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FTIR TALK LETTER

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FTIR Validation

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In this article, we will look at ways FTIR validation is performed. The word " validate " can be taken to mean " enable ". The process of having your parking ticket stamped at the cash register of your local department store after buying some products is an example of " validation ". " Validate " has come to be used to refer to the process of performing the required inspection for a system, checking that it operates properly, and "enabling" it for use. In other words, to " validate " a system is to recognize the propriety of that system. Similarly, " validation " is used to mean " verification "," qualification "," confirmation ",or " legitimization ".

Here, we will look at FTIR hardware and software

Hardware Validation

To perform " FTIR hardware validation " is to inspect an FTIR system and confirm that it is operating properly.

With dispersive IR, inspection (correction) was performed by measuring the spectra of polystyrene film and reading the peak wavenumber to correct wavenumber accuracy. With FTIR, the state of the system often manifests itself in power spectra and so checking the shape and size of power spectra is a relatively simple method that is used.

The method of checking the shape and size of power spectra is used with Shimadzu FTIR systems as part of daily inspection.

Several official bodies have issued standards related to the methods used to perform more detailed inspections of FTIR systems. Regulations are specified by industrial-standard bodies such as the American Society for Testing and Materials (ASTM) and the Japanese Industrial Standards (JIS, the Japanese version of ASTM) Committee and by publications such as the Japanese and European Pharmacopoeias.

Let us look at the kind of standards established by each body or publication.

JIS

Regulations are specified in JIS K0117 (General rules for infrared spectrophotometric analysis). Inspection methods are specified in *6.3 Calibration and Inspection Methods for Spectrophotometers*. Points related to wavenumber (precision), 0% transmittance, 100% transmittance, linearity, resolution, and repeatability are specified. I will briefly describe the methods specified by JIS. JIS does not, however, give specific details on procedures or criteria.

Wavenumber (Accuracy)

This is obtained from the difference between the peak wavenumber(s) positions for a substance with a well-known peak wavenumber(s) position (e.g., atmospheric carbon dioxide, water vapor, polystyrene, ammonia, or indene) and the values indicated by the system.

0% Transmittance

A sample that does not allow the transmission of light is measured in order to investigate the 0% transmittance, namely, the error caused by stray light and secondary emission spectra.

100% Transmittance

The 100% transmittance is investigated by performing analysis without a sample and measuring the transmittance.

Linearity

A calibration curve for the absorbance and the concentration is created and the linearity of this curve is inspected.

Resolution

The resolution of absorbance peaks obtained using, for example, ammonia or atmospheric carbon dioxide, is investigated.

Reproducibility

A stable sample is measured at least twice within a short period and it is confirmed that the variation in the measurement values obtained for wavenumber and transmittance is within the prescribed range.

ASTM

The ASTM standards are specified in *E1421-99 Standard Practice for Describing and Measuring Performance of Fourier Transform Mid-Infrared (FT-MIR) Spectrometers; Level Zero and Level One Tests*. With the ASTM standards, unlike the JIS standards and the pharmacopoeias described later, power spectra and spectrum of polystyrene films are measured and it is confirmed that there are no FTIR abnormalities or large changes over short and long periods. I will briefly describe the methods specified in the ASTM E1421-99 Level Zero tests.

Energy Spectrum Test – Changes in Power Spectra

Power spectra obtained in inspection are compared with reference data and the spectra are checked for changes over long periods.

One Hundred Percent Line Test – 100% Line Changes Over Short Periods

100%T line spectra are calculated for power spectra measured continuously in inspection and the spectra are checked for changes over short periods.

Polystyrene Test – Comparison of Polystyrene spectrum with Reference Data

Evaluation is performed using the differences between spectra obtained for polystyrene film in inspection and reference data.

The FTIR-8400S/IRPrestige-21 is equipped, as a standard feature, with a validation program that conforms to the ASTM E1421-99 Level Zero tests.

Japanese Pharmacopoeia and European Pharmacopoeia

The relevant specifications are given under *Instrument and adjustment* in *Infrared Spectrophotometry* in *General Tests,* in supplement 1 to the fourteenth edition of the Japanese Pharmacopoeia. Procedures and criteria are specified for four inspection items: resolution (resolving power), wave number precision, wave number reproducibility, and transmittance reproducibility. The specifications of supplement 1 to the fourteenth edition of the Japanese Pharmacopoeia have been brought in line with those of the European Pharmacopoeia (EP4.0).
The FTIR hardware validation methods used by Shimadzu are based on the Japanese Pharmacopoeia methods, which are aimed at the pharmaceutical industry and clearly specify procedures and standards, and not on the JIS/ASTM methods, which are aimed at industry and do not clearly specify procedures.

Pharmacopoeia of the United States of America

FTIR is mentioned in the Pharmacopoeia of the United States of America (USP). As shown below, however, it tells the reader to refer to manufacturers' instruction manuals for detailed instructions.

> Detailed instructions for operating spectrophotometers are supplied by manufacturers. To achieve significant and valid results, the operator of a spectrophotometer should be aware of its limitation and of potential sources of error and variation. The instruction manual should be followed closely on such matters as care, cleaning, and calibration of the instrument, and ......

Validation Program Conforming to Japanese Pharmacopoeia

I will describe the validation program used with the FTIR-8400S/IRPrestige-21. There are 5 inspection items: power spectrum, resolution (resolving power), wave number accuracy, wave number reproducibility, and transmittance reproducibility. The performance of the system is inspected by comparing measurement results with criteria values.

Power Spectrum

The most fundamental form of FTIR performance evaluation can be conducted using the size of a power spectrum. The sizes of a power spectrum at specified wavenumbers are investigated; if they are no less than the criteria values at each specified wavenumber then system performance regarding this item is judged to be satisfactory.

Resolving Power (Resdution)

The following specification for resolving power is given in supplement 1 to the fourteenth edition of the Japanese Pharmacopoeia and in EP4.0.

> When the spectrum of a polystyrene film about 0.04 mm thick is recorded, the depth of the trough from the maximum absorption at about 2850 cm^{-1} to the minimum at about 2870 cm^{-1} should be not less than 18% transmittance and that from the maximum at about 1583 cm^{-1} to the minimum at about 1589 cm^{-1} should not be less than 12% transmittance.

The respective differences in transmittance are measured and if they both are no less than the criteria values then system performance regarding this item is judged to be satisfactory.

Wave number Accuracy

The following specification for wavenumber accuracy is given in supplement 1 to the fourteenth edition of the Japanese Pharmacopoeia and in EP4.0.

> The wave number (cm^{-1}) scale is usually calibrated by the use of several characteristic absorption wave numbers (cm^{-1}) of a polystyrene film shown below. The number in parentheses indicates the permissible range.
>
> 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}

With this program, the peak wavenumbers measured for a polystyrene-film spectra with the wavenumbers used for evaluation given above are obtained. If all the peak wavenumbers are within the respective permissible ranges, system performance regarding this item is judged to be satisfactory.

Wave number Repeatability

The following specification for wavenumber repeatability is given in supplement 1 to the fourteenth edition of the Japanese Pharmacopoeia.

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

With this program, 3 peak wavenumber points are specified and the actual peak wavenumbers at these points are obtained for two measurements of polystyrene film. If the peak wavenumbers for the specified wavenumbers are all within the respective ranges, system performance regarding this item is judged to be satisfactory. There is no specification for wavenumber repeatability in EP4.0.

Transmittance Repeatability

The following specification for transmittance repeatability is given in supplement 1 to the fourteenth edition of the Japanese Pharmacopoeia.

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

With this program, 3 peak wavenumber points are specified and the transmittance values at these points are obtained for two measurements of polystyrene film. If the differences between the transmittance values are all within the respective ranges, system performance regarding this item is judged to be satisfactory.

Program Operation

The Japanese Pharmacopoeia-based validation program is incorporated, as a standard feature, in the IRsolution software that controls FTIR-8400S/IRPrestige-21. It can be executed simply by selecting it from the IRsolution menu and operation can be performed simply by following the instructions that are displayed. Inspection can be completely automated by using the Beam Switching Kit, which incorporates polystyrene film.
Reports summarizing inspection results can also be automatically printed out when measurement is completed.

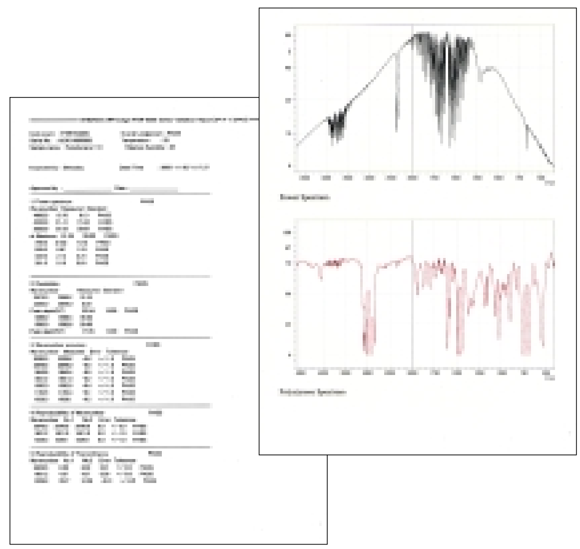

Fig. 1 Results Obtained by Executing Japanese Pharmacopoeia-Based Validation

Polystyrene Film Used for Inspections

The polystyrene film that is packed together with Shimadzu FTIR systems can be used for inspections. If traceability is required, however, use NIST (National Institute of Standards and Technology) standard polystyrene film: SRM 1921a – Infrared Transmission Wavelength Standard (Polystyrene Film).
In SRM 1921a, polystyrene film with a thickness of approx. 38 μm and a diameter of 25 mm is mounted to a paper holder of dimensions 5 × 11 cm. The handling method, storage method, and use-by date are all detailed on the certificate provided with the product.
When not using polystyrene film, cover it with the cover provided and store it in a desiccator. Do not touch the surface of the polystyrene film and blow off the dust that may accumulate on the surface using clean, dry air. The polystyrene film cannot be used if it is damaged or contaminated.

Changes Made with Supplement 1 to the Fourteenth Edition of the Japanese Pharmacopoeia

I imagine there are already people performing validation in accordance with the old version of the Japanese Pharmacopoeia. With supplement 1 to the fourteenth edition of the Japanese Pharmacopoeia, which was published on 27 December 2002, the specifications related to resolving power and wave-number precision were changed as shown in Table 1. Of particular note is the way that the definition of the figures in parentheses has been clarified, a point that caused a lot of misunderstanding.

Validation, Periodic Inspection, and Operational Qualification

Basically, the same way of thinking applies to validation, periodic inspection, and operational qualification. They all involve the inspection and correction of FTIR systems at regular intervals using specified techniques. At Shimadzu, we recommend using the validation program to perform periodic inspection and operational qualification.

Table 1 Changes Made to Japanese Pharmacopoeia

Item	Fourteenth edition of Japanese Pharmacopoeia	Supplement 1 to Fourteenth Edition of Japanese Pharmacopoeia
Resolving power (Resolution)	When the spectrum of a polystyrene film about 0.04 mm thick is recorded, the depth of the trough from the maximum absorption at about 2851 cm^{-1} to the minimum at about 2870 cm^{-1} should be not less than 18% transmittance and that from the maximum at about 1583 cm^{-1} to the minimum at about 1589 cm^{-1} should not be less than 10% transmittance.	When the spectrum of a polystyrene film about 0.04 mm thick is recorded, the depth of the trough from the maximum absorption at about 2850 cm^{-1} to the minimum at about 2870 cm^{-1} should be not less than 18% transmittance and that from the maximum at about 1583 cm^{-1} to the minimum at about 1589 cm^{-1} should not be less than 12% transmittance.
Wave number accuracy	The wave number (cm^{-1}) scale is usually calibrated by the use of several absorption bands of a polystyrene film, shown below. The numbers in parentheses indicate the precision with which these values have been established. 3027.1 (±0.3) 1801.6 (±0.3) 1069.1 (±0.3) 2924 (±2) 1601.4 (±0.3) 1028.0 (±0.3) 2850.7 (±0.3) 1583.1 (±0.3) 906.7 (±0.3) 1944 (±0.3) 1181.4 (±0.3) 698.9 (±0.5) 1871.0 (±0.3) 1154.3 (±0.3)	The wave number (cm^{-1}) scale is usually calibrated by the use of several characteristic absorption wave numbers (cm^{-1}) of a polystyrene film shown below. The number in parentheses indicates the permissible range. 3060.0 (±1.5) cm^{-1} 1154.5 (±1.0) cm^{-1} 2849.5 (±1.5) cm^{-1} 1028.3 (±1.0) cm^{-1} 1942.9 (±1.5) cm^{-1} 1601.2 (±1.0) cm^{-1} 1583.0 (±1.0) cm^{-1}

Software Validation

In addition to checking that the hardware is operating properly, it is also necessary to check that the software is operating properly. FTIR software has, however, become very complex and it is impossible for the user to check all the functions using black-box tests involving the input and output of test data.

Software differs from hardware in that the influence of the manufacturing process for each individual product on the quality of that product is minimal and the product quality is determined almost entirely by the development process. Therefore, the user checks that software's configuration files have not been corrupted or deleted using the alteration-check program and also checks that the main functions, such as the security functions and the basic data analysis functions, operate properly. The software development is validated by the appropriate implementation of computer validation at the time of development.

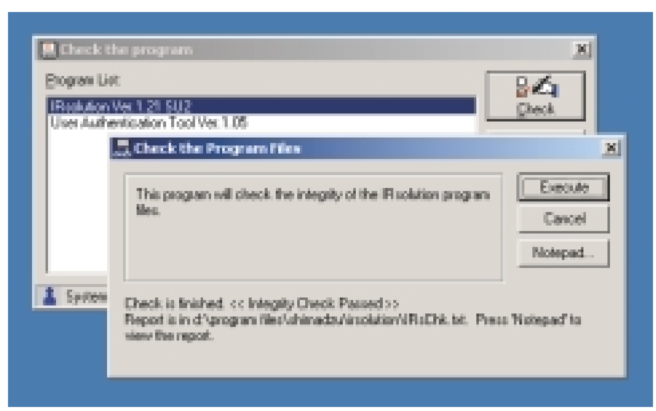

Fig. 2 Execution of Alteration-Check Program

References

JIS	http://www.jisc.go.jp/eng/
ASTM	www.astm.org
Japanese Pharmacopoeia	www.mhlw.go.jp/topics/bukyoku/iyaku/yakkyoku/
European Pharmacopoeia	http://www.pheur.org/
Pharmacopoeia of the United States of America	http://www.usp.org/
NIST	http://www.nist.gov/

Using Microscope Accessories

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In volume 3 of the FTIR Talk Letter, we provided descriptions of the accessories that are required, or are useful, for effective sampling in infrared microscopic measurement. Here, we will explain how to use infrared-microscope accessories to obtain high-quality spectra.

Transmission Measurement with Infrared Microscope

When performing transmission measurement with an infrared microscope, the sample is flattened and measured using a transmission window plate. Transmission windows are made from various materials; the well-known types include those made from KBr, BaF_2, diamond, and silicon wafer. The characteristics of these windows vary and are selected according to the actual measurement conditions.

1. KBr
Features: This is a commonly used type. It is relatively cheap and has an extremely high transmittance of 90% for infrared light. (See Fig. 1.) The wide wave-number region of 4,000 to 400 cm^{-1} makes it possible to obtain high-quality spectra.
Points to note: It is relatively soft and prone to damage. KBr dissolves when used for samples containing moisture and is therefore unsuitable for measurement in this case. Store it at a humidity level not exceeding 50%. If a KBr window plate is stored in a location with a high humidity level, because of deliquescence, the window will become clouded and it will not be possible to obtain high-quality spectra.

2. BaF_2
Features: This is a commonly used type. It is relatively cheap and has an extremely high transmittance of 90% for infrared light. It has greater water-resistance than the KBr type.
Points to note: It is relatively soft and prone to damage. There is BaF2 absorption at wave numbers of less than 800 cm^{-1} and measurement is possible only down to approx. 720 cm^{-1}. (See Fig. 1.) BaF_2 dissolves when it is used for samples containing acid or ammonia.

3. Diamond
Features: This is a commonly used type. It is easy to handle. It is a very hard substance and is extremely resistant to damage. It is also relatively stable in terms of chemical behavior and can be used for various types of sample. It has a high transmittance of approx. 70% for infrared light.
Points to note: It is more expensive than KBr and BaF_2 The area for which measurement is possible is small and, when using relatively large samples, it is sometimes necessary to cut and set the sample for measurement. The edges of the window are not suitable for measurement.
There is diamond absorption in a neighborhood of 2,000 cm^{-1} and the S/N ratio is lower in this range. (See Fig. 1.) Also, the refractive index of 2.4 is relatively high and the difference between that of general samples makes the appearance of interference fringes likely.

4. Silicon Wafer (High-Resistance Silicon Wafer)
Features: This type is not commonly used. It is relatively hard and easy to handle. Water can be used to clean it.
Points to note: It has a relatively low transmittance of approx. 55% for infrared light, making it difficult to obtain high-quality spectra. It also has the disadvantage of not allowing transmission observation with visible light. Also, the refractive index of 3.4 is high and the large difference between that of samples makes the appearance of interference fringes likely.

It can be seen from the above that, as for the type of window plate used for transmission measurement performed with plate an infrared microscope, diamond is suitable for general-purpose and hard samples, and KBr and BaF_2 are suitable for high-sensitivity analysis.

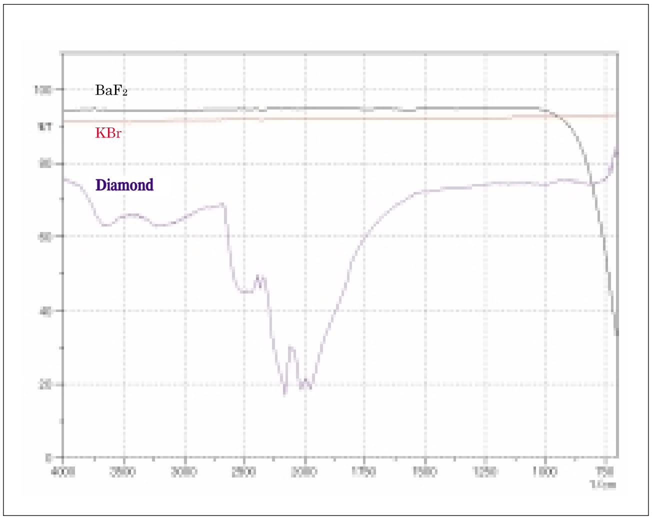


Fig. 1 Transmittance for Different Types of Window Material

Using Diamond Cells (Points to Note When Flattening Samples)

A diamond cell consists of two discs into which diamonds with dimensions of 2 to 3 mm are embedded. This accessory is useful for making hard or irregularly shaped samples thinner. Depending on the way it is used, however, it may not be possible to obtain high-quality spectra. Here I will describe how to use the diamond cell effectively.

Put an appropriate amount of the sample on a disk. Note that if an amount of the sample that could be spread out over the entire diamond cell is used, it will not be possible to perform background measurement.

Put the other disk on top of the sample to flatten it out. With soft samples, simply pressing with your hand is sufficient; there is no need to use screws. With small, hard samples, flattening the sample by turning the screw with a large force may, in exceptional cases, cause cracks to appear at the edge of the diamond. (See Fig. 2.)

It may not be possible to obtain high-quality spectra if measurement is performed with the upper disk in place. For example, the infrared light passes through windows twice, which may adversely affect the transmittance; the large diamond absorbance may also adversely affect the transmittance; the direction of the light may become parallel between the disks, making the appearance of interference fringes extremely likely. Therefore, remove the upper disk before measurement. Note that the sample may adhere to the upper disk.

Put the disk to which the sample has adhered in the holder and perform transmission measurement using an infrared microscope. (See Fig. 3.)

Clean the windows after use. A simple method is to scrape of any dust that has adhered to the windows using a swab that has been soaked in water or alcohol.

Fig. 2 Flattening the Sample

Fig. 3 Analyzing the Sample

Question

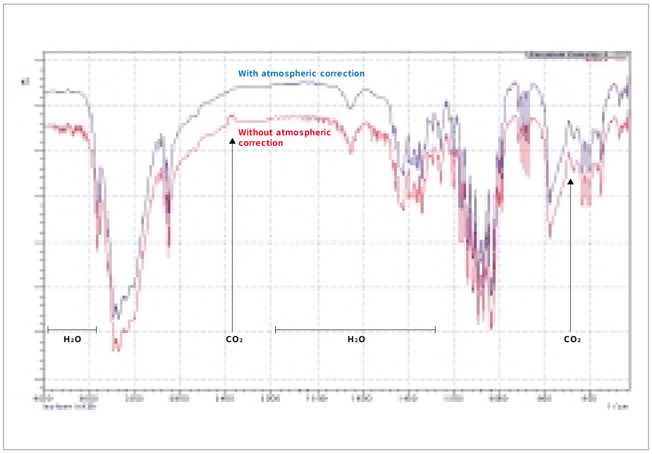
Noise can be observed in the 4,000 to 3,400-cm^{-1} and 2,000 to 1,300-cm^{-1} ranges. How can this be eliminated?

Answer

The phenomenon that can be observed in the 4,000 to 3,400cm^{-1} and 2,000 to 1,300cm^{-1} ranges is water vapor (H_2O) absorption. Absorption can be observed as noise because of a change in the amount of water vapor resulting from a change in the ambient conditions. In addition to water vapor, carbon dioxide (CO_2) absorption can be observed in neighborhoods of 2,350cm^{-1} and 670cm^{-1}.

The influence of water vapor and carbon dioxide can be minimized by performing sample measurement immediately after background measurement. It is also possible to reduce the influence of these gases by purging the system with dry air or nitrogen. This method, however, requires the use of special equipment, such as a dry-air supply unit or a nitrogen canister.

IRsolution software is equipped with an atmospheric-correction function. Using this function makes it possible to reduce the influence of water vapor and carbon dioxide. (See below.)



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UV-VIS-NIR Spectrophotometer SolidSpec-3700/3700DUV

UV-VIS-NIR Spectrophotometer
SolidSpec-3700/3700DUV

World First — High Sensitivity Achieved with Installation of 3 Detectors

In addition to a photomultiplier tube and a cooling-type PbS detector, this UV-VIS-NIR spectrophotometer also incorporates an InGaAs detector, giving it a much higher level of sensitivity in the near-infrared region.

Large Sample Compartment Designed to Facilitate Nondestructive Measurement

The compartment allows the measurement of horizontally placed samples with dimensions of up to 700 × 560 mm. Using the automatic X-Y stage (option) enables automatic multipoint measurement of samples with dimensions of up to 310 × 310 mm.

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Purging the optical path with nitrogen gas makes it possible for the SolidSpec-3700DUV to perform measurement in the 175 to 2,600-nm range with an integrating sphere and in the 165 to 3,300-nm range with an optional accessory.

UV-VIS-NIR Spectrophotometer UV-3600

UV-VIS-NIR Spectrophotometer
UV-3600

High Sensitivity — Equipped with 3 Detectors

In addition to a photomultiplier tube and a cooling-type PbS detector, this UV-VIS-NIR spectrophotometer also incorporates an InGaAs detector, giving it a much higher level of sensitivity in the near-infrared region.

High Resolution, Ultra-Low Stray Light, and Wide Measurement Range

This instrument achieves high resolution and ultra-low stray light using a high-performance double monochromator. It is capable of high-sensitivity measurement across the ultra-violet, visible, and near-infrared regions, with a measurement wavelength range of 185 to 3,300 nm.

A Variety of Accessories for a Wide Range of Applications

A variety of accessories, such as the integrating-sphere attachment, the electronic constant-temperature cell holder, or the ultra-micro cell holder can be mounted to the instrument, allowing it to handle a wide range of measurement applications.

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