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QUALIFICATION OF EQUIPMENT

QUALIFICATION OF UV-VISIBLE SPECTROPHOTOMETERS

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ANNEX 3 OF THE OMCL NETWORK GUIDELINE "QUALIFICATION OF EQUIPMENT"

QUALIFICATION OF UV-VISIBLE SPECTROPHOTOMETERS

Note: Mandatory requirements in this annex are defined using the terms "shall" or "must". The use of "should" indicates a recommendation. For these parts of the text other appropriately justified approaches are acceptable. The term "can" indicates a possibility or an example with non-binding character.

Introduction

The present document is the 3th Annex of the core document "Qualification of Equipment", and it shall be used in combination with it when planning, performing and documenting the UV-Visible spectrophotometer qualification process.

The core document contains the Introduction and general forms for Level I (Selection of instruments and suppliers) and II (Installation and release for use) of qualification, which are common to all type of instruments.

The present annex 3 contains general introduction and requirements for UV-Visible spectrophotometers. Level III (Periodic and motivated instrument calibration/checks) and IV (In-use instrument checks) qualifications must be carried out being an ISO 17025 requirement.

Requirements and (if applicable) corresponding typical acceptance limits given in bold should be applied; however other appropriately justified approaches are acceptable.

Exemplary procedures provided in this document have non-binding character. They can be helpful to carry out the required qualification. Nevertheless, it is left to the professional judgement and background experience of each OMCL to decide on the most relevant procedures to be undertaken in order to give evidence that their UV-Visible spectrophotometers are working properly and are suitable for their intended use.

If the qualification of equipment is done by the manufacturer or an external service provider, it is the responsibility of the OMCL to make sure that this is in line with the requirements set out in this guideline.

TABLE I

Level III. Periodic and motivated instrument checks

Recommendations for UV-visible spectrophotometers and related typical acceptance limits

Parameter to be checked	*Typical acceptance limits*
Spectral slit-width (if applicable)	± 10 %
Wavelength accuracy*	**According Ph. Eur. 2.2.25.**
Wavelength precision (for mechanically set wavelengths)	See manufacturer's specifications
Absorbance accuracy*	**According Ph. Eur. 2.2.25.**
Photometric linearity*	**According Ph. Eur. 2.2.25.**
Limit of stray light*	**According Ph. Eur. 2.2.25.**
Baseline noise	± 0.002 Absorbance units (500 nm) or ± 0.01 Absorbance units (200, 300, 400 nm)
Photometric drift	± 0.001 Absorbance units/h (250 nm) or ± 0.002 Absorbance units/h (500 nm)

*** following the instructions given in Ph. Eur. Chapter 2.2.25. "Control of equipment performance"**

TABLE II

Level IV. In-use instrument checks

Recommendations for UV-visible spectrophotometers and related typical acceptance limits

Parameter to be checked	*Typical acceptance limits*
System suitability check of the method - e.g. Repeatability - e.g. Resolution (if required for qualitative analysis)	According to Ph. Eur. Chapter 2.2.25 or Monographs or MAH dossier or validated in-house method
Control of cuvettes*	**According Ph. Eur. 2.2.25.**

* **following the instructions given in Ph. Eur. Chapter 2.2.25. "Control of cuvettes"**

Level III. Periodic and motivated instrument checks

This section contains practical examples of tests and their associated acceptance limits for several parameters related to the performance of a UV-Visible spectrophotometer.
These examples can be considered by the OMCLs as possible approaches to perform the Level III of the equipment qualification process: “Periodic and motivated instrument checks”.

GENERAL CONSIDERATIONS

- Measurements made by comparing samples against external standards should be made under conditions during which temperature is held constant. This is particularly relevant where the carrier solvent is organic and measurements may be distorted by expansion or evaporation of the solvent.

- It is recommended to perform the qualification within the spectral range corresponding to the region of analytical interest.

- Ensure that the spectrophotometer has stabilised, according to the manufacturer’s recommendations, before starting the qualification tests.

- When references are made to the European Pharmacopoeia, e.g. reagents R, then the reagent quality shall comply with the Ph. Eur. specifications.

- When using commercial filters as alternative to the proposed tests, a set of filters covering the entire range of interest should be used. They should be calibrated with traceability to national/international standards, preferable through a national metrology laboratory or NIST.

SPECTRAL SLIT WIDTH (if applicable)

When using an instrument on which the slit-width is variable at the selected wavelength, the slit-width must be small compared with the half-width of the absorption band but it must be as large as possible to obtain a high value of I_0. Therefore, a slit-width is chosen such that further reduction does not result in a change in absorbance reading.

Method and Limits:
1. Switch the system on and start the Scan module.

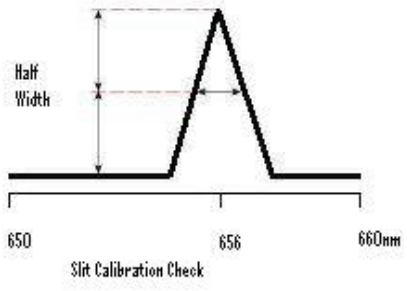
2. Select SETUP and set the following parameters:
   X Mode = Nanometres
   Start wavelength = 660.0 nm
   Stop wavelength = 650.0 nm
   Y Mode = % T
   Scan rate = 10 nm/min
   Gain = (100) see 4 below

3. Select Options tab and set the following parameters:
SWB = 4 nm
Beam mode = Single front
Lamps on = Deuterium
Source change = 700.0 nm

4. Start a scan and examine the trace for a spectral peak around 656.1 nm.
If no peak is seen or it is less than 50% T, increase the gain.
If the signal exceeds 100% T, reduce the gain.

5. Measure the width of the peak (in nanometres) at half the height of the peak.
This represents the spectral bandwidth and should be within ± 10% of that selected via the computer.

6. Check the calibration at a slit width of 0.2 nm. If the measured slits are too small then, for a selected width, the instrument will have more photometric noise than normal. If the slit width is unacceptable, then reset the slit calibration.



Effect of spectral slit width on absorbance fluctuation (performed with pure solvents).

Slit width 5.0 nm	Slit width 2.0 nm	Slit width 1.0 nm	Slit width 0.05 nm	Difference in Abs.	Theoretical Values	Test status
Cyclohexane						
0.016	0.015	0.015	0.015	< 0.001	< 0.010	Passed
Ethanol						
0.020	0.019	0.019	0.019	< 0.001	< 0.010	Passed
Methanol						
0.005	0.005	0.005	0.005	0.00	< 0.010	Passed

WAVELENGTH PRECISION (for mechanically set wavelengths)

Materials:
For this test, the same materials of the previous test can be used:
Holmium perchlorate solution R prepared, for example, with a 40 g/L solution of holmium oxide R in a solution of perchloric acid R containing 141 g/L of $HClO_4$ (Ph. Eur. Chapter 4.1.1. "Reagents", ref. 1043101).
If available, the built-in mercury lamp of the instrument may be used for this test.
Alternatively, suitable commercial certified filters may be used[1].

Method:
Carry out 6 measurements of the absorbance maxima.

Limits:
Repeatability: the relative standard deviation of the absorbance maxima should satisfy the manufacturer's specifications.
The difference between the 6 individual absorbance maxima values should comply with the manufacturer's specifications (e.g. < 0.5 nm).

BASELINE NOISE

For this test, 2 alternative methods are proposed.

TEST 1

Method:
Make 61 absorbance measurements with an integration time of 1 second at a wavelength of 500 nm, with no sample in the sample chamber, and calculate the mean.

Limits:
Mean ± 0.002 Absorbance units

TEST 2

Method:
Record the absorbance for 60 seconds at 200, 300 and 400 nm with a highly pure, synthetic Quartz block[1]. The measurement is made against air.

Note: If commercial filters are used, the wavelengths and the exact absorption values with the corresponding tolerance limits will depend on the type of filters.

Example of limits:

Filter	Wavelength (nm)	Maximum tolerance
Quartz block (against air)	200	0.049 ± 0.01
	300	0.033 ± 0.01
	400	0.031 ± 0.01

[1] e.g. Hellma filter 667-UV 0.

PHOTOMETRIC DRIFT

Photometric drift should be checked at both the visible and UV region, at appropriate wavelengths. The limits are in accordance with the user's requirements (as defined in Level I) and with manufacturer's specifications.

For this test, 2 alternative examples are proposed.

TEST 1

Method:
As routine test, the drift is measured at 250 nm over a period of 2 hours by using the Time Scan mode of the instrument, with no sample in the sample chamber.

Limits: ± 0.001 Absorbance units/h

Note: In certain cases, for example when several samples are measured over a long period of time (or when using auto sampler), the drift can also be determined at the wavelength reported in the analytical method, under the same operational conditions, before testing samples.

TEST 2

Method:
Record the baseline for 60 minutes at 500 nm and compare the absorbance with the initial value.

Limits: ± 0.002 Absorbance units/h

Level IV. In-use instrument checks

This Annex contains practical examples of tests and their associated acceptance limits for several parameters related to the performance of an UV-Visible spectrophotometer.
These examples can be considered by the OMCLs as possible approaches to perform the Level IV of the equipment qualification process: “In-use instrument checks”.

SYSTEM SUITABILITY TEST OF THE METHOD

- REPEATABILITY (for quantitative analysis)
- RESOLUTION (for both qualitative and quantitative analysis)

Method:
This test should be performed according to Ph. Eur., the MAH dossier or a suitably validated in-house method.

REFERENCES

(For all references, the latest version applies)

1) Ph Eur. 2.2.25, Absorption spectrophotometry, Ultraviolet and Visible.

2) Guidance on Equipment Qualification of Analytical Instruments: UV-Visible Spectro(photo)meters (UV-Vis). Valid Analytical Measurement (VAM) Programme.