Agilent Cary 630 FTIR Pharmacopoeia compliance

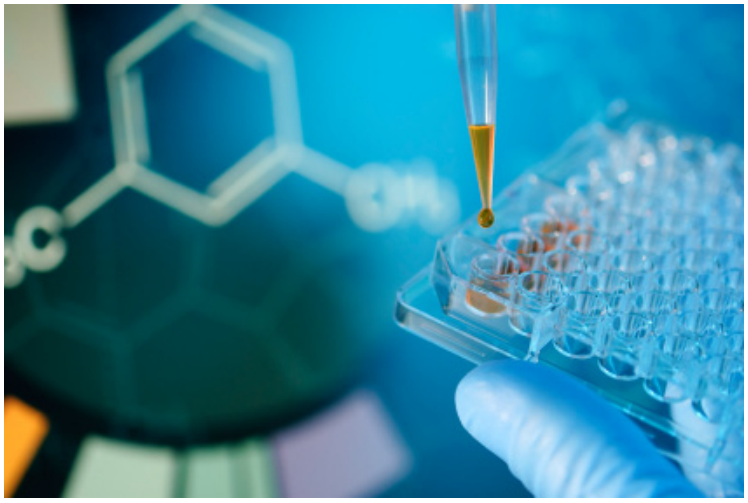
Application note

Pharmaceutical

Authors

Frank Higgins and John Seelenbinder

Agilent Technologies
Danbury, CT, USA



Instrument performance requirements

In an attempt to standardize pharmaceutical measurement and compounding, several countries publish Pharmacopoeia, which provide procedures and standards for identification of pharmaceuticals by many methods, including FTIR. The most often cited example is the US Pharmacopoeia, but there also exists a European Union, Japanese, Chinese and Indian Pharmacopoeia, as well as an international version. All versions give procedures and practices for identification of materials by FTIR. In addition, some give required instrument performance specifications. A good summary of the differences between the US, European, Japanese, Indian, Chinese and International Pharmacopoeias can be found in an article titled "FTIR Identification", Pharmaceutical Technology Europe (September 2011, pp 87–88).

The Agilent Cary 630 FTIR is uniquely suited for use in pharmaceutical quality control applications. The Cary 630 FTIR incorporates ease-of-use, ruggedness and unique dedicated sampling accessories in a highly compact system with class-leading performance. This provides the spectrometer with major advantages for routine measurement in an industry that is highly regulated. Additionally, Agilent's 21 CFR Part 11 compliant Microlab PC software package provides the data security and logging capabilities required in the pharmaceutical industry. Furthermore, the available automated Installation Qualification/Operational Qualification (Auto IQ/OQ) software can be used to routinely verify instrument performance. The Cary 630 FTIR is available with transmission, diffuse reflectance and ATR sample interfaces, which are specified in the US and other Pharmacopoeia for identification. This application note will document the compliance of the Cary 630 FTIR spectrometer with performance standards published in the US, European, Japanese, Chinese, Indian and International Pharmacopoeia.

Results and discussion

A Cary 630 FTIR system (serial number 11410805) was selected for compliance verification directly after completing the standard post-manufacturing system tests. This instrument was tested as it would be received by a customer, with no additional calibration or tuning. A method was created in the Microlab PC software for measurement of the frequency accuracy and resolution, as specified in the European, Japanese, Chinese and Indian Pharmacopoeia. For all tests measuring polystyrene, a NIST traceable, 38 micron thick polystyrene film was measured in transmission mode. The absorbance spectrum of this polystyrene standard with the specified bands labeled is shown in Figure 1.

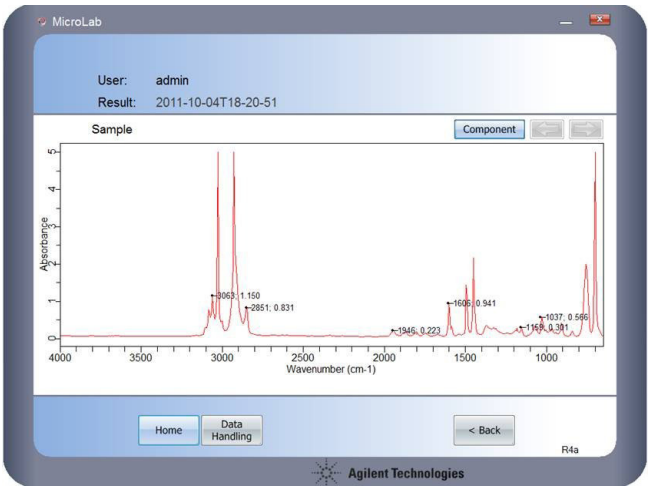


Figure 1. Spectrum of a 38 µm NIST traceable polystyrene film measured on an Agilent Cary 630 FTIR with specified bands labeled

Microlab PC methods are designed to make repetitive measurements easy to use. The method defines the entire analysis from collection of the spectrum to the quantitative or library search analysis. This method was configured to collect a spectrum at 4 cm^{-1} resolution using triangular apodization with no zero filling and a 30 second collection time (74 scans co-added). The component method was configured to find the peak center for each of the specified bands and calculate the ratios required for the resolution tests. An example of the output from the Microlab PC method established for these tests is shown in Figure 2.

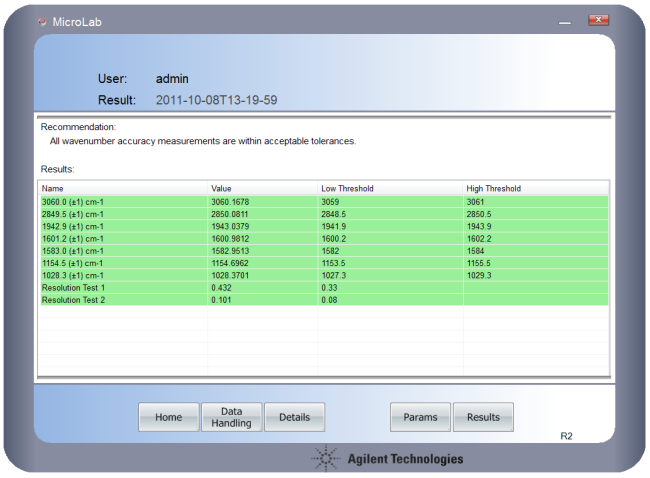


Figure 2. The FTIR results from a polystyrene European Pharmacopoeia performance test method. The values as well as the low and high thresholds are shown; and the green color-coding indicates that all wavenumber accuracy measurements are within acceptable tolerances. A red warning would appear if any results were outside of these ranges.

Table 1 shows the results of the tests performed on the Cary 630 FTIR, as specified in each individual Pharmacopoeia, and indicates that the system readily passes all of the listed specification requirements. As an example, frequency accuracy was measured between two- and ten-fold more accurate than required by even the strictest specification. These results indicate that the Cary 630 FTIR is compliant with the wavelength accuracy and resolution requirements of US, European, Japanese, Chinese, Indian and International Pharmacopoeia.

Pharmaceutical identification by FTIR

As referenced in each Pharmacopeia, the primary use of FTIR is for the identification of pharmaceutical ingredients and products. The infrared spectrum of a sample is compared to a reference spectrum; in the case of the Japanese and International Pharmacopoeia, reference spectra are available online. In general, the reference spectra have been measured in transmission mode, with the sample prepared as a potassium bromide (KBr) pellet. Sample spectra can also be measured by diffuse reflectance infrared Fourier transform (DRIFT) or attenuated total reflectance (ATR) techniques and both methods have the advantage of simple sample preparation. A comparison of the diffuse reflectance spectrum of furosemide measured by the Cary 630 FTIR and the reference spectrum of furosemide from the International Pharmacopoeia website is shown in Figure 3. The sample was prepared by mixing the API with dried KBr in a ratio of 1:5 and lightly grinding to form a homogeneous mixture. Excellent correlation of the frequencies present in the reference spectrum with those of the measured sample is observed.

Table 1. Measured Agilent Cary 630 FTIR performance compared to US, EU, Japanese, Chinese, Indian and International Pharmacopoeia requirements. Summary table adapted from Pharmaceutical Technology Europe, September 2011, pp 87–88.

Requirement	Pharmacopoeia						Cary 630 FTIR	
	US	European	Japanese	Indian	Chinese	International		
Approximate recommended polystyrene thickness	N/A	0.035 mm	0.04 mm	0.035 mm	0.04 mm	MFG	0.035 mm	0.035 mm
Resolution Test: Limit 1 The value between 2870 & 2849.5 cm^{-1}	N/A	>0.33 A	>18 %T	>0.33 A	>18 %T	MFG	0.4343 A Pass	25.01 %T Pass
Resolution Test:: Limit 2	N/A	>0.08 A	>12 %T	>0.08 A	>12 %T	MFG	0.1012A Pass	12.59 %T Pass
Resolution Test: Limit 3 7 resolved peaks between 3110 & 2850 cm^{-1}	N/A	None	None	None	Yes	MFG	Pass	7 bands observed
Wavenumber accuracy	N/A	cm^{-1} ±	cm^{-1} ±	cm^{-1} ±	cm^{-1} ±	MFG	Difference EU, Japan, India (cm^{-1})	Actual values (cm^{-1})
3060.0 cm^{-1}		±1.0	±1.5	±1.0	3027 ±5		+0.17 Pass	3060.16 3025.9
2849.5 cm^{-1}		±1.0	±1.5	±1.0	2851 ±5		+0.58 Pass	2849.75
1942.9 cm^{-1}		±1.0	±1.5	±1.0			+0.14 Pass	1943.12
1601.2 cm^{-1}		±1.0	±1.0	±1.0	1601 ±1		+0.22 Pass	1600.97
1583.0 cm^{-1}		±1.0	±1.0	±1.0			+0.05 Pass	1582.94
1154.5 cm^{-1}		±1.0	±1.0	±1.0	1028 ±1		+0.2 Pass	1154.31
1028.3 cm^{-1}		±1.0	±1.0	±1.0	907 ±1		+0.07 Pass	1028.37 906.60
Reproducibility (between 2 scans):	N/A	None		None	None	MFG		
%T			Δ<0.5 %T				Pass	0.146 %T
Wavenumber								
3000 cm^{-1}			5 cm^{-1}				Pass	0.32 cm^{-1}
1000 cm^{-1}			1 cm^{-1}				Pass	0.01 cm^{-1}

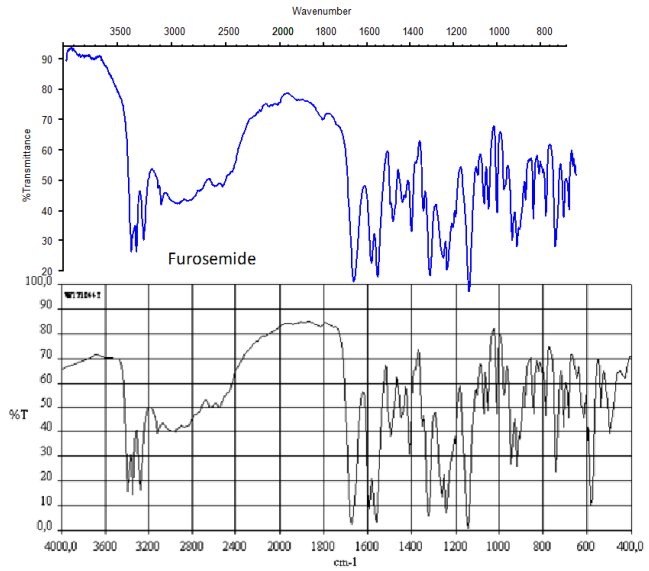


Figure 3. The FTIR spectra of furosemide, comparing the online spectrum from International Pharmacopoeia (Black, KBr pellet) and that measured on the Cary 630 FTIR (Blue, DRIFT)

Similarly, a comparison of the spectrum of caffeine measured on the Cary 630 FTIR using the ATR technique with that of the reference spectrum of caffeine from the International Pharmacopoeia website is shown in Figure 4. Again, the identity of caffeine can be confirmed by comparison of the infrared band frequencies. The intensities differ due to the pathlength differences; however, positive identification only requires a match of the band frequencies.

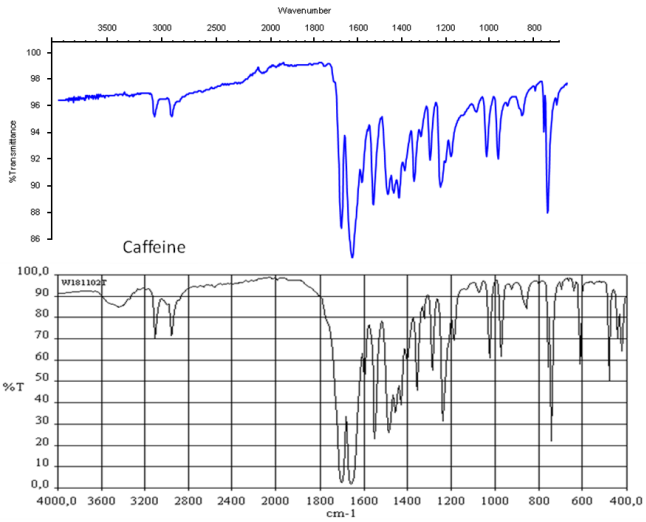


Figure 4. The FTIR spectra of caffeine, comparing the online spectrum from International Pharmacopoeia (Black, KBr Pellet) and that measured on the Agilent Cary 630 FTIR (Blue, ATR)

Conclusions

This application note demonstrates that the Agilent Cary 630 FTIR easily meets the performance specifications of the US, European, Japanese, Chinese, Indian and International Pharmacopoeia. Its combination of compact size, innovative technology, rugged design, intuitive and regulation-compliant software makes the Cary 630 FTIR an ideal instrument for use in pharmaceutical quality control.

www.agilent.com/chem

Published November 10, 2011
Publication number: 5990-9379EN

Agilent Technologies