C103-E119

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FTIR TALK LETTER

Vol. 27

Validation of FTIR Systems

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Methods for validating FTIR systems were described in FTIR Talk Letter Vol. 4 (2006). In recent years, the pharmacopoeia of respective countries, which serve as the basis for the FTIR hardware validation methods, were revised. Therefore, this article discusses the effects of those revisions. First, however, a review of the article from FTIR Talk Letter Vol. 4 is provided below. The word "validate" can mean to legally "enable." When a parking ticket is stamped with a free parking stamp at the cash register after shopping at a department store, for example, we refer to that as "validating" the ticket. For instruments, we use "validation" to indicate that the instrument has been verified to function properly and is "safe and enabled for use." Consequently, it means that the instrument's validity has been verified and it is certified for use. As a result, the noun "validation" is now used to refer to the process of "verifying or confirming the appropriateness, suitability, or legal compliance" of an instrument.

Actually, there are two types of instrument validation - hardware validation and software validation, but this article only addresses validation of FTIR hardware.

1. Hardware Validation

FTIR hardware validation is the process of inspecting FTIR hardware to confirm that it is functioning properly. For FTIR systems, the instrument status is often revealed in the power spectrum. Therefore, one simple validation method is to check the shape and intensity of the power spectrum. In the case of Shimadzu FTIR systems, the shape and intensity of power spectra are checked as part of routine inspections.

In addition, several public institutions have issued standards for methods used to inspect FTIR systems in more detail. For example, industrial standards have been specified by the Japanese Industrial Standards (JIS) and the American Society for Testing and Materials (ASTM), and pharmaceutical standards have been specified in the Japanese Pharmacopoeia (JP), European Pharmacopoeia (EP), United States Pharmacopeia (USP), and Chinese Pharmacopoeia (ChP). For FTIR hardware validation, rather than use JIS or ASTM methods, which do not clearly specify procedures for validating hardware intended for use in industry, Shimadzu uses procedures and standards specified for the pharmaceutical industry, which include clearly specified pharmacopoeia-based validation methods.

Therefore, this article reviews the standards specified in the most recent country-specific pharmacopoeias.

2. Japanese Pharmacopoeia

The 17th edition specifies requirements for instrument and adjustment under the section on Infrared Spectrophotometry in General Tests. It specifies procedures and criteria values for four inspection criteria—resolution, wavenumber accuracy, wavenumber repeatability, and transmittance repeatability.

3. European Pharmacopoeia

The European Pharmacopoeia 8th Edition specifies procedures and criteria values for two inspection criteria—resolution and wavenumber accuracy in the "Control of resolution performance" and "Verification of the wavenumber scale" sections of "Absorption Spectrophotometry, Infrared." It does not include the repeatability criteria specified in the Japanese Pharmacopoeia. Up to the 4th Edition, the European Pharmacopoeia and Japanese Pharmacopoeia standards were the same, but starting with the 5th Edition, European Pharmacopoeia "resolution" standards for FTIR were based on absorbance and the "wavenumber accuracy" standards became ±1.0 cm^{-1} for all wavenumbers.

4. United States Pharmacopeia

Until recently, the United States Pharmacopeia specified FTIR requirements under "851 Spectrophotometry and Light-Scattering", which specified referring to manufacturer instruction manuals for more specific FTIR system operating instructions.
However, section 854, Mid-Infrared Spectroscopy, was added to the United States Pharmacopeia 38th Edition, released in 2015. That section includes wavenumber accuracy as an inspection criterion under "Qualification of IR Spectrophotometers," which specifies the same wavenumber and accuracy inspection requirements as the European Pharmacopoeia wavenumber accuracy requirements.
Until May 2016, inspections based on 851 were permitted on an interim basis, but now inspections based on 854 are required.

5. Chinese Pharmacopoeia

The Chinese Pharmacopoeia specifies procedures and criteria values for three inspection criteria—resolution, wavenumber accuracy, and peak separation function, which are specified in the "Equipment and Calibration" section of "Appendix IV C Infrared Spectrophotometry." Of these inspection criteria, the Chinese Pharmacopoeia specifies validation at different wavenumbers for wavenumber accuracy than either the Japanese Pharmacopoeia, European Pharmacopoeia, or United States Pharmacopeia, and only the Chinese Pharmacopoeia specifies peak resolution function as an inspection criterion.

6. Content of the Pharmacopoeia-Compliant Validation Program

The following describes the validation program that is used in IRTracer-100/IRAffinity-1S systems and is compliant with all the pharmacopoeias. Instrument performance is inspected by comparing measurement results to criteria values, where inspection criteria include power spectrum, resolution, wavenumber accuracy, wavenumber repeatability, transmittance (absorbance) repeatability, and peak resolution function (only for Chinese Pharmacopoeia). The European Pharmacopoeia-compliant validation program is used for validation based on United States Pharmacopeia requirements.
A polystyrene film about 0.04 mm thick (Japanese Pharmacopoeia) is used as the sample for validation.

● Power Spectrum

The most basic FTIR performance can be evaluated based on the power spectrum size. The program determines whether or not the power spectrum at a specified wavenumber is larger than the criterion value, where the sample is considered normal if the spectrum value is higher than the criteria value at all specified wavenumbers.

● Resolution

Resolution is inspected as follows, based on an absorption spectrum measured from a polystyrene film about 0.04 mm thick. The difference between respective vertical axis values is determined and if both are greater than the criteria values, then it passes the inspection.

	Japanese Pharmacopoeia	European Pharmacopoeia	United States Pharmacopeia	Chinese Pharmacopoeia
Difference Between Minimum Vertical Axis Value Near 2870 cm^{-1} and Maximum Near 2850 cm^{-1}	not less than 18 %	greater than 0.33	Not specified	not less than 18 %
Difference Between Minimum Vertical Axis Value Near 1589 cm^{-1} and Maximum Near 1583 cm^{-1}	not less than 12 %	greater than 0.08	Not specified	not less than 12 %

● Wavenumber Accuracy

Wavenumber accuracy is inspected based on the wavenumbers of polystyrene spectrum peaks being within an allowable range. It passes the inspection if all specified peak wavenumbers are within the allowable range.

Japanese Pharmacopoeia	European Pharmacopoeia United States Pharmacopeia	Chinese Pharmacopoeia
3060.0 (±1.5) cm^{-1} 2849.5 (±1.5) cm^{-1} 1942.9 (±1.5) cm^{-1} 1601.2 (±1.0) cm^{-1} 1583.0 (±1.0) cm^{-1} 1154.5 (±1.0) cm^{-1} 1028.3 (±1.0) cm^{-1}	3060.0 (±1.0) cm^{-1} 2849.5 (±1.0) cm^{-1} 1942.9 (±1.0) cm^{-1} 1601.2 (±1.0) cm^{-1} 1583.0 (±1.0) cm^{-1} 1154.5 (±1.0) cm^{-1} 1028.3 (±1.0) cm^{-1}	3027 (±1.5) cm^{-1} 2851 (±1.5) cm^{-1} 1601 (±1.0) cm^{-1} 1028 (±1.0) cm^{-1} 907 (±1.0) cm^{-1}

● Wavenumber Repeatability

The Japanese Pharmacopoeia includes the following about wavenumber repeatability.

> As the repeatability of transmittance and wavenumber, ..., when the spectrum of a polystyrene film is measured twice at several wavenumbers from 3000 to 1000 cm^{-1}, and the difference of wavenumber should be within 5 cm^{-1} at about 3000 cm^{-1} and within 1 cm^{-1} at about 1000 cm^{-1}.

The program specifies three peak wavenumber points and determines the actual peak wavenumber at each point from two measurements of a polystyrene film. Then it decides whether or not the difference between the two measurements is within the allowable range. It passes the inspection if the peak wavenumbers at the specified wavenumber points are all within the allowable range. Though the European Pharmacopoeia, United States Pharmacopeia, and Chinese Pharmacopoeia do not specify wavenumber repeatability requirements, the program performs the inspection based on the Japanese Pharmacopoeia criteria.

> 3060.0 (±5) cm^{-1}
> 1601.2 (±1) cm^{-1}
> 1028.3 (±1) cm^{-1}

● Transmittance (Absorbance) Repeatability

The Japanese Pharmacopoeia includes the following about transmittance repeatability.

> As the repeatability of transmittance and wavenumber, the difference of transmittance should be within 0.5 % when the spectrum of a polystyrene film is measured twice at several wavenumbers from 3000 to 1000 cm^{-1}...

The program specifies three peak wavenumber points and determines the transmittance at each point from two measurements of a polystyrene film. Then it decides whether or not the difference between the two measurements is within the allowable range. It passes the inspection if the difference at each specified wavenumber point is within the allowable range. Note that transmittance (absorbance) repeatability requirements are not specified in the European Pharmacopoeia, United States Pharmacopeia, or Chinese Pharmacopoeia. The validation program for the Chinese Pharmacopoeia performs inspections based on the same standards as the Japanese Pharmacopoeia, whereas the validation program for the European Pharmacopoeia performs inspections based on absorbance standards.

Japanese Pharmacopoeia Chinese Pharmacopoeia	European Pharmacopoeia
3060.0 cm^{-1} : ±0.5% 1601.2 cm^{-1} : ±0.5% 1028.3 cm^{-1} : ±0.5%	3060.0 cm^{-1} : ±0.03 1601.2 cm^{-1} : ±0.05 1028.3 cm^{-1} : ±0.03

● Peak Resolution Function

The Chinese Pharmacopoeia specifies that the resolution must resolve seven peaks within the wavenumber range of 3110 cm^{-1} to 2850 cm^{-1}. The Chinese Pharmacopoeia does not specify a specific wavenumber for each peak, but the program inspection confirms that peaks are present within the following ranges, based on actual peak wavenumbers.

> 3102.63 (±5.0) cm^{-1}
> 3082.38 (±5.0) cm^{-1}
> 3060.20 (±5.0) cm^{-1}
> 3025.48 (±5.0) cm^{-1}
> 3001.37 (±5.0) cm^{-1}
> 2921.32 (±5.0) cm^{-1}
> 2849.95 (±5.0) cm^{-1}

● Program Functionality

The validation program compliant with the Japanese Pharmacopoeia, European Pharmacopoeia, United States Pharmacopeia, and Chinese Pharmacopoeia are included standard in the LabSolutions IR software used to control IRTracer-100 and IRAffinity-1S systems. The program can be executed by simply selecting it on the LabSolutions IR launcher menu and operated by following the instructions displayed on the screen. Inspections can be performed fully automatically by using an external beam switching kit that includes a polystyrene film.

When measurements are finished, it automatically prints a report with a summary of inspection results.

Since inspections require only about five minutes, they can even be performed instead of routine inspections.

● Polystyrene Film Used for Inspections

The polystyrene films included with Shimadzu FTIR systems can be used for inspections. However, if traceability is required, use an NIST (National Institute of Standards and Technology) SRM 1921b infrared transmission wavelength standard polystyrene film or other conforming secondary standard.

SRM 1921b 25 mm diameter and approximately 38 µm thick polystyrene film samples are attached to a 5×11 cm paper holder. The provided certificate includes information about handling and storage methods, expiration date, and so on. Conforming secondary samples are available from companies such as International Crystal Laboratories (ICL).

When not in use, cover the polystyrene film with the included cover and store it in a desiccator. Also, avoid touching the polystyrene film surface and blow off any dust with clean dry air. Needless to say, scratched or contaminated polystyrene film cannot be used.

References

Japanese Pharmacopoeia

http://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000066597.html

European Pharmacopoeia

https://www.edqm.eu/

United States Pharmacopeia

http://www.usp.org/

National Institute of Standards and Technology (NIST)

https://www.nist.gov/

International Crystal Laboratories (ICL)

http://www.internationalcrystal.net/home1.htm

AIM-9000 Infrared Microscope

Infrared Microscope
—Convenience of a Wide-View Camera

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Shimadzu has released the AIM-9000 infrared microscope as an automatic failure analysis system. The AIM-9000 includes a variety of new functionality that enables the series of steps involved in failure analysis to be performed quickly and easily. This article describes one of those new features, the wide-view camera, which can be used to view a broad area of the sample.

1. Introduction

Using an infrared microscope to obtain an infrared spectrum from a tiny contaminant, for example, involves the following general steps.

(1) Pretreat the sample, as necessary.
(2) Place the item being measured on the infrared microscope stage and position it so that the target measurement location is within the field of view.
(3) Select the location to be measured and specify the measurement range (aperture).
(4) Measure the background and sample.

Of those steps, one of the most time-consuming steps is step (2). It can be the most difficult step, particularly for those unfamiliar with operating an infrared microscope or those that use one infrequently. It was for that reason that the wide-view camera feature was developed.

2. Wide-View Camera

With infrared cameras included in typical infrared microscopes, images are viewed via a reflecting objective mirror used for measuring infrared spectra, which provides an extremely narrow field of view only about a few hundred microns square. Consequently, it can take a long time to find the target item being measured.

The new microscope includes both a conventional microscope camera and a wide-view camera that can show a large field of view. That means measurement targets can now be found more quickly. Fig. 1 shows the surface of an electronic circuit board viewed using the wide-view camera. In addition to enabling a macroscopic view size (10×13 mm), the wide-view camera also includes a zoom function that can magnify images by up to five times (2.0×2.6 mm). Fig. 2 shows the electronic part surface from Fig. 1 viewed via the high-magnification microscope camera. The microscope camera and wide-view camera share position information, so that users can switch smoothly between the cameras without the fields of view shifting out of alignment. Furthermore, the microscope camera includes a 10x zoom function (0.03×0.04 mm), which provides a total of about a 330x zoom capability.

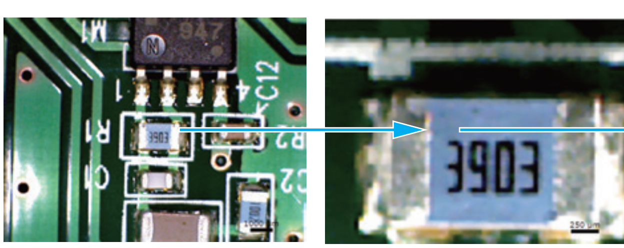


Fig. 1 Wide-View Camera Images
Left: 10×13 mm Field-of-View
Right: 2×2.6 mm Field-of-View (5x zoom)

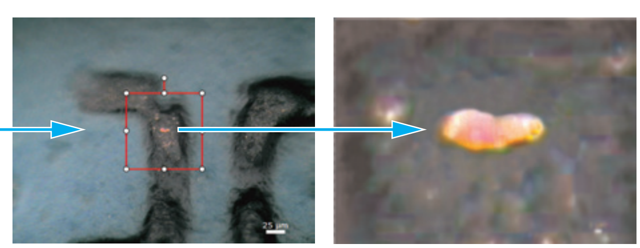


Fig. 2 Microscope Camera Images
Left: 0.3×0.4 mm Field-of-View
Right: 0.03×0.04 mm Field-of-View (10x zoom)

3. Example Using the Wide-View Camera

The Japanese 10-yen coin is engraved with an image of the Phoenix Hall from the Byodoin Temple. If you have an infrared microscope, are you able to smoothly zoom in on one of the phoenixes on the roof of the Phoenix Hall, so that it remains in the field of view?

Fig. 3 shows an image of a 10-yen coin placed on the stage. It was viewed using the microscope camera through the reflecting objective mirror (Cassegrain). The actual process involved moving the stage in X (left-right), Y (up-down), and Z (focus) directions, while also checking the position of light projected from the reflecting objective mirror and the degree of convergence. The target object does not appear in the field of view unless the stage is moved properly in the X, Y, and Z-directions.

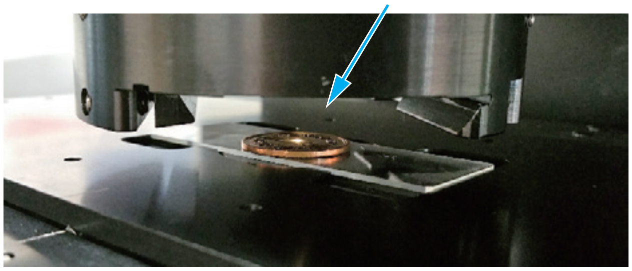


Fig. 3 10-Yen Coin Placed on the Stage and Viewed via the Reflecting Objective Mirror (Cassegrain)

Next, the coin was viewed using the wide-view camera. Fig. 4 shows an image of the coin viewed via the wide-view camera. The stage is set to its lowest position and the focus is not adjusted. Fig. 5 shows the wide-view camera image in that state. It shows an approximate image of the design on the 10-yen coin.

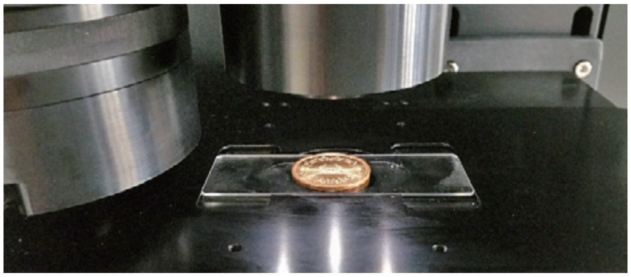


Fig. 4 Viewing the 10-Yen Coin Placed on the Stage via the Wide-View Camera

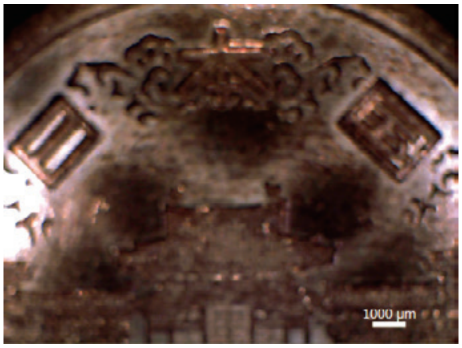


Fig. 5 Wide-View Camera Image of 10-Yen Coin (Before Adjusting Focus)

After adjusting the focus, double-clicking on the center of the Phoenix Hall moves the point that was double-clicked to the center of the window, so that a sharp image of the Phoenix Hall is displayed as shown in Fig. 6.

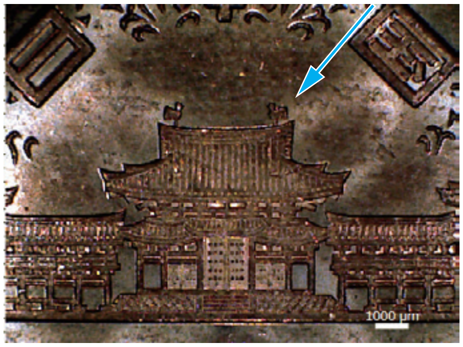


Fig. 6 Wide-View Camera Image of 10-Yen Coin (After Adjusting Focus)

Double-clicking on a phoenix on the roof of the Phoenix Hall moves the phoenix to the center of the window. If the digital zoom function is used, even the approximate shape of the phoenix becomes visible, as shown in Fig. 7.

Fig. 7 Magnified Image of Phoenix Using Wide-View Camera

Double-clicking the head of the phoenix moves it to the center of the window, and the field of view is switched from the wide-view camera to the reflecting objective mirror (microscope camera). Because the wide-view camera shares its position information with the microscope camera, the field of view switches smoothly from wide-view to microscope without moving out of alignment. The upper image in Fig. 8 shows the image displayed immediately after switching to the microscope camera. By slightly adjusting the focus, a sharp image of the phoenix head area can be obtained, as shown in the lower image in Fig. 8.

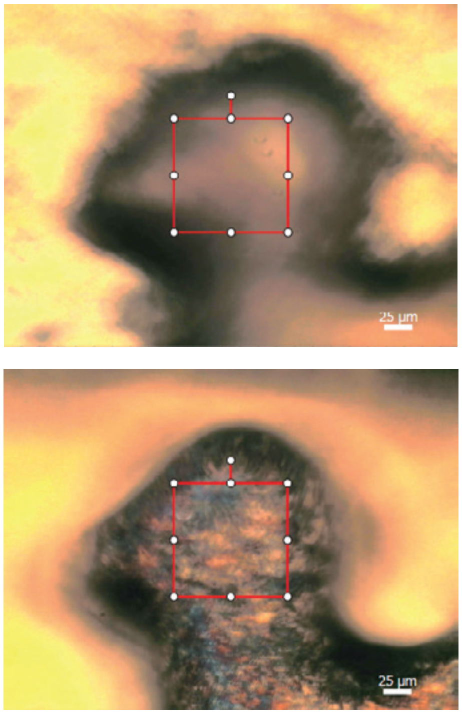


Fig. 8 Microscope Camera Image of the Phoenix Head
Upper: Before Focusing
Lower: After Focusing

4. Example of Analysis Using Wide-View Camera

The following is an example of analyzing a brown substance adhered to a metal plate. Fig. 9 is an image of a metal plate surface viewed via the wide-view camera. It shows several dots of a brown substance adhered to the surface, spaced a few millimeters apart. The capture function can be used to hold the image in a fixed position in the software window.

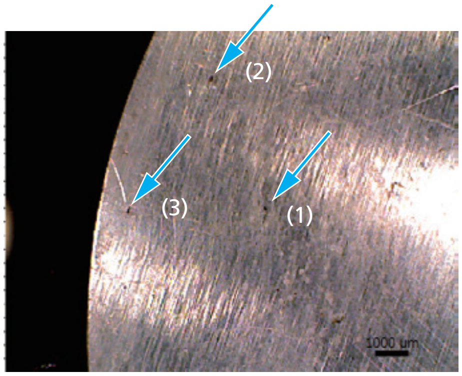


Fig. 9 Image of Metal Plate Surface Viewed via Wide-View Camera

By double-clicking in the window to further zoom in and focus on adhesion (1) shown in Fig. 9, a clear image of the overall shape of the adhesion can be confirmed, as shown in Fig. 10.

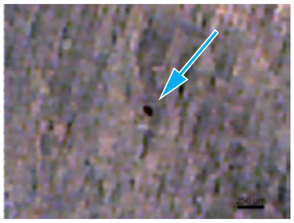


Fig. 10 Magnified Image of Adhesion Using Wide-View Camera

Next, the field of view is switched from the wide-view camera to the microscope camera. Even if the image is slightly out of focus, the target item always remains within the field of view of the microscope camera, which eliminates any need to move the stage in X or Y direction. Therefore, only the focus needs to be adjusted to obtain a reliable clear image of the adhesion, as shown in Fig. 11. By specifying a background measurement range (yellow square) and sample measurement range (red square), the reflection method was used to measure the IR spectrum of the adhesion. In this example, the aperture size was set to 30×30 µm and the number of scans was set to 40. The spectrum obtained is shown in Fig. 12.

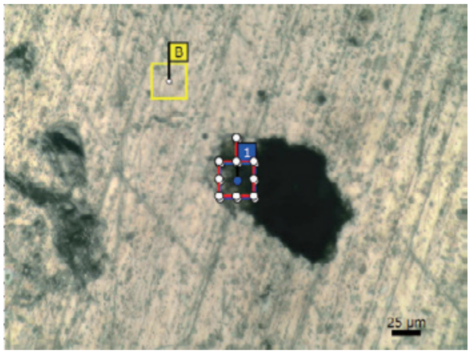


Fig. 11 Specifying the Measurement Range in the Microscope Camera Image of Adhesion (1)

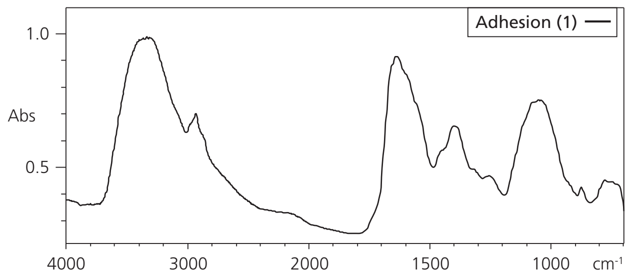


Fig. 12 Infrared Spectrum of Adhesion (1)

Then the captured wide-view camera image, shown in the upper image of Fig. 13, can be used for measuring adhesion (2) next. Double-clicking on adhesion (2) positions adhesion (2) within the microscope camera field of view. Then the measurement process can be started smoothly by simply fine-focusing the image, as shown in the lower image of Fig. 13.

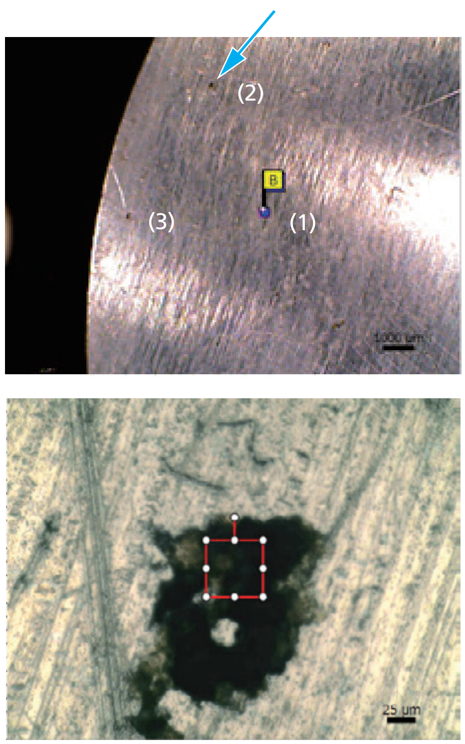


Fig. 13 Captured Wide-View Camera Image (Upper) and Microscope Camera Image of Adhesion (2) (Lower)

By following the above steps, spectra from the three adhesions can be obtained smoothly. An overlay of the measurement results from the three adhesions is shown in the upper graph of Fig. 14. It shows that the spectra from the three adhesions are very similar. Spectrum search results indicate that the adhesions are similar to sodium carboxymethyl cellulose, shown in the lower graph of Fig. 14.

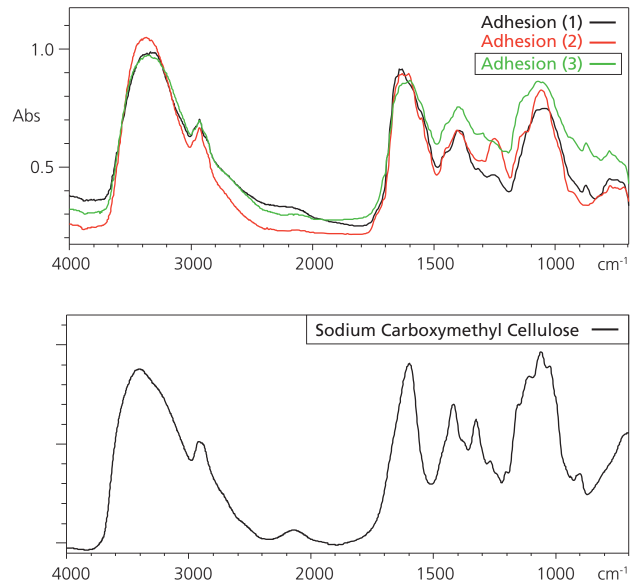


Fig. 14 Overlay of Infrared Spectra from Three Adhesions (Upper) and Library Spectrum of Sodium Carboxymethyl Cellulose (Lower)

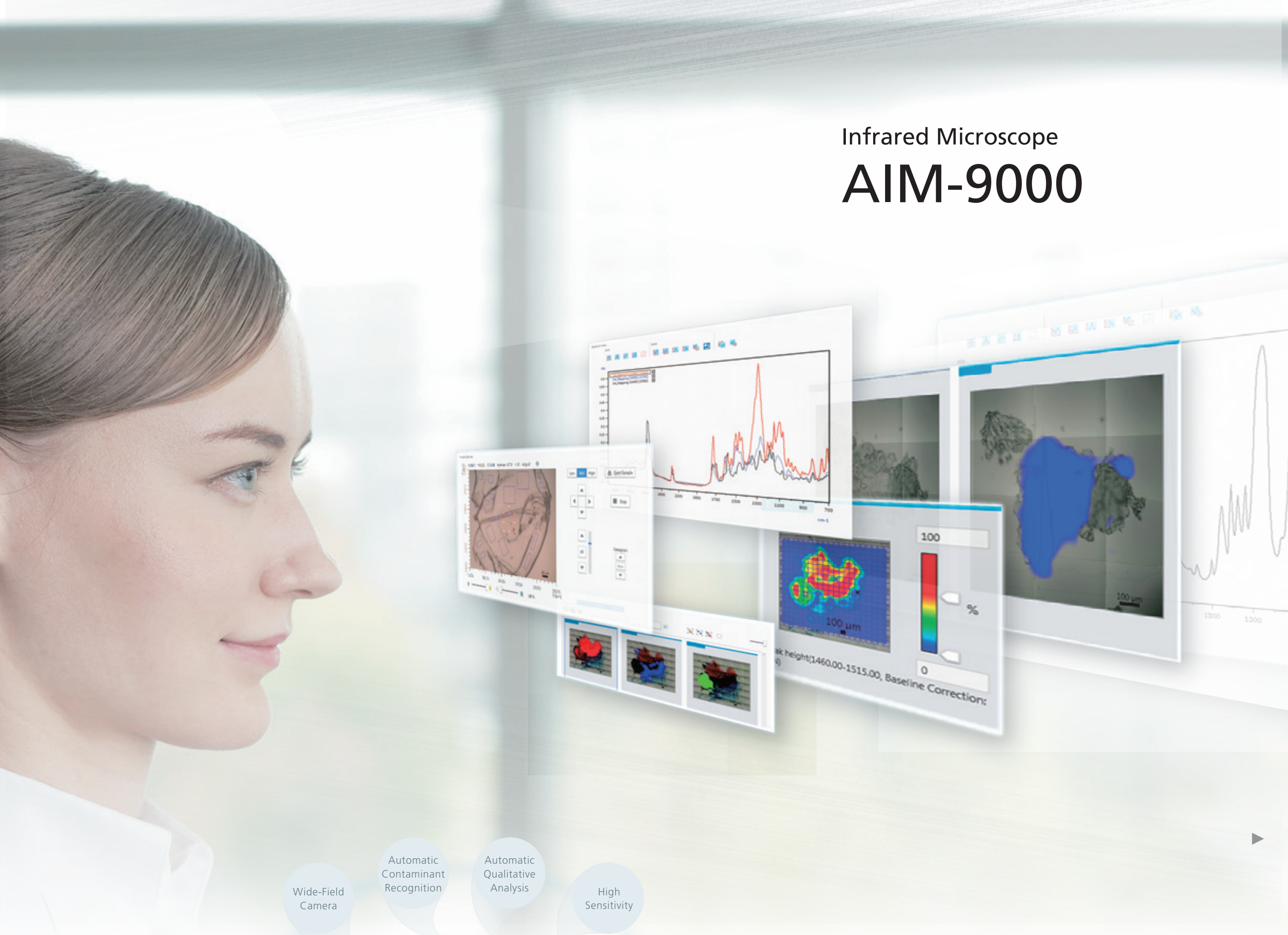
5. Conclusion

The wide-view camera was developed to minimize the burden on those without significant experience operating an infrared microscope, but when highly experienced operators at Shimadzu used the wide-view camera, even they definitely appreciated its convenience. Consequently, it has dramatically increased the productivity of contract analysis work and customer-attended analysis work that Shimadzu performs for customers. We would be grateful if customers were given the opportunity to experience the new infrared microscope as well.

Due to publication space limitations, the Q&A section has been omitted in this issue.

Infrared Microscope

AIM-9000



Finally, a wide view on micro sample analysis

Contaminant Analysis
Surface Analysis
Micro Analysis

IRTracer-100 +AIM-9000

IRAffinity-1S+AIM-9000

SHIMADZU AIMs to provide analysis systems for all users.

The system is automated to ensure all steps involved in micro analysis can be performed quickly and easily.
All our accumulated know-how in micro analysis is concentrated in the AIM-9000 to strongly support analysts.

Three steps for micro analysis

Observe	Measure	Analyze
Visible 330× digital zoom	Automatic contaminant recognition system	Contaminant analysis program

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First Edition: November 2017