Technical Note: 51686

Performance Verification of the Evolution 300 UV-Visible Spectrophotometer in the Regulated Laboratory

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Key Words

- Calibration Validation Carousel (CVC)
- Certified Reference Materials
- Good Laboratory Practices (GLP)
- Good Manufacturing Practices (GMP)
- International Organization of Standardization (ISO)
- Mercury Lamp Accessory
- Performance Verification
- Regulatory Compliance
- Standard Operating Procedures (SOPs)

Introduction

Analytical and quality control laboratories are frequently regulated by industry guidelines and agencies such as Good Manufacturing Practices (GMP) and Good Laboratory Practices (GLP) instituted by the Food and Drug Administration (FDA) in the United States and the European Medicines Agency (EMEA) in Europe; Pharmacopoeia testing protocols such as those defined by the United States (USP), European Union (EP), and Japan (JP); or seek quality certification from secondary agencies such as ISO (International Organization of Standardization). The goal of these guidelines and agencies is to ensure product quality and measurement consistency. Compliance with these standards generally includes the incorporation of some type of performance verification (PV) testing into the Standard Operating Procedures (SOPs) for instruments used throughout the regulated laboratory. For UV-Visible spectrophotometers, Thermo Fisher Scientific provides a comprehensive suite of resources to assist laboratories in achieving and maintaining a regulatory compliant system, within industry guidelines.

Tools for Automated PV Testing

PV testing for the Thermo Scientific Evolution™ 300 spectrophotometer is simplified by the use of the Smart Calibration Validation Carousel (CVC). The CVC fully automates PV testing using certified reference materials traceable to the NIST (National Institute of Standards and Technology, USA) or NPL (National Physical Laboratory, UK). The calibrated value of the standards and the instrument specifications are stored in a single data file matched to the serial number of the CVC. This secure link eliminates transcription and other sources of human error that might enter the PV testing process. To perform testing, the user must simply select the desired tests, press the test button to run them and return to the instrument after the tests are complete. Fully-automated testing saves time and reduces errors. The CVC fully automates testing for:

- Wavelength accuracy with holmium oxide in perchloric acid solution
- Wavelength repeatability with the instrument's xenon lamp
- Photometric accuracy using NIST or NPL traceable neutral density filters
- UV photometric accuracy using a sealed solution of potassium dichromate in perchloric acid solution
- Stray light
- Photometric noise
- Photometric stability
- Baseline flatness

Further PV testing of the Evolution 300 can be accomplished using the mercury lamp accessory. The emission lines of a mercury lamp are fundamental, primary standards that require no certification or re-calibration. The mercury lamp accessory covers the entire wavelength range capabilities of the Evolution 300 from the ultraviolet to the near-IR region (254 to 810 nm). Recommended by the USP as the preferred standard for testing wavelength accuracy, the mercury lamp accessory allows automated testing of:

- Wavelength accuracy
- Wavelength repeatability
- Bandwidth accuracy

The mercury lamp is not only a useful tool for PV testing, it also gives laboratory personnel the ability to perform a calibration of the Evolution 300 instrument exactly as it was performed at the factory. The calibration method uses seven mercury lamp lines from wavelength 253.65 nm to 810 nm (Figure 1). A unique calibration curve is used for every spectral bandwidth available with the Evolution 300. This means the calibration at a SBW of 0.5 nm is performed and stored independently of the calibration at a SBW of 1.0 nm. For more details on the mercury lamp and wavelength accuracy see Thermo Fisher Scientific Application Note No. 51171 *Wavelength Accuracy – Measurement and Effect on Performance in UV-Visible Spectrophotometry*.

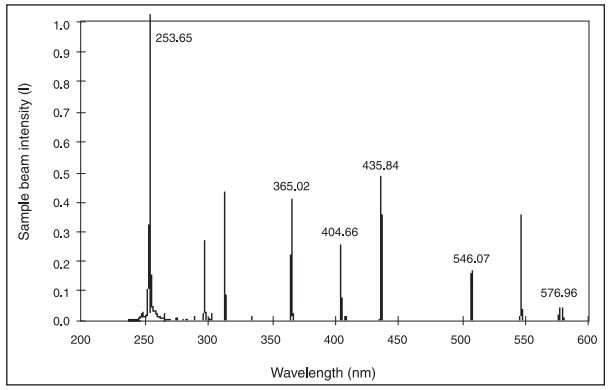

Figure 1: The emission from a mercury lamp accessory measured on an Evolution 300 spectrophotometer.

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Recommendations for Performance Verification Testing

This application note serves as a guide for ensuring reliable performance of the Evolution 300 spectrophotometer. For more specific information on USP and EP requirements, see Thermo Fisher Scientific Application Note No. 51111 *U.S. and European Pharmacopoeias and UV-Visible Spectrophotometers*. The suggestions provided in this note are simply suggestions for GMP and GLP and should not be extended further.

Although each laboratory must ultimately make its own decision on the frequency and type of performance verification testing required to comply with its internal SOPs and applicable industry regulations and guidelines, the following PV testing schedule is offered for ensuring reliable performance of the Evolution 300 spectrophotometer in a well-controlled laboratory environment. Extremes in temperature, humidity, dust, and corrosive solvents and vapors should be avoided. If these extremes cannot be avoided or are difficult to control, a more frequent PV testing schedule is recommended.

Tier 1 Tests

Suggested Frequency: Weekly

Tier 1 tests evaluate instrument performance and control over the wavelength and photometric axes of measurement. These tests are representative of the requirements of most Pharmacopeias and regulatory agencies. Tier 1 tests are designed to quickly identify discrepancies in instrument performance that could produce erroneous data and give a relevant and useful snapshot of instrument performance.

Tier 1 Tests include the following:

- Wavelength accuracy
- Photometric accuracy (two separate tests)
  - Absorbance accuracy
  - UV absorbance accuracy
- Photometric noise (noise)
- Baseline flatness

Tier 2 Tests

Suggested Frequency: Six-week intervals

Tier 2 tests are designed to examine long-term aspects of the instrument's mechanical performance. Most compromises in instrument performance arising from these tests would also be identified during Tier 1 testing. For example, a major component failure that causes wavelength repeatability to fail during Tier 2 testing would also be likely to cause a wavelength accuracy failure in Tier 1 testing.

Tier 2 Tests include the following:

- Photometric (absorbance) repeatability
- Wavelength repeatability
- Stray light

Tier 3 Tests

Suggested Frequency: At time of installation qualification and requalification and at 6 to 12-month intervals thereafter

Tier 3 tests are designed to examine instrument performance criteria that are less indicative of overall instrument performance and failure modes.

Tier 3 Tests include the following:

- Photometric drift
- Bandwidth accuracy

It is important to note that the drift test may be sensitive to environmental fluctuations, such as electrical and temperature fluctuations, method design and development, and user error that are not indicative of a fault in instrument performance and may necessitate additional analysis of test results, SOP and method development, or analyst training.

Considerations for Instruments in Continuous Use

The Evolution 300 uses a xenon lamp that is only "on" when the instrument is taking data. Thus, many laboratories will leave the spectrophotometer on for long periods of time. Over the course of a week or more, environmental conditions in the laboratory are likely to fluctuate, causing minor changes in the spectrophotometer. To account for these changes, it is recommended that an optical initialization be performed prior to PV testing. Version 4.2 of the Thermo Scientific VISION™ software is designed to force an optical initialization at user-defined intervals. This feature allows the administrator to set a maximum amount of time that can elapse before an optical initialization is required (Figure 2). The default setting of one day is the factory recommended interval.

Requiring the performance of an optical initialization prior to PV testing, ensures the most accurate evaluation of the instrument's performance. The dialog box (Figure 3) shows the PV tests that are available when a CVC and mercury lamp accessory are installed. Here, only the Tier I tests have been selected. You will note that the user cannot perform the PV tests until an optical initialization is performed.

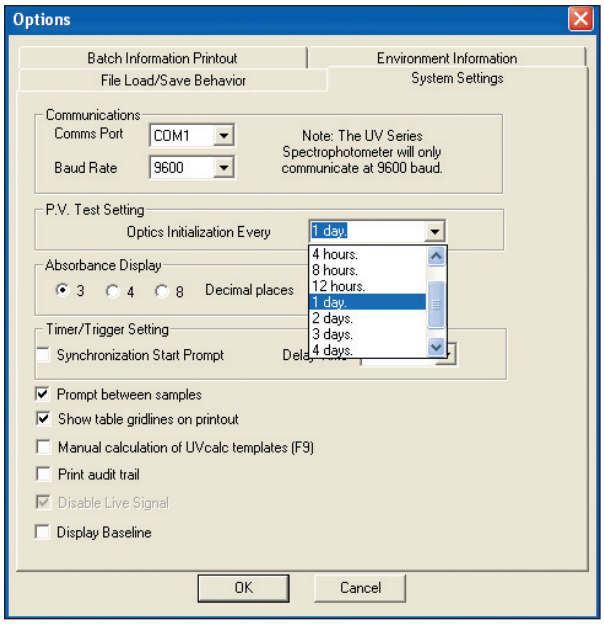

Figure 2: Thermo Scientific VISION*pro*™ and Thermo Scientific VISION*security*™ 4.2 software allow you to specify the interval of time between optical initializations. This allows you to operate the instrument in an "always on" state and still ensure optimum performance.

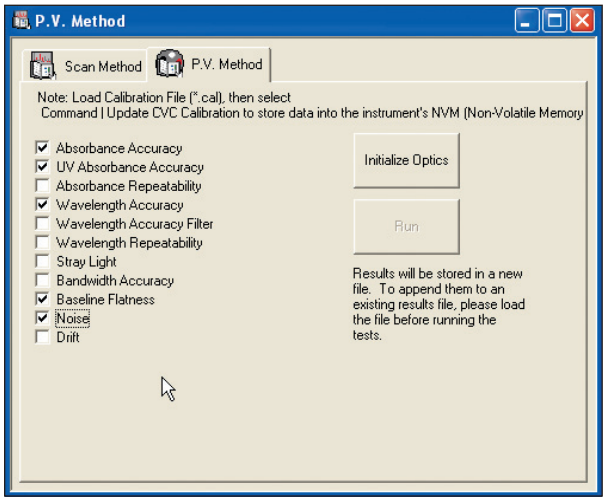

Figure 3: Tier 1 tests selected in a PV test method. Note that the Run button is disabled until an optical initialization is performed.

Conclusion

Performance verification testing plays an important role in ensuring the quality of results obtained from the Evolution 300 spectrophotometer. This document serves as a guideline for performance verification of the instrument in a well-controlled laboratory environment. In the development of SOPs, laboratory managers should consider the environmental factors present in their laboratory that may impact the performance of their instrument, the desired function of the instrument, as well as the knowledge and experience levels of laboratory personnel. Data collected over time from PV testing may support more or less frequent testing at each tier level and should be tailored to meet the needs of each individual laboratory.

In addition to the aforementioned Smart CVC and mercury lamp accessories, Thermo Fisher Scientific offers a wide array of other certified reference materials, which may provide additional flexibility in performance verification testing. These standards include Potassium Dichromate Solution in Perchloric Acid for UV Photometric Accuracy and Toluene in Hexane Solution for UV bandwidth and resolution.

In addition to these offices, Thermo Fisher Scientific maintains a network of representative organizations throughout the world.

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