CTech™ Beams™ System: Qualification and Pharmacopeia Compliance

Technical Note

Introduction

Global pharmacopeial conventions require that a UV-Vis spectrometer must be qualified for critical instrument parameters in order to be certified as “suitable for intended use.” The most widely acknowledged conventions are the United States Pharmacopeia (USP), European Pharmacopoeia (EP), and Japanese Pharmacopoeia (JP).

Each pharmacopeia dictates testing methods to qualify the instrument. Among these procedures are tests for wavelength and resolution, which are designed to ensure the mechanics of the system can separate broadband light and transmit the correct wavelength with sufficient accuracy and precision. Thus, the prescribed tests assume the spectrometer uses a multi-wavelength or broadband light source with a monochromator that selects a nominal output wavelength to transmit.

The CTech™ Beams™ System consists of a monochromatic light source and data acquisition module for integration with the CTech FlowVPX® System. Internal to each Beams source is a steady-state LED with wavelength stabilization, ensuring a consistent, fixed output wavelength. There are no internal moving parts for wavelength selection, as assumed in the USP, EP, and JP protocols. While some of the pharmacopeia tests can be run, certain tests apply only to spectrometers with multi-wavelength light sources and thus cannot be carried out using the Beams system. However, the Beams system can satisfy the objectives of the pharmacopeia tests regarding wavelength accuracy, absorbance accuracy, stray light, and resolution.

The purpose of this document is to establish the Beams system’s compliance with the principles of the pharmacopeia tests. The following sections will show that the Beams system can be verified as suitable for its intended use as a UV-Vis spectrometer.

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Operational Qualification Summary

The operational qualification (OQ), also called control of equipment performance, consists of several tests designed to evaluate critical instrument parameters and establish "fitness for purpose" of the spectrometer. The parameters in question include wavelength, absorbance, stray light, and resolution, though the exact requirements for qualification vary across pharmacopeial conventions.

In each test, the instrument's capabilities are measured using certified reference materials (CRMs) traceable to the National Institute of Standards and Technology (NIST) or another accredited metrological institute.

Table 1 below summarizes the four OQ tests as they apply to the Beams system. The sections that follow describe the tests in more detail and further explain how the Beams system can be qualified as a suitable UV-Vis spectrometer.

Acceptance criteria for each major pharmacopeia can be found in the Appendix.

Table 1. Summary of USP Tests as Applied to Beams System

Test	Does it Apply?	Details
Control of Wavelength	No	The Beams source emits at a single wavelength.*
Control of Absorbance	Yes	Use ND filters as the reference standard.
Estimation of the Limit of Stray Light	Yes	Use acetone as the reference standard.
Control of Resolution	No	The Beams source has a certified bandwidth of 1 nm or less.*

*A certificate is provided with each Beams system showing guaranteed performance data.

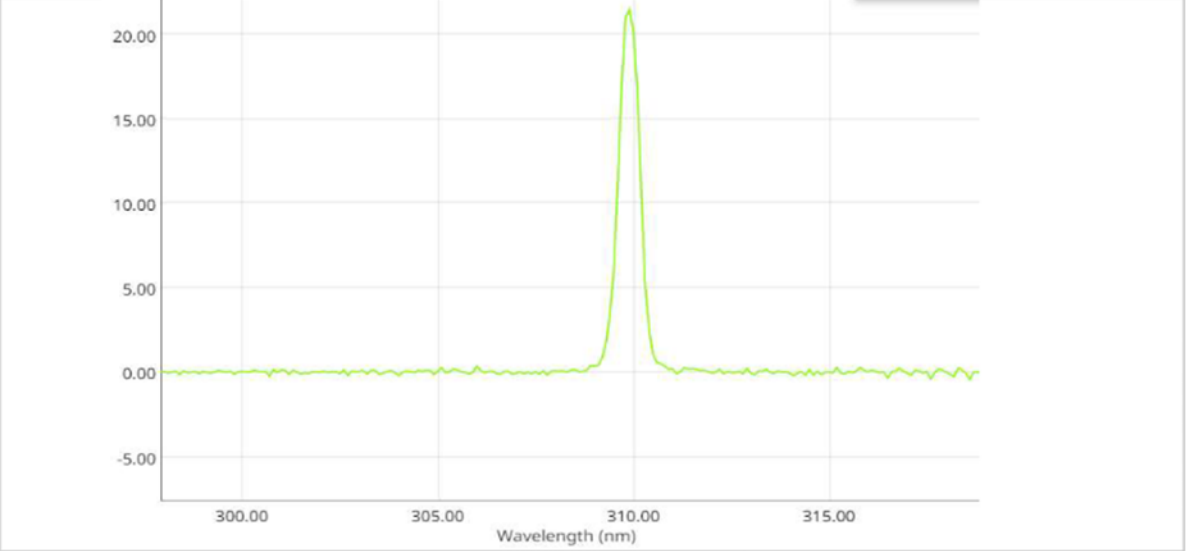
Operational Qualification Procedures

Control of Wavelength

The control of wavelength test ensures the accuracy of the spectrophotometer's output wavelength. The objective is to verify that the actual center wavelength emitted by the light source falls within a small margin of error relative to the nominal or specified output wavelength.

This test is typically done by measuring the absorbance of one or more CRMs over the intended operation range. The wavelengths of the absorbance peaks in the measured spectrum are then compared against the accepted peak absorbance wavelengths of the CRM.

The Beams source emits at a single, fixed wavelength. Therefore, the instrument is not able to generate a full spectrum for comparison to the CRM's absorbance spectrum. However, each Beams light source is certified using a calibrated Ibsen spectrometer to determine the LED center wavelength. A certificate is provided with each Beams system that states the certified center wavelength value. This value can be verified by the analyst to comply with the acceptance criteria stated in the relevant pharmacopeia. A sample certificate is shown in Figure 1 below.



Test Performed By:	Charles Findlay		Test Date:	12-Aug-22

Test Results

Parameter	Criteria	Measurement	Result
Central Wavelength	310 +/- .25 nm	309.80 nm	Pass
Full Width Half Max	<=0.700 nm	0.65 nm	Pass
Max Intensity	>= 2.0 mW	22 mW	Pass

Figure 1. Beams Source Sample Wavelength Certification

Control of Absorbance

The control of absorbance test ensures the photometric accuracy of the system. The objective is to confirm that the spectrometer will measure the correct amount of absorbance by the sample.

When performing this test using the Beams system, the absorbance should be evaluated using neutral density filters, a type of reference standard with a specified absorbance at a given design wavelength. The design wavelength of the filter must be chosen to match the output wavelength of the Beams source, and at least three different absorbance levels at the appropriate wavelength should be measured.

Estimation of the Limit of Stray Light

The limit of stray light test determines the presence of radiation that reaches the detector but falls outside the desired wavelength, called “stray light.” This can occur due to mechanical imperfections and increases with the age of the optical components in the system. The objective of this test is to confirm that the system is minimally impacted by the presence of stray light.

Stray light is measured by comparing the absorbance of a cut-off solution against an appropriate reference blank (10 mm cuvette filled with water or air, depending on the cut-off solution used). The analyst then records the difference in measured absorbance or transmission for the two materials at the recommended wavelength.

When performing this test on the Beams system, acetone should be selected as the CRM, as it has a known absorbance spectrum that includes the wavelengths of the Beams sources.

Control of Resolution

The control of resolution test ensures that the spectrometer can distinguish nearby features of an absorbance spectrum from one another. A spectrometer with high resolution, or a narrow emission spectrum, can measure absorbance at a specified wavelength without influence from nearby wavelengths. Low resolution, or a wide spectrum, can lead to inaccurate data, as the sample may interact with multiple wavelengths during a single measurement. The objective of this test is to verify that the emission spectrum of the light source is sufficiently narrow.

This test is done by measuring the absorbance of a reference standard at two different wavelengths, typically a solution of toluene in *n*-hexane at 266 nm and 269 nm. The ratio of the absorbance at these two wavelengths is then calculated to determine if the spectrometer can resolve the features of the absorbance spectrum.

As the Beams system uses a steady-state, monochromatic LED light source with a single, fixed wavelength, the instrument cannot be adjusted in order to take absorbance measurements at two different wavelengths. However, each Beams system is provided with a certificate that guarantees the light source bandwidth (full width at half maximum), which can be verified by the analyst to comply with the acceptance criteria stated in the relevant pharmacopeia. A sample certificate is shown in Figure 1 on the previous page.

Conclusion

The CTech Beams system has a steady-state design, not requiring mechanical wavelength selection from a broadband source and ensuring performance parameters do not change over time. The wavelength certification provided with each unit attests that the wavelength and resolution meet acceptance criteria. This, in addition to the control of absorbance and limit of stray light tests performed during the qualification, ensures that each Beams system complies with industry-standard requirements for operation under intended use.

Appendix: Pharmacopeia Acceptance Criteria

The tables below provide acceptance criteria values for the USP, EP, and JP standards. The standards shown are valid for the wavelengths of the Beams sources, in the range of 260 nm to 310 nm. In cases where criteria vary based on testing method, the criteria corresponding to the method recommended in this technical note are shown.

Control of Wavelength

Parameter	USP	EP	JP
Wavelength Accuracy	±1 nm	±1 nm	±0.5 nm
Wavelength Precision	≤0.5 nm	Not Required	≤0.2 nm

Control of Absorbance

Parameter	USP	EP	JP
Photometric Accuracy	±0.008 AU for A < 1.00 AU ±0.80% for A > 1.00 AU	±0.010 AU or ±1%, whichever is greater	Dependent on Individual Test Filter Used
Photometric Precision	≤0.005 AU for A < 1.00 AU; ≤0.50% for A > 1.00 AU	Not Required	≤0.002 AU for A ≤ 0.500 AU; ≤0.004 AU for A > 0.500 AU
Photometric Linearity	Not Required	$R^2 \geq 0.999$	Not Required

Estimation of Limit of Stray Light

Parameter	USP	EP	JP
Limit of Stray Light	A ≥ 2.0 AU or T ≤ 1%	Dependent on Individual Test Filter Used	Not Required

Control of Resolution

Parameter	USP	EP	JP
Spectral Bandwidth	≤2 nm	Not Specified	Not Required

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