Valid Analytical Measurement (VAM) Programme

Guidance on Equipment Qualification of Analytical Instruments: UV-Visible Spectro(photo)meters (UV-Vis)

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Preface

Original guidance on equipment qualification [1] was prepared by LGC with assistance from an Instrumentation Working Group. Following the original guidance the decision was taken to produce a series of specific guides for particular techniques. This guide, produced by a sub-group of the Instrumentation Working Group, provides specific guidance for users of UV-Visible spectrophotometry (UV-Vis). The contributions from this sub-group, the members of which are listed below are gratefully acknowledged. The secretariat would also like to thank those who commented informally during the drafting process.

It is intended that after a period of use, the content of this document will be reviewed, and the amended text republished. Users are invited to comment on the content of the existing text and suggest additional material in writing to:

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1. Glossary

Many of the terms relating to equipment qualification are used in different ways to convey a
variety of meanings. In this document the term “spectrometer” refers to a spectrometer or
spectrophotometer (as defined in this section) which operates in the UV-visible region of the
electromagnetic spectrum [2]. This section explains how other terms should be interpreted in
this guidance document.

1.1 **Accessory**: an additional or alternative component of the system that may be used to extend the
capability of the distinct component of the system (*e.g.* a multiple sample-cell holder).

1.2 **Analytical Quality Control**: procedures, which give insight into the precision and accuracy of
a result [3].

1.3 **Calibration**: the set of operations which establish, under specified conditions, the relationship
between values indicated by a measuring instrument or process and the corresponding known
values of the measurand.

1.4 **Certified Reference Material (CRM)**: a reference material, accompanied by a certificate, one
or more of whose property values are certified by a procedure which establishes traceability to
an accurate realisation of the unit in which the property values are expressed, and for which
each certified value is accompanied by an uncertainty at a stated level of confidence.

1.5 **Design Qualification (DQ)**: covers all procedures prior to the installation of the system in the
selected environment. DQ defines the *user requirement specification*, and details the conscious
decisions in the selection of the supplier. Thus it defines the overall requirements for the
instrument, the key performance characteristics of the instrument and ranges over which the
instrument is required to operate and consistently perform, and other critical factors relating to
its use.

1.6 **Equipment Qualification (EQ)**: the overall process of providing evidence that an instrument is
fit for its intended purpose and that it is kept in a state of calibration and maintenance consistent
with its use.

1.7 **Holistic testing**: the process of verifying the correct functioning and performance of the entire
instrument system.

1.8 **Installation Qualification (IQ)**: covers all procedures relating to the installation of the
instrument in the selected environment. IQ establishes that the instrument is received as
designed and specified, that it is properly installed in the selected environment, and that this
environment is suitable for the operation and use of the instrument.

1.9 **Instrument**: an entire UV-Visible spectro(photo)meter measurement system comprising either a
fully integrated system or an optical system attached to a computerised controller.

1.10 **Instrument Diagnostics**: routines within an instrument or system that perform self-checks on
the functions of the instrument or system and which can be used for fault finding.

1.11 **National Measurement Institutes**: national laboratories with responsibility for the
maintenance of primary metrology standards, *e.g.* the National Physical Laboratory in the UK.
1.12 **Operational Qualification (OQ):** the process of undertaking confirmatory checks to verify key aspects of performance in the absence of any contributory effects which may be introduced by the method.

1.13 **Performance Qualification (PQ):** the process of demonstrating that an instrument consistently performs according to a specification appropriate for its routine use.

1.14 **Reference Material (RM):** material or substance one or more of whose property values are sufficiently homogeneous and well established to be used for the calibration of an apparatus, the assessment of a measurement method, or for assigning values to materials.

1.15 **Regulatory Authorities:** in the context of this document, these are organisations which monitor compliance against quality standards or protocols, *i.e.* accreditation bodies, certification bodies, and Good Laboratory/Manufacturing/Clinical Practice monitoring authorities.

1.16 **Resolution:** the spectrometer’s ability to distinguish between two absorbance bands which are close together. Related terms are bandwidth and spectral bandwidth. Band width is the width of the peak at half height, see diagram. Spectral band width should be set to about one tenth of the band width.

1.17 **SOP – Standard Operating Procedure/Practice:** a term used in Good Laboratory/Manufacturing/Clinical Practice to describe written procedures or practices that have been standardised within an organisation or industry which describe how to perform tests or other activities.

1.18 **Spectrometer:** an instrument that establishes the ratio, or a function of the ratio, of the radiant power of two beams as a function of spectral wavelength. These two beams may be separated in time, space, or both.

1.19 **Spectro(photo)meter:** a spectrometer consisting of an entrance aperture, a dispersing device, and one or more exit apertures, so that radiant power or a function of radiant power can be measured at selected wavelengths within the spectral range, or by scanning over the range.

1.20 **Supplier:** the instrument manufacturer, vendor, lessor or approved agent.

1.21 **System Suitability Checking (SSC):** a series of tests to check the performance of a measurement process. SSC may form part of the process of validation when applied to a particular measuring procedure. SSC establishes that the operational conditions required for a
specific measurement process are being achieved and can be used to provide evidence of satisfactory instrumental performance during actual use.

1.22 **Traceability**: the property of a result of a measurement whereby it can be related to appropriate standards, generally national or international standards, through an unbroken chain of comparisons.

1.23 **User**: the organisation purchasing the instrument including its management and staff.

1.24 **Validation**: the process of evaluating the performance of a specific measurement process and checking that the performance meets certain pre-set criteria. Validation establishes and provides documented evidence that the measuring procedure is fit for a particular purpose.
2. The equipment qualification process

2.1 Equipment qualification (EQ) is a formal process that provides documented evidence that an instrument is fit for its intended purpose and kept in a state of maintenance and calibration consistent with its use.

2.2 EQ is divided into four stages: design qualification (DQ); installation qualification (IQ); operational qualification (OQ); and performance qualification (PQ). The role of each stage is summarised in Figure 1.

![Diagram of EQ process]

- **Design Qualification (DQ)**
  - Defines the specifications of the instrument and details the conscious decisions in the selection of the supplier.

- **Installation Qualification (IQ)**
  - Establishes that the instrument is received as designed and specified, that it is properly installed in the selected environment, and that this environment is suitable for the operation of the instrument.

- **Operational Qualification (OQ)**
  - Confirmatory checks to verify key aspects of performance in the absence of contributory effects which might be introduced by the method.

- **Performance Qualification (PQ)**
  - The process of demonstrating that an instrument performs according to a specification appropriate for its routine use.

Figure 1 - The EQ process

2.3 DQ is the ‘planning’ part of the EQ process and is most often undertaken as part of the process of purchasing a new instrument, although it may be appropriate to repeat aspects of DQ following a major change to the instrument or its use. Whilst qualification of the actual instrument design is for manufacturers of instruments, users of instruments have an important role in DQ by ensuring adoption of a user requirement specification (URS) which meets the intended use.

2.4 IQ, OQ and PQ are the ‘implementation’ stages of the EQ process and provide an assurance that the instrument is installed properly, that it operates correctly, and that its ongoing performance remains within the limits required for its actual use. IQ covers the installation of the instrument up to and including its response to the initial application of power. OQ should be carried out after the initial installation of the instrument (IQ) and repeated following a major event (e.g. relocation or maintenance) or periodically at defined intervals (e.g. annually).
2.5 PQ is undertaken regularly during the routine use of the instrument. The role of PQ is to provide continued evidence that, even though the performance of the instrument may change due to factors such as wear or contamination, its performance remains within the limits required for its actual use. As such, much of the evidence needed for PQ is available from ‘everyday’ procedures, for example, method validation, system suitability checking (SSC), routine calibration and analytical quality control.

2.6 The terms ‘validation’ and ‘qualification’ are used widely and often to convey the same meaning. The approach taken in this guidance document is that validation is application orientated and relates to a specific measurement method or process, whereas qualification is instrument orientated and relates primarily to providing evidence of satisfactory performance of the instrument.

2.7 Increasingly, both analytical laboratories and regulatory authorities are acknowledging that, under most circumstances, both method validation and equipment qualification are important prerequisites for obtaining reliable data. In particular, OQ provides an assurance that an instrument functions correctly independently of the applications or methods with which it is used.

2.8 Although formal quality standards [4, 5, 6 7, 8] all require various combinations of method validation and equipment qualification, there is a lack of clear guidance on when EQ is appropriate, what is actually required, how it should be achieved and how it should be documented. A key objective in developing guidance [1] has been, therefore, to provide users and suppliers of analytical instruments, as well as those responsible for the assessment, certification and monitoring of analytical laboratories, with a clear and consistent approach to EQ. The guidance has been prepared with the primary aim of assisting the interpretation of formal quality standards in order to satisfy regulatory and accreditation requirements.

2.9 Nowadays many instruments contain internal calibration routines, which calibrate the instrument against an internal standard and may additionally include automatic adjustment of the instrument. It may be difficult to establish the traceability of these internal routines to national standards, for example by relating them to external calibration. Furthermore it may be unclear whether these internal standards require periodic re-calibration and how this can be achieved. Consequently it is important that associated documentation establishes exactly what these routines do and provide advice for re-calibration and establishing traceability to the levels required by regulatory authorities.

2.10 EQ must be documented (Section 4 of the general guidance [1] provides more detailed guidance on requirements for EQ documentation). EQ documentation can be prepared and provided by the user, the supplier, or both. Where it is provided by the supplier (e.g. in a qualification protocol), it should be written in such a way that it can be readily followed and understood by the user.

2.11 The responsibility for equipment qualification rests with the users of analytical instruments. Suppliers can be expected to make available documentation, tools and services to assist EQ and, in particular, to provide clear instructions and details of tests and checks required to demonstrate satisfactory performance. Although such performance testing can be carried out by the supplier or the user, it must remain under the control of a suitably qualified user.
2.12 The user must establish the level of EQ required and what aspects of EQ (particularly OQ) will be done in-house and what will be carried out by an external organisation. Where any aspect of EQ, and/or a performance check or test is undertaken, users must satisfy themselves that it has been carried out competently and correctly (evidence of current competence should be established, for example, through a valid training record or certificate).

2.13 This document is not intended to describe an exhaustive series of compulsory tests that must be carried out under all circumstances. Those undertaking EQ must exercise their professional judgement and common sense to decide on which tests are relevant, and on what test criteria and tolerance limits are appropriate. An important consideration in determining what is checked and verified during EQ is the supplier’s track record and the user’s experience with previously supplied equipment.

2.14 EQ provides important evidence of an instrument’s satisfactory performance and its fitness for the purpose for which it is used. However, EQ is just one of a range of activities which contribute towards achieving and demonstrating reliable and valid data.
3. UV-Visible Spectro(photo)metry

3.1 The guidance in this document is intended to cover spectrometers operating in the ultra-violet and visible regions. It is not intended to include stand-alone near-infrared instruments but does include UV-Vis instruments with working ranges that extend into the near infrared region. It covers single and double beam instruments, scanning and non-scanning, and instruments with photodiode array detection. It specifically does not include instruments that operate using the Fourier transform principle.

3.2 A spectrometer system usually consists of a completely integrated ‘box’, or an optical unit controlled by an external personal computer (PC). Optional accessories to automate sample handling may include ‘sipper’ devices, which in turn may be coupled to auto-samplers, and temperature regulation devices. The spectrometer and its accessories may be obtained from one or more suppliers or as an integrated system from a single supplier.

3.3 Whilst suppliers will be able to assist and undertake qualification of their own instruments, they may not be able to perform qualification of other suppliers’ instruments. Testing of the complete system (holistic testing), such as that carried out in PQ, will normally have to be undertaken by the user.

3.4 This document provides guidance on the equipment qualification of the principle components of an UV-Vis system. The vast majority of modern spectrometers depend to some extent on computers or microprocessors for operation. Implicit in the demonstration of fitness-for-purpose is the checking of the associated hardware, software and firmware. The requirement for such checks is laid down in various regulations, e.g. [8, 9, 10]. It is beyond the scope of this guide to provide detailed advice on qualification of computer systems. Such advice is available elsewhere, e.g. [11, 12]. An assurance of the correct functioning of computerised systems can be inferred from holistic performance checks such as those carried out in PQ. Testing algorithms with standard data sets may also be possible.

3.5 The subsequent sections of this document provide more detailed guidance on the requirements of each stage of qualification (DQ⇒IQ⇒OQ⇒PQ) and how each stage should be applied to the qualification of the main features and functions of an UV-Vis instrument.

3.6 Many quality standards and regulatory authorities stipulate that “where possible calibrations should be traceable to national or international standards” in order to ensure accuracy. This leads to confusion as to the need for certified reference materials (CRMs) and calibrated apparatus when checking an instrument’s operating parameters. Tests to verify the accuracy of the critical parameters of wavelength and absorbance will require the use of CRMs.
4. Design Qualification (DQ)

4.1 Design Qualification is concerned with what the instrument is required to do and links directly to fitness for purpose. DQ provides an opportunity for the user to demonstrate that the instrument’s fitness for purpose has been considered at an early stage and built into the procurement process.

4.2 DQ should, where possible, establish the intended or likely use of the instrument and should define an appropriate user requirement specification (URS). The URS defines the key performance characteristics of the instrument and the ranges over which the instrument is required to operate and consistently perform along with other critical factors relating to its use. The URS may be a compromise between the ideal and the practicalities of what is actually available. Whilst it is the responsibility of the user to ensure that specifications exist, and that they are appropriate, they may be prepared by the user, the supplier(s), or by discussion between the two.

4.3 In undertaking DQ, information and knowledge of existing equipment should be taken into account. If an instrument is mature in design and has a proven track record, this may provide a basic confidence and evidence about its suitability for use. For new techniques or instruments DQ may require more effort. For a variety of reasons customers may favour particular manufacturers.

4.4 The selection of the supplier and instrument is entirely at the discretion of the user. One possible way to do this is to score candidate instruments according to the extent to which they meet the client’s requirements [13]. However, in making this selection, the user should bear in mind that regulatory authorities may require, and in some cases are likely to require, evidence that the manufacturer has used:

- fully documented quality control and quality assurance procedures, including design and specification;
- suitably qualified and experienced personnel;
- comprehensive and planned testing of all parts of the system, and;
- stringent change control, error reporting and corrective procedures.

4.5 A suitable questionnaire, third party audit, or independent certification of the supplier to an approved quality scheme may provide the user with the necessary evidence that regulatory requirements have been met during design and manufacture of the instrument. Where such evidence is not available, it is the responsibility of the user to carry out more extensive qualification in order to provide the necessary assurance of the instrument’s fitness for use. It would be reasonable for the supplier to assist the client with this stage.

4.6 Where instruments are intended to be used to make measurements which support regulatory studies, the user may also need to seek confirmation that the manufacturer is prepared, if required, to allow regulatory authorities access to detailed information and records relating to the instrument’s manufacture and development, for example: source codes; instrument development records and procedures; calibration and qualification documentation; batch test records and reports; hardware and software qualification documentation; and credentials of staff involved with the development of the instrument.
4.7 Tables 1-2 summarise key features that might be considered during the development of the URS. The user should decide what are the specific requirements for each parameter. A report of the Analytical Methods Committee also gives a useful checklist [13].

<table>
<thead>
<tr>
<th>Feature</th>
<th>Consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instrument set-up &amp; control</td>
<td>PC based or integrated system.</td>
</tr>
<tr>
<td></td>
<td>Software control of operating conditions and parameters.</td>
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<tr>
<td></td>
<td>Data acquisition, processing and presentation needs.</td>
</tr>
<tr>
<td></td>
<td>In-built diagnostic facilities.</td>
</tr>
<tr>
<td></td>
<td>Self-testing diagnostics.</td>
</tr>
<tr>
<td></td>
<td>Detector options.</td>
</tr>
<tr>
<td></td>
<td>Source options.</td>
</tr>
<tr>
<td>Sample introduction &amp; throughput</td>
<td>Sample throughput, presentation and introduction needs.</td>
</tr>
<tr>
<td></td>
<td>Sample thermostating requirements.</td>
</tr>
<tr>
<td></td>
<td>Sample volume requirements.</td>
</tr>
<tr>
<td>Materials of construction</td>
<td>Resistance to corrosion, contamination by solvents and samples.</td>
</tr>
<tr>
<td>Installation requirements</td>
<td>Size and weight in shipped form.</td>
</tr>
<tr>
<td></td>
<td>Access restrictions to permanent site.</td>
</tr>
<tr>
<td>Operational requirements</td>
<td>Limitations on, requirements for and expected consumption of services, utilities, and consumables (e.g. lamps).</td>
</tr>
<tr>
<td></td>
<td>Ventilation requirements.</td>
</tr>
<tr>
<td></td>
<td>Controlling software embedded or separate package.</td>
</tr>
<tr>
<td>Environmental conditions</td>
<td>Environmental conditions within which, or range over which, the instrument is required to work within specification.</td>
</tr>
<tr>
<td></td>
<td>Recyclability of instrument.</td>
</tr>
<tr>
<td>Maintenance &amp; support</td>
<td>Ease of user maintenance and cleaning.</td>
</tr>
<tr>
<td></td>
<td>Cost, longevity, and availability of spares and parts.</td>
</tr>
<tr>
<td></td>
<td>Cost and availability of service contracts and technical support.</td>
</tr>
<tr>
<td></td>
<td>Suggested intervals between and procedures for maintenance and calibration of the instrument.</td>
</tr>
<tr>
<td></td>
<td>The period for which support (qualification, maintenance, parts etc.) for the instrument can be guaranteed.</td>
</tr>
<tr>
<td>Training requirements</td>
<td>The level of skill required to operate the instrument and details of any training necessary and courses provided by the supplier.</td>
</tr>
</tbody>
</table>
Table 1 (continued)- Design Qualification - General Considerations

<table>
<thead>
<tr>
<th>Feature</th>
<th>Consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accessories</td>
<td>Desired adaptation of the system.</td>
</tr>
<tr>
<td>Documentation</td>
<td>Clarity and ease of use of documentation (e.g. operating manuals, qualification protocols, model SOPs).</td>
</tr>
<tr>
<td>Health and Safety</td>
<td>Health and safety and environmental issues and/or requirements.</td>
</tr>
<tr>
<td></td>
<td>Significant generation of ozone.</td>
</tr>
</tbody>
</table>

Table 2 – Design Qualification of UV-Vis Instruments

<table>
<thead>
<tr>
<th>Feature</th>
<th>Consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>System control and communication *</td>
<td>Spectrometer parameters selected/controlled/ stored/retrieved either locally within the optical instrument, or via a remote PC or system controller. Ability to send / accept / store / retrieve signals (e.g. through contact closures) and to communicate (e.g. RS232) with other devices.</td>
</tr>
<tr>
<td>Source type</td>
<td>Lamp life, warm-up time, susceptibility to drift.</td>
</tr>
<tr>
<td></td>
<td>Wavelength at which lamp changes (if at all).</td>
</tr>
<tr>
<td>Samples *</td>
<td>Sample types accommodated (conventional, turbid, solid).</td>
</tr>
<tr>
<td></td>
<td>Ability to handle discrete samples (single cell or matched cells) or continuous (flowcell). Range of sample sizes possible (cell volume and path length, minimum flushing volume for flowcells). Ability to handle multiple samples either attended or unattended, and possible batch size. Facility for control of sample cell temperature: range (including sub-ambient facility), accuracy, stability, type (Peltier or circulating). Ease of interchange of different cell types or accessories.</td>
</tr>
<tr>
<td>Detector type</td>
<td>Ability to monitor single, multiple or variable wavelengths and/or full spectral characteristics, required acquisition speed of full spectra.</td>
</tr>
<tr>
<td>Wavelength accuracy</td>
<td>Ability to select required wavelengths accurately and reproducibly.</td>
</tr>
<tr>
<td>Wavelength range</td>
<td>Ability to select and monitor required wavelengths, with or without changing source, filter or detector.</td>
</tr>
<tr>
<td>Linear dynamic range</td>
<td>Ability for accurate quantitation over a large absorbance range.</td>
</tr>
<tr>
<td>Optical and electronic noise</td>
<td>Low noise facilitates improved sensitivity and lower detection limits (note whether peak-to-peak or RMS).</td>
</tr>
<tr>
<td>Wavelength drift</td>
<td>Low drift facilitates improved sensitivity and lower detection limits.</td>
</tr>
<tr>
<td>Resolution</td>
<td>Important for accurate measurement of narrow bands.</td>
</tr>
<tr>
<td>Photometric accuracy</td>
<td>Good accuracy required for absolute absorbance measurements.</td>
</tr>
</tbody>
</table>
Table 2 (Continued) – Design Qualification of UV-Vis Instruments

<table>
<thead>
<tr>
<th>Feature</th>
<th>Consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photometric drift</td>
<td>Stability of the measurement over time, making comparisons meaningful.</td>
</tr>
<tr>
<td>Stray light</td>
<td>Affects accuracy and linearity. Define method used.</td>
</tr>
<tr>
<td>Data collection *</td>
<td>Expression of data on % Absorption or % Transmission scales.</td>
</tr>
<tr>
<td></td>
<td>Single or repeat scan facility.</td>
</tr>
<tr>
<td></td>
<td>Single or multiple wavelength monitoring.</td>
</tr>
<tr>
<td></td>
<td>Full spectral data (e.g., diode array).</td>
</tr>
<tr>
<td>Data manipulation *</td>
<td>Spectral subtraction.</td>
</tr>
<tr>
<td></td>
<td>Spectral derivatives.</td>
</tr>
<tr>
<td></td>
<td>Audit trail facility.</td>
</tr>
<tr>
<td></td>
<td>Is raw data uncorruptable?</td>
</tr>
<tr>
<td></td>
<td>Back-up and restore capabilities.</td>
</tr>
<tr>
<td>Data storage *</td>
<td>No storage.</td>
</tr>
<tr>
<td></td>
<td>Embedded memory.</td>
</tr>
<tr>
<td></td>
<td>File transmission to external device.</td>
</tr>
<tr>
<td></td>
<td>Stored output via optical or magnetic media.</td>
</tr>
<tr>
<td></td>
<td>System security.</td>
</tr>
<tr>
<td>Data output *</td>
<td>Inbuilt hardcopy output –data only, spectrum only, data + spectrum.</td>
</tr>
<tr>
<td></td>
<td>PC based data processing.</td>
</tr>
<tr>
<td></td>
<td>Custom report generation.</td>
</tr>
</tbody>
</table>

* Note that features relating to system or sample control, or collection, manipulation, storage and output of data may be required to comply with particular requirements for regulatory purposes, e.g. 21 CFR 11 [9].
5. Installation Qualification (IQ)

5.1 IQ covers the installation of the instrument up to and including its response to the initial application of power. IQ involves formal checks to confirm that the instrument, its modules and accessories have been supplied as ordered and that the instrument is properly installed in the selected environment.

5.2 IQ may be carried out either by the supplier and/or the user. However, it should be noted that, in some cases, the complexity of the instrument alone may preclude the user performing IQ and, in others, the unpacking of the equipment by the user may invalidate the warranty.

5.3 IQ must be undertaken in accordance with the supplier’s instructions and procedures. The success or failure of each of the IQ checks performed should be formally recorded and, where these have been carried out by the supplier, the results of these tests must be communicated to the user.

5.4 The principles relating to IQ are primarily generic in nature. For convenience, a checklist covering the main requirements for IQ is provided below:

- Has the instrument been delivered as ordered, e.g. according to the DQ or purchase order?
- Has the instrument been checked and verified as undamaged?
- Has the appropriate documentation been supplied, is it of correct issue and uniquely identified by part number, version number and date?
- Have details of all services and utilities required to operate the instrument been provided (preferably in advance of the delivery)?
- Is it clear which maintenance, calibration and performance tests should be carried out by the user and which by the supplier or their agent.
- Have details of recommended service and calibration intervals (carried out by the supplier) been provided?
- Have intervals, methods and instructions for user-maintenance and calibration been provided along with contact points for service and spare parts?
- Has the correct hardware, firmware and software been supplied and is it of correct issue and uniquely identified by part number?
- Has information been provided on consumables required during the normal operation of the instrument system?
- Is the selected environment for the instrument system suitable, with adequate room for unpacking, installation, operation and servicing, and have appropriate services and utilities (electricity, water, etc.) been provided?
- Has health and safety and environmental information relating to the operation of the instrument been provided and is the proposed working environment consistent with these requirements?
- Is the response of the instrument to the initial application of power as expected and have any deviations been recorded?
6. Operational Qualification (OQ)

6.1 The purpose of Operational Qualification (OQ) is to verify that key aspects of instrumental performance (e.g. wavelength, absorbance, resolution, stray light, noise and drift) are satisfactory, and within specification, in the absence of any contributory effects which may be introduced by the analytical method. OQ tests are designed to check the performance of an individual instrument in such a way that any variation noted is attributable to the instrument itself, rather than cells, or particular solvents or chromophores.

6.2 Whilst many methods might be robust to small differences between the selected and actual value of an operating condition (e.g. wavelength range, absorbance range, resolution), significant differences may impact on the validity of the method and the data generated by it. The role of OQ can, therefore, be considered as the process of checking that key operating conditions are within specified limits for accuracy and precision.

6.3 OQ testing should be carried out after the initial installation of the instrument and then at defined intervals throughout the instrument’s life. It is usually carried out either periodically or following an event, which may affect the performance of the instrument (see 6.6). Some aspects of performance (such as stray light) may be more sensitive to a particular event than other aspects (such as resolution). Thus a full suite of OQ checks may not be required on every occasion and the planning for OQ should tailor the testing programme to concentrate on the parameters most likely to be affected.

6.4 The responsibility for defining the frequency and extent of OQ testing rests with instrument users. However, manufacturers should provide advice on recommended intervals and identify the sort of checks that will be required following particular events. The frequency at which periodic OQ testing is undertaken will typically depend on:

- manufacturer’s recommendations;
- required instrument performance;
- level of instrument use (higher workloads might accelerate component wear, leading to more rapid deterioration in overall performance and therefore necessitate more frequent OQ testing);
- operating environment (an instrument in a mobile laboratory is likely to require more frequent OQ testing (e.g. to verify wavelength accuracy) than a similar model housed in a permanent location);
- use inconsistent with manufacturer’s recommendations;
- experience of intervals during which the instrument has been found to remain within required performance limits under the conditions used.

6.5 For event-driven OQ, the extent to which OQ is repeated will depend on the impact that the event has on the performance of the instrument. For example, whilst the replacement of the pump tubing is likely to affect the performance of a peristaltic pump based ‘sipper’ system, it is unlikely to impact on the optical performance of the spectrometer. Therefore, although it will be necessary to repeat OQ to verify the performance of the sample introduction by the sipper, it should not be necessary to repeat OQ testing to verify the optical performance of the
spectrometer. However changes made inside the sample cell compartment, such as reconfiguration of the sample cell holders, would prompt an examination that stray light levels were still acceptable, or a check on absorbance accuracy to confirm that vignetting has not occurred.

6.6 Examples of events that may necessitate repeating OQ include:

- routine maintenance, servicing and replacement of parts;
- movement or relocation;
- interruption to services and/or utilities (other than by accepted close-down procedures);
- modification or upgrades; and
- as part of troubleshooting / fault-finding following PQ failure.

6.7 A list of the checks and tests that might be carried out during OQ is provided in Table 3. It is important to emphasise that this is not intended to be an exhaustive list of checks and tests that must be carried out under all circumstances. Users must exercise their professional judgement to decide which checks are relevant and to what extent.
### Table 3 - Operational Qualification of UV-Vis Instruments

<table>
<thead>
<tr>
<th>Parameter [Refs]</th>
<th>Reason</th>
<th>Procedure / Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectrometer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wavelength</td>
<td></td>
<td></td>
</tr>
<tr>
<td>accuracy</td>
<td>[14, 15, 16, 17, 18, 19, 20]</td>
<td>Important for accuracy of results and comparability when transferring methods between systems. This can be determined by comparing the measured absorbance maxima with the absorbance maxima of a CRM (e.g. holmium perchlorate solution or holmium oxide filter). These are available in limited quantities as ‘Primary’ materials direct from National Measurement Institutes, and include a table of wavelengths and acceptable tolerances. ‘Secondary’ materials with well established traceability, and acceptable uncertainty values on the calibration values, are available from a variety of sources. However, the quality of the chain of traceability is likely to vary from supplier to supplier and should always be established. Other ways to verify accuracy include use of lines from the deuterium lamp (656.1 and 486.0 nm), low pressure mercury lamp (its UV lines are considered as physical reference values, quoted to 0.01 nm e.g. 253.65 nm), Xenon lamps (these are increasingly popular as they may be used right across the normal working range), and various standard solutions at additional wavelengths in the ultraviolet and visible regions. Care should be taken with small low-pressure mercury lamps - if the optical aperture is not completely filled a slight wavelength shift will result. Where wavelength is set manually check whether there is a difference in setting the wavelength either from higher wavelength or lower wavelength. Calibration of diode arrays is ideally done using several sources instead of just one.</td>
</tr>
<tr>
<td>Wavelength precision [18]</td>
<td>“play” or wear in wavelength-drive mechanism can affect precision.</td>
<td>For mechanically set wavelengths evaluate difference from setting the wavelength either from higher wavelength or lower wavelength.</td>
</tr>
<tr>
<td>Wavelength linearity</td>
<td>Obtained from checking accuracy at a number of isolated points across the range. It is dangerous to try to extrapolate the linearity beyond the highest and lowest measured wavelengths.</td>
<td></td>
</tr>
<tr>
<td>Photometric accuracy [15, 16, 17, 18, 21]</td>
<td>Important for accuracy of results and comparability when transferring methods between systems. This can be determined by comparing the measured absorbance value with the absorbance value of a CRM (e.g. Neutral Density glasses or solutions of high purity compound/mixtures). These are available in limited quantities as ‘Primary’ materials direct from National Measurement Institutes, or as ‘Secondary’ materials. The latter, available from a variety of sources, usually have well established traceability, and acceptable uncertainty values on the calibration values. However, the quality of the chain of traceability may vary from supplier to supplier and should always be established. In addition to the above, metal-on-quartz filters are available – however these materials essentially work on reflection, and may not be suitable for use on all types of spectrometer.</td>
<td></td>
</tr>
</tbody>
</table>
### Table 3 (continued) - Operational Qualification of UV-Vis Instruments

<table>
<thead>
<tr>
<th>Parameter [Refs]</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Spectrometer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Photometric linearity</td>
<td>Measurement made at a number of nominal absorbance or transmittance values provide a check on photometric linearity. Extrapolation beyond the highest standard is inadvisable. Repeatability of absorbance is obtained when the sample is removed then remeasured several times.</td>
<td></td>
</tr>
<tr>
<td>Photometric precision [17, 18]</td>
<td>Important for accuracy of results and comparability when transferring methods between systems.</td>
<td>Can be estimated using either; the width at ‘half-peak height’ of an emission line e.g. deuterium line at 656.1 nm, or a suitable solvent/vapour spectrum that is resolution dependent, e.g. benzene vapour, or 0.020% v/v solution of toluene in hexane. Also can use the peak width at half height of a number of the lines in the spectrum of a mercury lamp. Care should be taken with small low-pressure mercury lamps - if the optical aperture is not completely filled a slight wavelength shift will result.</td>
</tr>
<tr>
<td><strong>Resolution</strong> [15, 22, 23]</td>
<td>Important for accuracy of results and comparability when transferring methods between systems. Increasing stray light may be symptomatic of a failing source or contaminated optics. Stray light will influence the photometric accuracy particularly at higher absorbance.</td>
<td>Can be detected using solution/solvent cut-off filters. The use of filters, solutions (of various salts) and solvents covering the range 165 - 385 nm are fully documented by the American Society for Testing and Materials (ASTM). Stray light is a function of the sample: the measurement of x % stray light with a cut-off filter does not mean that x % will again be present when a different absorber is in the beam. It is better to regard the filter method as one that detects stray light rather than measures it. Always state the method of measurement used. The design of diode-arrays make them particularly susceptible to stray light.</td>
</tr>
<tr>
<td><strong>Stray light</strong> [14, 15, 16, 19, 20, 23, 24, 25]</td>
<td>Important for accuracy of results and comparability when transferring methods between systems. Increasing stray light may be symptomatic of a failing source or contaminated optics.</td>
<td>Can be detected using solution/solvent cut-off filters. The use of filters, solutions (of various salts) and solvents covering the range 165 - 385 nm are fully documented by the American Society for Testing and Materials (ASTM). Stray light is a function of the sample: the measurement of x % stray light with a cut-off filter does not mean that x % will again be present when a different absorber is in the beam. It is better to regard the filter method as one that detects stray light rather than measures it. Always state the method of measurement used. The design of diode-arrays make them particularly susceptible to stray light.</td>
</tr>
<tr>
<td><strong>Photometric drift</strong></td>
<td>Important for sensitivity and limit of detection.</td>
<td>Can be determined, after instrument warm-up, from the slope of the amplitude of random variations in the detector’s signal over a period of time longer than the sample measuring time.</td>
</tr>
<tr>
<td><strong>Noise</strong> [26]</td>
<td>Important for sensitivity and limit of detection. A worsening signal to noise ratio is symptomatic of a failing source or misaligned optics.</td>
<td>Can be determined from the amplitude of random variations in the detector’s signal over time using an in-built algorithm. The method of measurement must be specified, e.g. peak to peak or RMS.</td>
</tr>
<tr>
<td><strong>Baseline flatness</strong></td>
<td>Check effectiveness of (automatic) baseline correction.</td>
<td>Zero the instrument on air in the sample path(s), and take measurements across the wavelength band of interest to determine variations from zero.</td>
</tr>
<tr>
<td><strong>Software</strong></td>
<td>Importance for precise and accurate measurement of peaks including partially resolved, broad and asymmetric peaks – does it do its sums properly? Is the software fully and correctly loaded</td>
<td>Can be determined and verified using software packages or using reference materials. Where instruments are designed to accept checking using datasets, these should be used. The extent of checks may need to satisfy regulatory requirements.</td>
</tr>
</tbody>
</table>

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7. Performance Qualification (PQ)

7.1 The aim of PQ is to provide evidence that, following initial assembly, the entire UV-Vis instrument is functioning correctly and within specification and that its performance remains satisfactory during routine use. PQ can, therefore, be considered as having two stages: initial holistic testing to provide evidence that the complete instrument functions correctly; and system suitability checking (SSC) to provide evidence of fitness for purpose and satisfactory performance during actual use. The client should be able to ask the supplier for help in designing their own PQ protocols.

7.2 For convenience, PQ can be considered as having two stages:

- **Initial PQ** - performance testing following OQ to provide evidence that the complete UV-Vis instrument system functions correctly (some suppliers may include this type of holistic testing as part of OQ); and
- **Ongoing PQ** - system suitability checking (SSC) to ensure fitness for purpose and continued satisfactory performance during actual use.

7.3 Following OQ, a supplier would normally be expected to carry out a holistic performance test to verify the correct functioning and performance of the entire instrument system. This ‘Initial PQ’ usually involves measuring a ‘test sample’ under defined operating conditions. This enables the performance of the method to be established over a period of time. It also enables the performance of the instrument to be compared with that of other instruments, either in the same laboratory or elsewhere. As such, this provides evidence that the instrument is functioning not only correctly, but that its performance is also predictable, comparable and within specification. Typical parameters verified during PQ are summarised in Table 4.

7.4 However, whilst this type of holistic testing provides valuable evidence of satisfactory performance under one particular set of conditions, the actual conditions or range of conditions under which an instrument is normally used may be different. During normal routine use it is also highly likely that the performance of an UV-Vis instrument will change over time. Gradual deterioration in performance may result from contamination and normal wear of parts (e.g. contamination of mirrors, wear to mechanical wavelength drive, or loss of intensity from a source). There may also be more sudden changes in performance due to failure of the instrument or one of its components.

7.5 The user must, therefore, carry out further checks and tests to demonstrate system suitability and satisfactory instrumental performance before and during use. The user should establish appropriate procedures to monitor key performance characteristics and set warning and action thresholds outside which the instrument’s performance is deemed to be no longer acceptable for use (e.g. when the response to a CRM is not as expected). These checks and tests need not be burdensome and can be built into system suitability checking and analytical quality control (AQC). They may need to be established for a variety of conditions.

7.6 For example, prior to performing a fixed wavelength measurement, absorbance linearity should be assessed by calibrating the instrument with, e.g. a series of neutral density filters, covering the range of anticipated results, plus a suitable safety margin (typically a further 20%). This type of calibration should be performed before sample analysis or at an interval specified in a
standard operating procedure, the frequency of which should, as a minimum, be based on the period over which the instrument has previously been found to remain within calibration. The precision should be determined from the coefficient of variation (CV) of responses to replicate measurements of a CRM. Acceptable precision is often defined in methods as part of system suitability requirements but, as a rule of thumb, CVs greater than, e.g. 1% are generally unacceptable. During use, a control sample should be analysed at regular intervals to confirm that the instrument remains within calibration.

7.7 SSC can also provide an indication of which parts of the measurement system are not performing satisfactorily. Using a variety of tests may be beneficial for tracing faults when they occur.

7.8 For routine use, the most important parameters are wavelength reproducibility, photometric reproducibility and photometric linearity. Calibration under the same environmental conditions as used for samples usually compensates for temperature effects on wavelength and photometric inaccuracies.
<table>
<thead>
<tr>
<th>Parameter [Refs]</th>
<th>Reason</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Spectrometer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wavelength calibration [14, 15, 16, 17, 18, 19, 20]</td>
<td>Critical to accuracy of results</td>
<td>Can be determined using only two calibration wavelengths, preferably bracketing the analytical wavelength.</td>
</tr>
<tr>
<td>Photometric accuracy [15, 16, 17, 18]</td>
<td>Critical to accuracy of results</td>
<td>Can be determined for particular absorbance at particular wavelengths using calibrated filters or cuvettes filled with standard solutions.</td>
</tr>
<tr>
<td>Linearity of photometric response [26]</td>
<td>Critical to accuracy of results.</td>
<td>Can be determined by checking the accuracy of a number of nominal absorbances across the desired absorbance range. Extrapolation beyond highest standard is inadvisable.</td>
</tr>
<tr>
<td>Signal to noise ratio</td>
<td>Important for sensitivity and limit of detection.</td>
<td>Can be determined from the response of a detector to a dilute standard solution and/or a blank.</td>
</tr>
<tr>
<td>Stray light [19, 20]</td>
<td>Important measure of “health” of whole system.</td>
<td>Record uncorrected spectrum in single beam mode for double beam instruments or with baseline correction switched off for single beam instruments.</td>
</tr>
<tr>
<td><strong>Software</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accuracy and precision, derivatives [9, 10, 11, 15, 20, 26]</td>
<td>Importance for precise and accurate measurement of peaks including partially resolved, broad and asymmetric peaks – does it do its sums properly? Is the software fully and correctly loaded? Does manipulation and storage corrupt the raw data?</td>
<td>Can be determined and verified using software packages or using reference materials. Where instruments are designed to accept checking using datasets, these should be used. The extent of checks may need to satisfy regulatory requirements.</td>
</tr>
<tr>
<td><strong>Absorption Cells</strong> [15, 18]</td>
<td>Important for accuracy and precision of results, checks that the optical faces of the cell are parallel.</td>
<td>Can be determined by filling the cell with water, measuring at required wavelength(s), using air as the reference and repeating the process after rotating the cell through 180°.</td>
</tr>
</tbody>
</table>
8. Bibliography


7. Various NIST Special Publication and materials in the program 260-XX, SRMs 930, 935, 1930 and 2034.


9. References


   *This standard is in the process of revision and is likely to be reissued as BS EN ISO 9001:2000. Its relevance to equipment qualification is likely to remain unchanged.*


   Note that national regulations may contain requirements over and above those of the OECD Principles, *e.g.* see reference 6 below.


Optical Radiation Measurement (ORM) Newsletter, #9, Spring 2000, National Physical Laboratory, Teddington, UK.

A Guide to the Use and Calibration of Detector Based Array Equipment, A/1482/00/WP700/2, SIRA/NPL, Sira Electro-Optics Ltd, Chislehurst, UK.


