application note

Automation of Good Manufacturing Practice Requirements for a UV-Visible Spectrometer.

Lindsay Moore and John Bishop
GBC Scientific Equipment Pty Ltd

Introduction

All analytical techniques—particularly those in the pharmaceuticals industry—involve the generation of data for quality management. Regulatory authorities demand that this data complies with current Good Manufacturing Practices (GMP). Compliance with GMP quite often demands considerable time and resources, and requires detailed documentation. The automation of GMP tests saves valuable time, reduces the opportunity for operator error, and enhances productivity.

A range of performance tests for UV-Visible spectrometers is specified by the British Pharmacopoeia V.6.19 and the Australian Code of GMP for Therapeutic Goods—Guidelines for Laboratory Instrumentation Appendix D2. The specifications in these tests are a minimum set of criteria for a general purpose UV-Visible spectrometer. An instrument which meets these specifications is considered necessary for analyses based on published data.

The British Pharmacopoeia V.6.19 sets minimum specifications for Wavelength Accuracy, Photometric Accuracy, Stray Light and Resolution. The Australian Code of GMP for Therapeutic Goods—Guidelines for Laboratory Instrumentation Appendix D2 sets minimum specifications for Wavelength Accuracy, Photometric Accuracy, Stray Light, Resolution and Baseline Flatness. These performance tests should be performed routinely on a monthly basis or whenever the instrument has been disturbed or serviced, or when malfunction is suspected.

British Pharmacopoeia

Wavelength Accuracy
The wavelength accuracy should be better than ± 1 nm for the ultraviolet range and ± 3 nm for the visible range.

Photometric Accuracy
The photometric accuracy should be within ± 0.010 AU.

Stray Light
The stray light should not exceed 1 % transmittance (2 AU) at 200 nm.

Resolution
The instrument should be able to resolve the absorbance peak due to toluene from a solution of toluene in hexane.

Australian Code of GMP for Therapeutic Goods—Guidelines for Laboratory Instrumentation Appendix D2

Wavelength Accuracy
The wavelength accuracy should be better than ± I nm for 200 to 400 nm and ± 3 nm for 400 to 700 nm.

Photometric Accuracy
Between 200 nm and 700 nm the photometric accuracy should be within±O.O1OAU in the range 0.25 to 0.75 AU.

Stray Light
The stray light should not exceed 1%

transmittance (2 AU) at 200 nm and 370 nm.

Resolution
The instrument should be able to resolve the absorbance peak due to toluene from a solution of toluene in hexane.

Baseline Flatness
The I_o line (100% transmittance line) at wavelengths between 220 nm and 700 nm should be flat to within 2% transmittance.

GBC provides an optional dedicated GMP application program for its 914/916/918/920 range of double beam UV-Visible spectrometers which automates the tests required by the British Pharmacopoeia V.6.19 and the Australian Code of GMP for Therapeutic Goods—Guidelines for Laboratory Instrumentation Appendix D2. In this note, the features of this software package are described using the British Pharmacopoeia V.6.19 tests as an example.

Experimental

Reagents and Materials

The following solutions and materials are required as part of the GMP Application for the British Pharmacopoeia V.6.19.

Wavelength Accuracy
A 4% w/v solution of holmium oxide (99.5%) in 1.4M perchloric acid.

Photometric Accuracy
A solution of 60.06 mg of A.R. grade potassium dichromate in I L of O.OIN sulphuric acid. A O.OIN sulphuric acid solution is required as a reference solution for this test.

Stray Light
A 1.2% m/v solution of potassium chloride in distilled water.

Resolution
A 0.020% v/v solution of toluene in hexane (UV grade).

Instrument

A GBC 918 double beam UV/Visible spectrometer running “GMP” application software was used in this study. A matched pair of 10 mm path length standard quartz cells was used.

Software

The GMP tests involve measurements made on a number of inorganic solutions. These tests have been automated so that the operator need only insert the test solution and initiate the test.

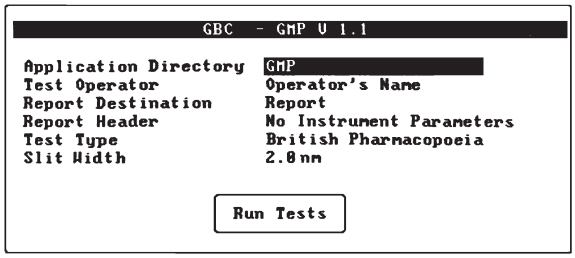

Fig. 1. GMP application main menu

The main menu of the software provides the operator with:

1. The choice of the Australian Code of GMP for Therapeutic Goods—Guidelines for Laboratory Instrumentation Appendix D2 or the British Pharmacopoeia V.6.19.
2. The choice of a full report including instrument operating parameters or brief report that includes only the test results.
3. The facility to enter the test operator’s name.
4. A command button to initiate the test.

Once the test is initiated the operator is prompted as to the specific test that is required. Figure 2 shows the test menu for the British Pharmacopoeia V.6.19.

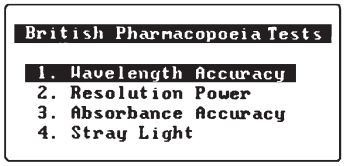

Fig. 2. British Pharmacopoeia V.6.19 test selection menu.

For each test the operator is prompted to insert the relevant test solution and initiate the test. The relevant instrument operating parameters are automatically set once a test is initiated. At the conclusion of the test the results are reported and the operator has the option of repeating the test or selecting a new test.

Results

A set of results generated by the GMP application is given in Table 1.

Table 1: Results printout from the GMP application program using the British Pharmacopoeia V.6.19.

GBC 918 - GMP V 1. I

Performance tests as specified by the British Pharmacopoeia (V6.19).

---Test

Operator: Lindsay Moore
Date: 21-Jun-1993 I
TEST - WAVELENGTH ACCURACY Measurement Mode: Absorbance
Slit Width: 2.0 nm
Upper Wavelength: 570.0 nm
lower Wavelength: 220.0 nm
Scan Speed: 240 nm/min
Wavelength Step: 0. 10 nm
Lamp Change: 350.0 nrn
Beam Mode: Double Beam
D2 On: When Necessary

Check Calibration at 536.3 nm
Peak found at: 536.2 nm
(expected 536.3 ± 3.0 nm)
Test Passed
Check Calibration at 361.5 nm
Peak found at: 361.6 nm
(expected 361.5 ± 1.0 nm)
Test Passed
Check Calibration at 287.15 nm
Peak found at: 287.2 nm
(expected 287.1 ± 1.0 nm)
Test Passed
Check Calibration at 241.15 nm
Peak found at: 241.2 nm
(expected 247.1 ± 1.0 nm)
Test Passed
TEST PASSED

TEST - RESOLUTION POWER
Measurement Mode: Absorbance
Slit Width: 2.0 nm
Upper Wavelength: 275.0 nm
Lower Wavelength: 265.0 nm
Scan Speed: 240 nm/min
Wavelength Step: 0.10 nm
Lamp Change: 350.0 nm
Beam Mode: Double Beam
D2 On: When Necessary
Peak found at: 268.00 nm
Absorbance = 0.490
Abs Trough found at: 266.30 nm
Absorbance = 0.286
Abs Expected ratio (peak/trough)
greater than or equal to: 1.5
Calculated ratio: 1.72
TEST PASSED

TEST - ABSORBANCE ACCURACY
Measurement Mode: Absorbance
Slit Width: 2.0 nm
Wavelengths: 235.0, 257.0, 313.0, and 350.0 nm
Integration Time: 2.00 s
Lamp Change: 350.0 nm
Beam Mode: Double Beam
D2 On: When Necessary

60.06 mg/L Potassium Dichromate Solution

Wavelength (nm)	Expected Reading (Abs)	Measured (Abs)	Result
235.0	0.748 ± 0.010	0.746	Passed
257.0	0.865 ± 0.010	0.860	Passed
313.0 ± 0.010	0.292	0.296	Passed
350.0	0.640 ± 0.010	0.644	Passed

TEST PASSED

TEST - STRAY LIGHT TEST
Measurement Mode: %T
Slit Width: 2.0 nm
Wavelength: 200.0 nm
Integration Time: 2.00 s
Lamp Change: 350.0 nm
Beam Mode: Double Beam
D2 On: When Necessary

1.2% m/v Potassium Chloride reading: 0.84 %T
Expected Reading less than or equal to: 1.00 %T
Test Passed
TEST PASSED

Summary

GBC provides optional dedicated GMP application software for its 914/916/918/920 range of double-beam UV/Visible spectrometers. This application program automates the series of regular performance tests that are required by the British Pharmacopoeia V.6.19 and the Australian Code of GMP for Therapeutic Goods—Guidelines for Laboratory Instrumentation Appendix D2. These tests have been automated so that the operator needs only to insert the relevant test solution and initiate the test thus saving valuable time, reducing the opportunity for operator error, and enhancing laboratory productivity. Whilst the GMP tests are required by regulatory authorities in the pharmaceutical industry, these tests may be used by any analyst interested in checking instrument performance on a regular basis.