATR measurement mode, wavenumber setpoints and limits were adapted based on the Ph. Eur. transmission measurement mode.

Table 2 shows the test parameters, and their limits for ATR measurement mode as well as the test outcome for the two Cary 630 FTIR instruments. Figure 6 shows the automatically created PDF report for the Cary 630 FTIR with ZnSe optics.

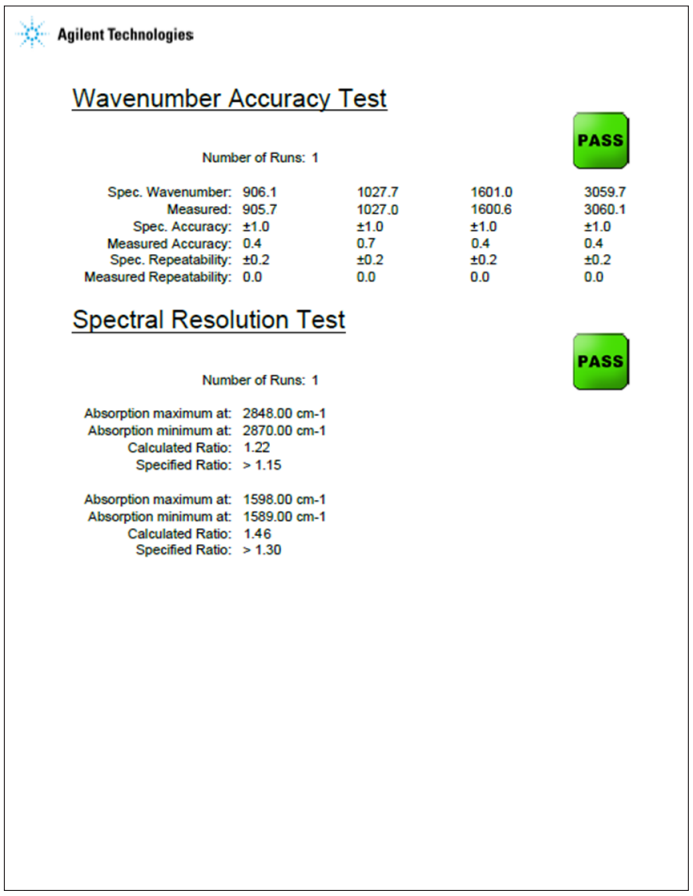


Figure 6. Extract from the Operational Qualification (OQ) report generated using MicroLab OQ. It verifies that the Cary 630 FTIR with ZnSe optics operated in ATR measurement mode met the Ph. Eur. requirements. Results are reported with all test parameters along with easy to ready pass/fail results.

***** *Test parameters and test limits recommended by Agilent in accordance with Ph. Eur. guidance.*

Table 3. USP system verification test descriptions and test limits as well as the test outcome for the two tested Cary 630 FTIR instruments in transmission measurement mode.

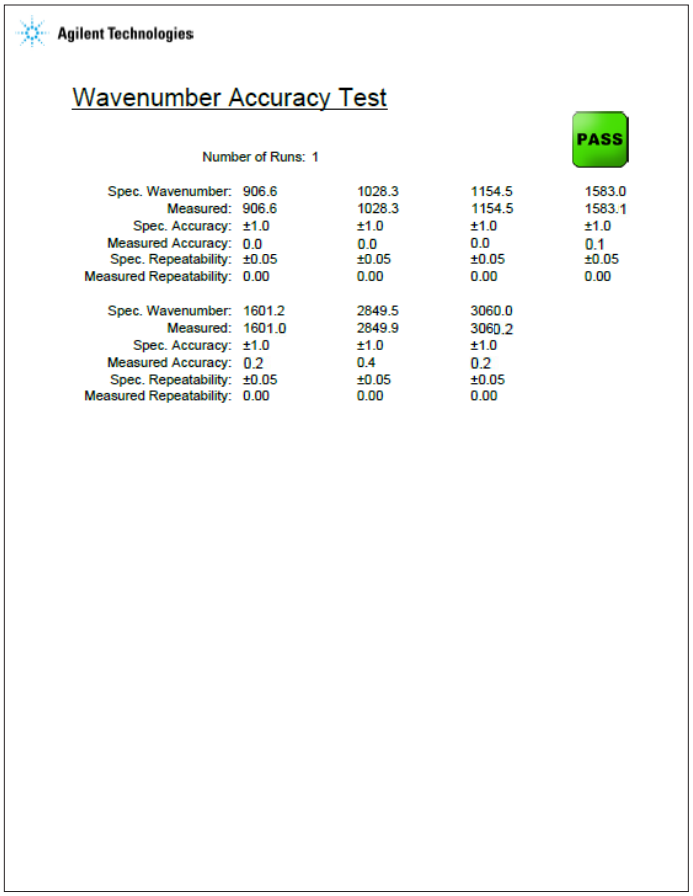
		Results	
Test description and limits		Cary 630 with KBr optics	Cary 630 with ZnSe optics
Wavenumber Accuracy			
Position of band maxima of polystyrene film			
1028.3 cm^{-1} 1154.5 cm^{-1} 1583.0 cm^{-1} 1601.2 cm^{1} (1942.9 cm^{-1})(*1*) 2849.5 cm^{-1}. 3060.0 cm^{-1}	±1.0 cm^{-1}	✓	✓
Overall Verification Result		Pass	Pass

United State Pharmacopeia (USP)

Chapter <854>, Mid-FTIR spectrometers, in the USP describes the instrument qualification requirements for mid-IR instruments. Operation Qualification according to USP Chapter <854> requires determining the *Wavenumber Accuracy* of the spectrometer. The USP Chapter <854> references several sharp bands of a polystyrene film that can be used to check the *Wavenumber Accuracy.* The chapter advises that the most frequently selected band for determining *Wavenumber Accuracy* is at 1601.2 cm^{-1}. There is no requirement to measure at multiple wavenumbers.

Passing the "Laser Frequency Calibration Check" (= *Wavenumber Accuracy*) in the MicroLab OQ software indicates that the instrument is performing to USP Chapter <854> specifications. The "Laser Frequency Calibration Check" in MicroLab OQ utilizes all band positions given in USP Chapter <854> (except for the band at 1942 cm^{-1})[1]. An additional band at 906 cm^{-1} is included in the "Laser Frequency Calibration Check" test that is not listed in the USP Chapter <854>.

The MicroLab OQ software was used to evaluate the two Cary 630 FTIR spectrometers performance, in accordance with USP Chapter <854> requirements (number of runs set to "1"). Table 3 summarizes the test parameters, and their limits as well as the test outcome for the two tested Cary 630 FTIR instruments. Figure 7 shows the automatically created PDF report for the Cary 630 FTIR with ZnSe optics.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Wavenumber Accuracy Test

PASS

Number of Runs: 1

Spec. Wavenumber:	906.6	1028.3	1154.5	1583.0
Measured:	906.6	1028.3	1154.5	1583.1
Spec. Accuracy:	±1.0	±1.0	±1.0	±1.0
Measured Accuracy:	0.0	0.0	0.0	0.1
Spec. Repeatability:	±0.05	±0.05	±0.05	±0.05
Measured Repeatability:	0.00	0.00	0.00	0.00

Spec. Wavenumber:	1601.2	2849.5	3060.0
Measured:	1601.0	2849.9	3060.2
Spec. Accuracy:	±1.0	±1.0	±1.0
Measured Accuracy:	0.2	0.4	0.2
Spec. Repeatability:	±0.05	±0.05	±0.05
Measured Repeatability:	0.00	0.00	0.00

Figure 7. Extract from the Operational Qualification (OQ) report generated using MicroLab OQ. It verifies that the Cary 630 FTIR, with ZnSe optics operated in transmission measurement mode met the USP requirements. Results are reported with all test parameters along with easy to read pass/fail results.

Table 4. Indian pharmacopeia system verification test descriptions and test limits as well as the test outcome for the two tested Cary 630 FTIR instruments in transmission measurement mode.

		Results	
Test description and limits		Cary 630 with KBr optics	Cary 630 with ZnSe optics
Verification of Wave Number Scale			
Position of band maxima of polystyrene film			
1028.3 cm^{-1} 1154.5 cm^{-1} 1583.0 cm^{-1} 1601.2 cm^{-1} (1942.9 cm^{-1})(*1*) 2849.5 cm^{-1} 3060.0 cm^{-1}	±1.0 cm^{-1}	✓	✓
*Spectral Resolution**			
Ratio between absorbance value at:			
the absorption minimum at 2870 cm^{-1} and the absorption maximum at 2849.5 cm^{-1}	>0.33	✓	✓
the absorption minimum at 1589 cm^{-1} and the absorption maximum at 1583 cm^{-1}	>0.08		
	Overall Verification Result	Pass	Pass

Indian Pharmacopeia (IP)

The Indian Pharmacopeia (IP) outlines the tests and limits to verify infrared spectrometers in Chapter 2.4.6. The IP requires *Verification of Wave Number Scale* (equivalent to wavenumber accuracy) and *Control of Resolution Performance* (equivalent to spectral resolution) for instrument qualification.

Passing the "Laser Frequency Calibration Check" (= *Verification of Wave Number Scale*) and the "Spectral Resolution Check" (= *Control of Resolution Performance*) in the MicroLab OQ software indicates that the instrument is performing to IP specifications.

The MicroLab OQ software was used to evaluate the Cary 630 FTIR spectrometers performance in accordance to the IP requirements (number of runs set to "1" for both tests). The "Laser Frequency Calibration Check" utilizes all band positions given in IP Chapter 2.4.6 (except for the band at 1942 cm^{-1})(*1*). An additional band at 906 cm^{-1} is included in the "Laser Frequency Calibration Check" test that is not required for the *Verification of Wave Number Scale* according to the IP. Table 4 shows the test parameters, and their limits as well as the test outcome for the two tested Cary 630 FTIR instruments. Figure 8 shows the automatically created PDF report for the Cary 630 FTIR with ZnSe optics.

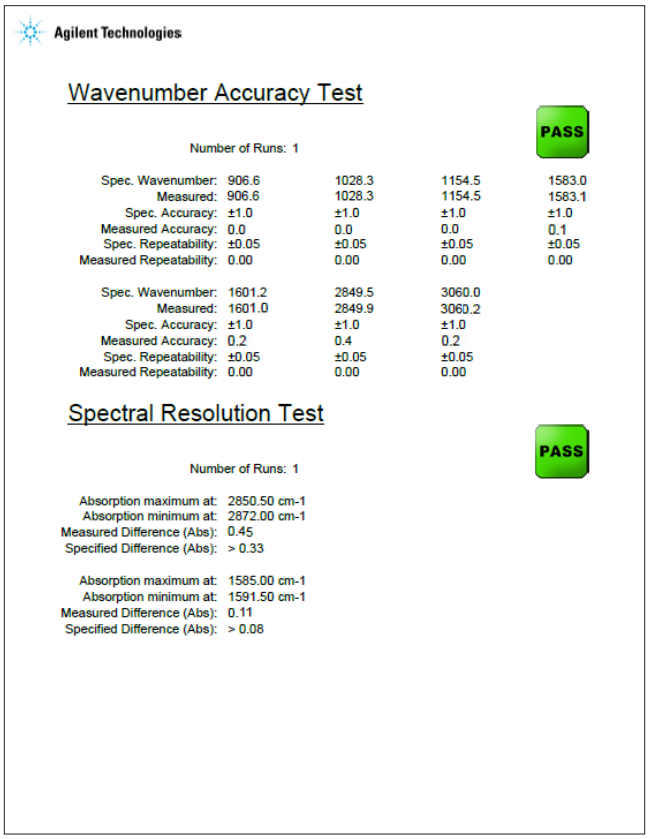


Figure 8. Extract from the Operational Qualification (OQ) report generated using MicroLab OQ. It verifies that the Cary 630 FTIR with ZnSe optics operated in transmission measurement mode met the IP requirements. Results are reported with all test parameters along with easy to read pass/fail results.

Japanese Pharmacopeia (JP)

The Japanese Pharmacopeia (JP) defines instrument qualification for infrared spectrophotometry in chapter 2.25. For an FTIR instrument to be qualified in accordance to the JP, *Wave Number Scale* (equivalent to wavenumber accuracy) and *Resolving Power* (equivalent to spectral resolution) must be verified. The JP describes two more parameters not found in the Ph. Eur., USP or IP. These are *Transmittance Reproducability* and *Wave Number Reproducability.*

The MicroLab PC software was used to validate the Cary 630 FTIR spectrophotometers, performance in accordance to the JP requirements. Suitable methods were generated to run the performance tests in accordance to the JP specifications using MicroLab PC.

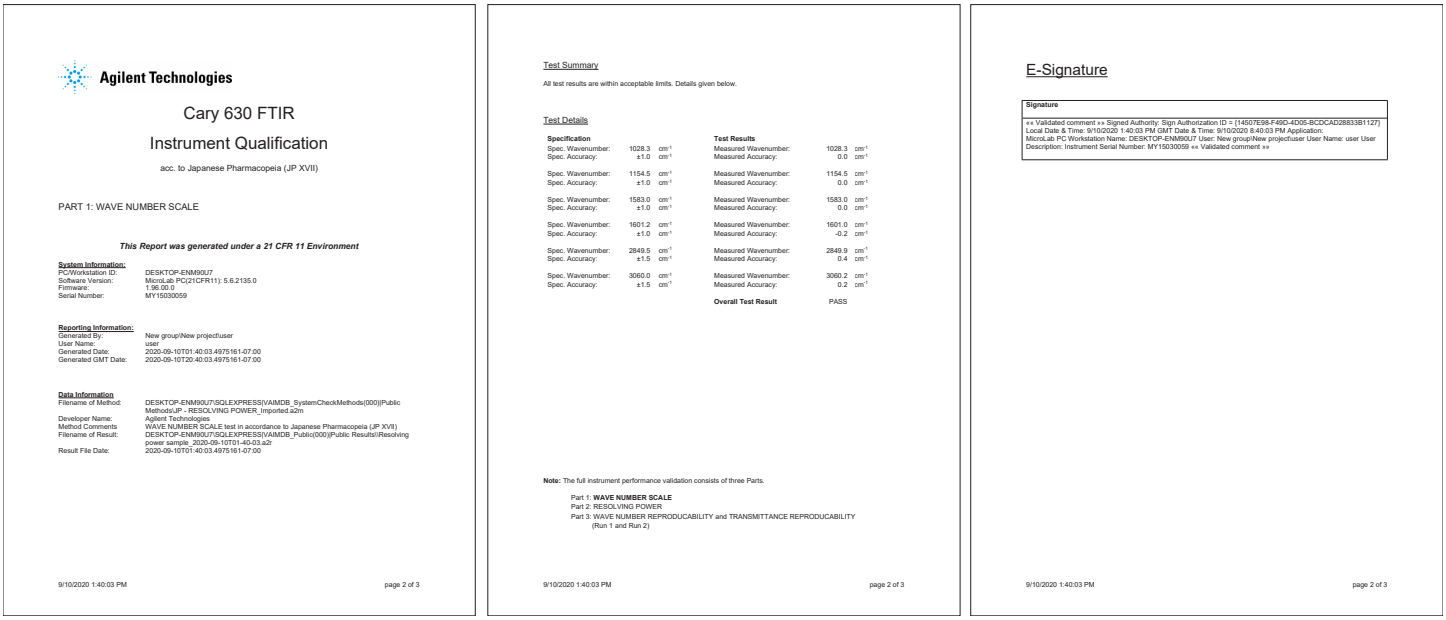
For the full verification according to the JP, three MicroLab methods were used. After a method is started, the software guides the user through the test procedure using picture-driven workflows. At the end of the analysis, color-coded results are presented, and a customized PDF report is created for future reference.

Wave Number Scale

To verify the *Wave Number Scale,* the pre-installed method "LaserFreqCalTest_Transmission" was customized to align with the test requirements given in the JP. Specifically, the acceptance limits for the bands at 3060.0 cm^{-1} and 2849.5 cm^{-1} have been adjusted to ±1.5 cm^{-1} and the band at 906.6 cm^{-1} has been removed from the test. The band at 1942.9 cm^{-1} is not used to verify the *Wave Number Scale*.(*1*) Figure 9 shows the automatically created PDF report for the *Wave Number Scale* test for the Cary 630 FTIR with ZnSe optics.

Resolving Power

To verify the *Resolving Power* the preinstalled method "EP_TransRes_Poly_Test_Rev04" was customized to align with the test requirements given in the JP. Specifically, the method was adjusted for "transmittance" and the acceptance limit for the difference of the maximum absorption at about 2850 cm^{-1} and the minimum at about 2870 cm^{-1} was set to 18% transmittance. The acceptance limit for the difference of the maximum absorption at about 1583 cm^{-1} and the minimum at about 1589 cm^{-1} was set to 12% transmittance. Figure 7 shows the automatically created PDF report for the Cary 630 FTIR with ZnSe optics.



Agilent Technologies

Cary 630 FTIR

Instrument Qualification

acc. to Japanese Pharmacopeia (JP XVII)

PART 1: WAVE NUMBER SCALE

This Report was generated under a 21 CFR 11 Environment

System Information:
PC/Workstation ID: DESKTOP-ENM90U7
Software Version: MicroLab PC(21CFR11): 5.6.2135.0
Firmware: 1.96.00.0
Serial Number: MY15030059

Reporting Information:
Generated By: New group\New projectfuser
User Name: user
Generated Date: 2020-09-10T01:40:03.4975161-07:00
Generated GMT Date: 2020-09-10T20:40:03.4975161-07:00

Data Information
Filename of Method: DESKTOP-ENM90U7\SQLEXPRESS|VAIMDB_SystemCheckMethods(000)|Public Methods|JP - RESOLVING POWER_Imported.a2m
Developer Name: Agilent Technologies
Method Comments: WAVE NUMBER SCALE test in accordance to Japanese Pharmacopeia (JP XVII)
Filename of Result: DESKTOP-ENM90U7\SQLEXPRESS|VAIMDB_Public(000)|Public Results\\Resolving power sample_2020-09-10T01-40-03.a2r
Result File Date: 2020-09-10T01:40:03.4975161-07:00

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Test Summary

All test results are within acceptable limits. Details given below.

Test Details

Specification			Test Results		
Spec. Wavenumber:	1028.3	cm^{-1}	Measured Wavenumber:	1028.3	cm^{-1}
Spec. Accuracy:	±1.0	cm^{-1}	Measured Accuracy:	0.0	cm^{-1}
Spec. Wavenumber:	1154.5	cm^{-1}	Measured Wavenumber:	1154.5	cm^{-1}
Spec. Accuracy:	±1.0	cm^{-1}	Measured Accuracy:	0.0	cm^{-1}
Spec. Wavenumber:	1583.0	cm^{-1}	Measured Wavenumber:	1583.0	cm^{-1}
Spec. Accuracy:	±1.0	cm^{-1}	Measured Accuracy:	0.0	cm^{-1}
Spec. Wavenumber:	1601.2	cm^{-1}	Measured Wavenumber:	1601.0	cm^{-1}
Spec. Accuracy:	±1.0	cm^{-1}	Measured Accuracy:	-0.2	cm^{-1}
Spec. Wavenumber:	2849.5	cm^{-1}	Measured Wavenumber:	2849.9	cm^{-1}
Spec. Accuracy:	±1.5	cm^{-1}	Measured Accuracy:	0.4	cm^{-1}
Spec. Wavenumber:	3060.0	cm^{-1}	Measured Wavenumber:	3060.2	cm^{-1}
Spec. Accuracy:	±1.5	cm^{-1}	Measured Accuracy:	0.2	cm^{-1}
			Overall Test Result	PASS	

Note: The full instrument performance validation consists of three Parts.

Part 1: **WAVE NUMBER SCALE**
Part 2: RESOLVING POWER
Part 3: WAVE NUMBER REPRODUCABILITY and TRANSMITTANCE REPRODUCABILITY (Run 1 and Run 2)

9/10/2020 1:40:03 PM page 2 of 3

E-Signature

Signature

«« Validated comment »» Signed Authority: Sign Authorization ID = {14507E98-F49D-4D05-BCDCAD28833B1127} Local Date & Time: 9/10/2020 1:40:03 PM GMT Date & Time: 9/10/2020 8:40:03 PM Application: MicroLab PC Workstation Name: DESKTOP-ENM90U7 User: New group\New projectfuser User Name: user User Description: Instrument Serial Number: MY15030059 «« Validated comment »»

9/10/2020 1:40:03 PM page 2 of 3

Figure 9. Full report automatically generated using MicroLab PC used to verify that the *Wavenumber Scale* of the Cary 630 FTIR with ZnSe optics operated in transmission measurement mode met the JP requirements. The report can be customized to include all relevant information and test results.

Wave Number Reproducibility and *Transmittance Reproducibility*

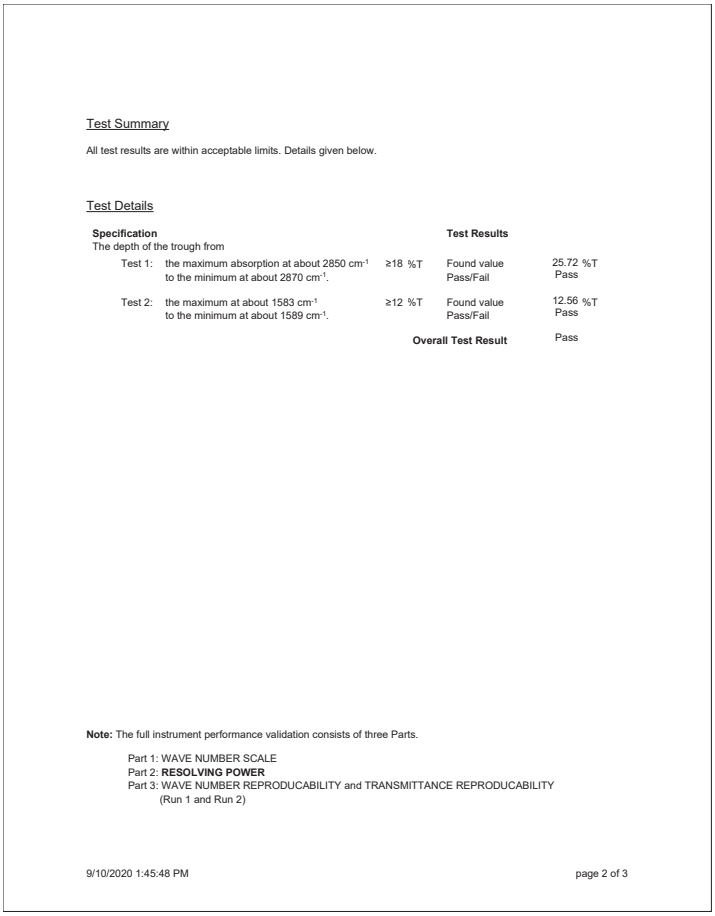
To verify the *Wave Number Reproducibility* and *Transmittance Reproducibility* a customized MicroLab method has been created. The method automatically reports the band positions for the bands at about 3060 cm^{-1} and 1028 cm^{-1}, and the %T of the band maxima at about 3060 cm^{-1}, about 2849 cm^{-1}, about 1601 cm^{-1}, about 1583 cm^{-1}, about 1154 cm^{-1} and about 1028 cm^{-1}.

The method was run twice and the differences of wavenumbers at about 3060 cm^{-1} and about 1028 cm^{-1} between the two runs were used to verify that the *Wave Number Reproducibility* was within the limits given in the JP. Likewise, the difference between the %T values of the two runs at each band maximum has been used to verify that the *Transmittance Reproducibility* was within the limits given in the JP.

The PDF reports for the two runs serve as record that the instrument passes the JP performance criteria for *Wave Number Scale* and *Wave Number Reproducibility.*

Figure 10 shows extractions of the automatically created PDF reports for the *Resolving Power* test and the *Wave Number Reproducability* and *Transmittance Reproducibility* test for the Cary 630 FTIR with ZnSe optics.

Table 5 shows the test parameters, and their limits as well as the results obtained for the two Cary 630 FTIR instruments tested. It further details the measured values for *Wave Number Reproducibility* and *Transmittance Reproducability* for both instruments.



Test Summary

All test results are within acceptable limits. Details given below.

Test Details

Specification			Test Results	
The depth of the trough from				
Test 1:	the maximum absorption at about 2850 cm^{-1} to the minimum at about 2870 cm^{-1}.	≥18 %T	Found value Pass/Fail	25.72 %T Pass
Test 2:	the maximum at about 1583 cm^{-1} to the minimum at about 1589 cm^{-1}.	≥12 %T	Found value Pass/Fail	12.56 %T Pass
			Overall Test Result	Pass

Note: The full instrument performance validation consists of three Parts.

Part 1: WAVE NUMBER SCALE
Part 2: **RESOLVING POWER**
Part 3: WAVE NUMBER REPRODUCABILITY and TRANSMITTANCE REPRODUCABILITY
(Run 1 and Run 2)

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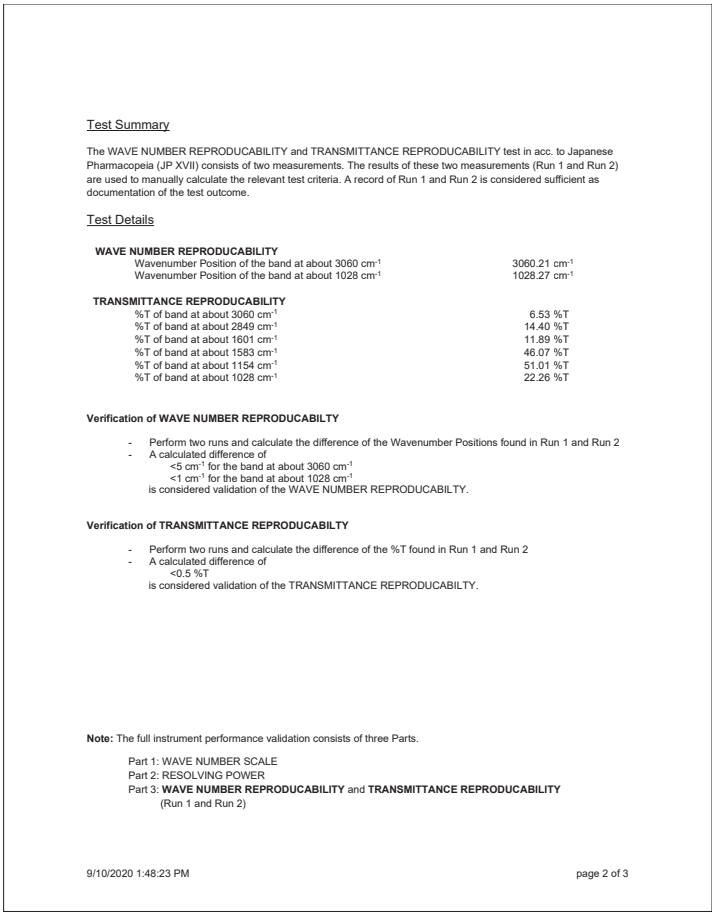

Test Summary

The WAVE NUMBER REPRODUCABILITY and TRANSMITTANCE REPRODUCABILITY test in acc. to Japanese Pharmacopeia (JP XVII) consists of two measurements. The results of these two measurements (Run 1 and Run 2) are used to manually calculate the relevant test criteria. A record of Run 1 and Run 2 is considered sufficient as documentation of the test outcome.

Test Details

WAVE NUMBER REPRODUCABILITY	
Wavenumber Position of the band at about 3060 cm^{-1}	3060.21 cm^{-1}
Wavenumber Position of the band at about 1028 cm^{-1}	1028.27 cm^{-1}
TRANSMITTANCE REPRODUCABILITY	
%T of band at about 3060 cm^{-1}	6.53 %T
%T of band at about 2849 cm^{-1}	14.40 %T
%T of band at about 1601 cm^{-1}	11.89 %T
%T of band at about 1583 cm^{-1}	46.07 %T
%T of band at about 1154 cm^{-1}	51.01 %T
%T of band at about 1028 cm^{-1}	22.26 %T

Verification of WAVE NUMBER REPRODUCABILTY

- Perform two runs and calculate the difference of the Wavenumber Positions found in Run 1 and Run 2
- A calculated difference of
  <5 cm^{-1} for the band at about 3060 cm^{-1}
  <1 cm^{-1} for the band at about 1028 cm^{-1}
  is considered validation of the WAVE NUMBER REPRODUCABILTY.

Verification of TRANSMITTANCE REPRODUCABILTY

- Perform two runs and calculate the difference of the %T found in Run 1 and Run 2
- A calculated difference of
  <0.5 %T
  is considered validation of the TRANSMITTANCE REPRODUCABILTY.

Note: The full instrument performance validation consists of three Parts.

Part 1: WAVE NUMBER SCALE
Part 2: RESOLVING POWER
Part 3: **WAVE NUMBER REPRODUCABILITY** and **TRANSMITTANCE REPRODUCABILITY**
(Run 1 and Run 2)

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Figure 10. Extract from the reports automatically generated using MicroLab PC used to verify that the *Resolving Power* (left) and the *Wave Number Reproducibility* and *Transmittance Reproducibility* (right) of the Cary 630 FTIR with ZnSe optics operated in transmission measurement mode met the JP requirements. The report can be customized to include all relevant information and test results.

Table 5. JP system verification test descriptions and test limits as well as the test outcome for the two tested Cary 630 FTIR instruments in transmission measurement mode. Measured values for *Wave Number Reproducibility* and *Transmittance Reproducibility*.

		Results			
Test description and limits		Cary 630 with KBr optics		Cary 630 with ZnSe optics	
Wave Number Scale					
Position of band maxima of polystyrene film					
1028.3 cm^{-1} 1154.5 cm^{-1} 1583.0 cm^{-1} 1601.2 cm^{-1} (1942.9 cm^{-1})(*1*) 2849.5 cm^{-1} 3060.0 cm^{-1}	±1.0 cm^{-1} ±1.0 cm^{-1} ±1.0 cm^{-1} ±1.0 cm^{-1} ±1.5 cm^{-1} ±1.5 cm^{-1} ±1.5 cm^{-1}	✓		✓	
Resolving Power					
The depth of the trough from:					
the maximum absorption at about 2850 cm^{-1} to the minimum at about 2870 cm^{-1}	≥18% transmittance	✓		✓	
the maximum at about 1583 cm^{-1} to the minimum at about 1589 cm^{-1}	≥12% transmittance				
Wave Number Reproducibility					
Difference of wavenumber of two spectra at:		**Measured values (cm^{-1})**		**Measured values (cm^{-1})**	
about 3060 cm^{-1}	<5cm^{-1}	Run 1: 3059.90 Run 2: 3059.91 **Difference: 0.01**	✓	Run 1: 3060.21 Run 2: 3060.18 **Difference: 0.03**	✓
about 1028 cm^{-1}	<1cm^{-1}	Run 1: 1028.30 Run 2: 1028.30 **Difference: 0.00**		Run 1: 1028.27 Run 2: 1028.27 **Difference: 0.00**	
Transmittance Reproducibility					
Difference of transmittance of several bands measured twice from 3000 to 1000 cm^{-1} at:					
about 3060 cm^{-1}	<0.5%	Run 1: 8.15 Run 2: 8.17 **Difference: 0.02**	✓	Run 1: 6.53 Run 2: 6.59 Difference: 0.06	✓
about 2849 cm^{-1}		Run 1: 14.77 Run 2: 14.79 **Difference: 0.02**		Run 1: 14.40 Run 2: 14.42 Difference: 0.02	
about 1601 cm^{-1}		Run 1: 11.36 Run 2: 11.36 **Difference: 0.00**		Run 1: 11.89 Run 2: 11.91 Difference: 0.02	
about 1583 cm^{-1}		Run 1: 45.72 Run 2: 45.68 **Difference: 0.04**		Run 1: 46.07 Run 2: 46.08 Difference: 0.01	
about 1154 cm^{-1}		Run 1: 50.34 Run 2: 50.34 **Difference: 0.00**		Run 1: 51.01 Run 2: 50.94 Difference: 0.07	
about 1028 cm^{-1}		Run 1: 22.01 Run 2: 21.97 **Difference: 0.04**		Run 1: 22.26 Run 2: 22.31 Difference: 0.05	
	Overall Verification Result	Pass		Pass	

Conclusion

Qualification and ongoing monitoring of instrument performance is an important aspect of ensuring accurate and reproducible measurements in pharmaceutical laboratories.

This white paper demonstrates how the Agilent MicroLab software suite can be used to verify that Cary 630 FTIR spectrometers meet the performance specifications required by the US, European, Japanese, and Indian Pharmacopoeias.

The MicroLab OQ software application covers the qualification requirements for the US, European, and Indian Pharmacopoeias while MicroLab PC can be used to create customized testing methods including automatic reporting for pharmacopeia not covered under MicroLab OQ which has been, as demonstrated here for the Japanese Pharmacopeia.

The Agilent Cary 630 FTIR spectrometer is ultra compact, easy to use, and has exceptional performance. With its flexible sampling technology, the Cary 630 FTIR is a capable spectrometer for QA/QC, analytical services, and method development in regulated pharmaceutical industry environments.

The optional MicroLab Pharma software package also supports users in regulated environments and provides tools to help achieve compliance with electronic record regulations such as 21 CFR Part 11 and EU Annex 11.

End note

1. The band at around 1942.9 cm^{-1} was determined in NIST SRM 1921b by “extrapolated center of gravity”. MicroLab uses “center of gravity” peak determination. It is therefore justifiable that this setpoint is omitted from the Wavenumber Accuracy test without compromising the qualification requirements. For details, please contact your local Agilent representative.

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