SPOTLIGHT feature

Reagents, Reference Materials & Laboratory Chemicals

UV-Vis: 5 steps to Pharmacopoeia compliance

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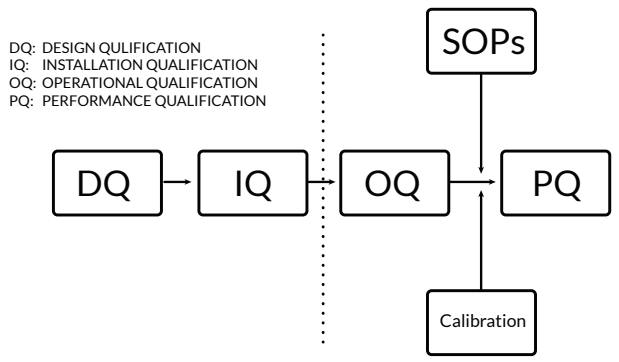
'UV-Vis', UV-Visible spectro(photo)metry, is one of the most widely used instrumental techniques in pharmaceutical analysis; the Unites States Pharmacopeia contains no less than 155 monographs describing UV-vis methods. Instrument qualification, the process of demonstrating that an instrument can perform the required analysis, is now an integral part of any laboratory quality regime. Recent changes in the pharmacopoeias have made compliance more complicated, but still achievable by following a few simple steps.

Analytical Instrument Qualification (AIQ)

USP guidance document <1058> describes the four stages of AIQ: design qualification (DQ), installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ). Good quality control also requires that documented Standard Operating Procedures (SOPs) are used and that instruments are regularly calibrated.



The four stages of Analytical Instrument Qualification (AIQ)

DQ - Design Qualification defines the operational specifications of the instrument. Many users would see this as the responsibility of the instrument manufacturer, but as it is the application that determines the performance required, onus is on the user to select an instrument capable of performing to the necessary standard and consequently 'fit-for-purpose'. The recent revision of USP <857> includes metrics to assist this selection process. Careful selection can also avoid the purchase of over-specified and hence expensive instrumentation!

IQ - Installation Qualification establishes that an instrument is properly installed and works to the manufacturer's specification.

OQ –Operational Qualification demonstrates that the instrument is suitable for the intended use and analytical procedures for which it is to be used. It is not just that it performs to specification! This is usually accomplished by the measurement of recognised calibration standards with accurately known properties. It is the choice of these standards that the recent pharmacopoeia changes have made more complicated.

PQ – Performance Qualification demonstrates on an ongoing basis that the instrument continues to perform and that it can produce test results of the required accuracy and precision. While the former can be tested using the same calibration standards used for OQ, the latter could involve the analysis of standard samples of the actual analyte.

The five steps to compliance

1. Identify the standards that you need to comply with (e.g. European Pharmacopoeia, US Pharmacopeia)

2. Select the monographs describing the analyses you wish to perform.

3. Confirm that the specifications of the available instruments meet the requirements of the monograph(s) or, if the monographs do not state specific instrument performance limits, the generic criteria given in the pharmacopoeias. If selecting a new instrument, this is the user's DQ process.

4. Identify the appropriate wavelength and photometric (absorbance) ranges over which you will be working.

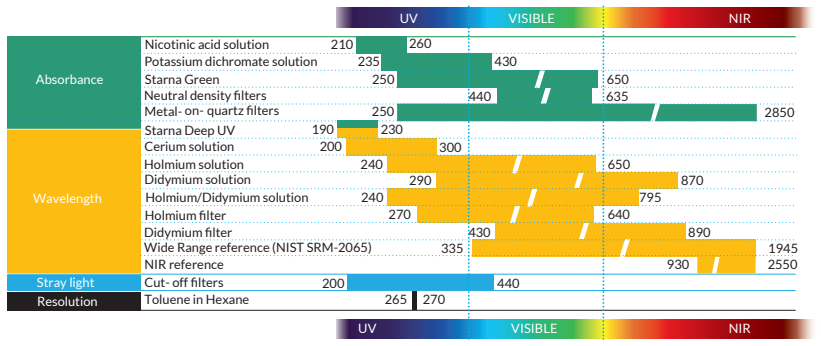
5. Select appropriate reference materials from a properly accredited supplier

Qualification – parameter ranges

Earlier versions of the pharmacopoeias described a limited set of generic tests to qualify an instrument for wavelength, absorbance, stray light and resolution (spectral bandwidth) – in some cases one test per parameter. If the instrument passed these tests, in could be described as 'pharmacopoeia compliant'. The same parameters must still be qualified, but now users must demonstrate 'fitness for purpose', i.e. that the instrument has the performance to perform the analysis to the required accuracy and precision. The qualification measurements must therefore be made at parameter values that match, as closely as possible, those used in the analysis. It is also recommended that the values of the references used for qualification should 'bracket' the values expected in the analysis. Two references at the extreme ends of the parameter ranges could not be said to bracket the analytical values, so if a wide variety of analyses is to be carried out, several references will be needed to cover the range of parameter values involved. To facilitate this, several new reference materials are cited in both standards, all of which are commercially available as Certified Reference Materials (CRMs). Both EP and USP allow the use of CRMs, indeed the USP strongly advocates their use in preference to laboratory-prepared references.

Reference material selection

The next step, then, is to identify the analytical wavelengths to be used and the absorbance values to be expected. The chart below gives an indication of the wavelength ranges of various commercially available CRMs for the four usually qualified parameters.

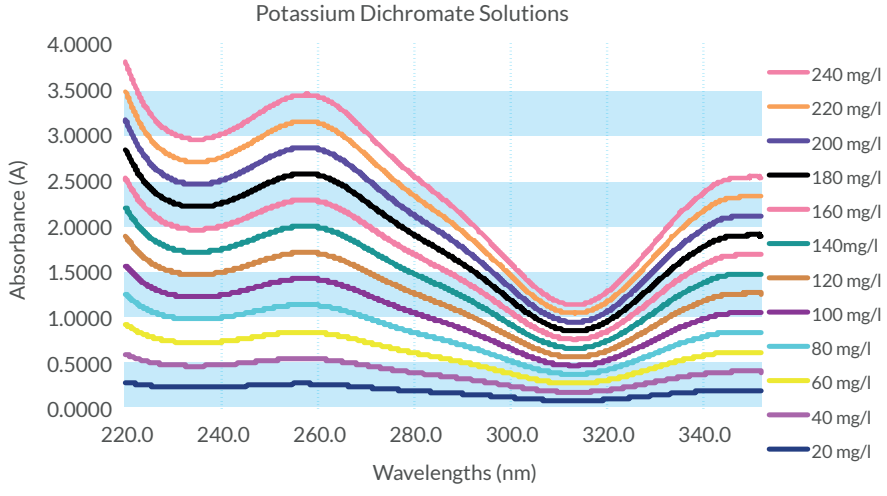


Wavelength ranges of various commercially available CRMs

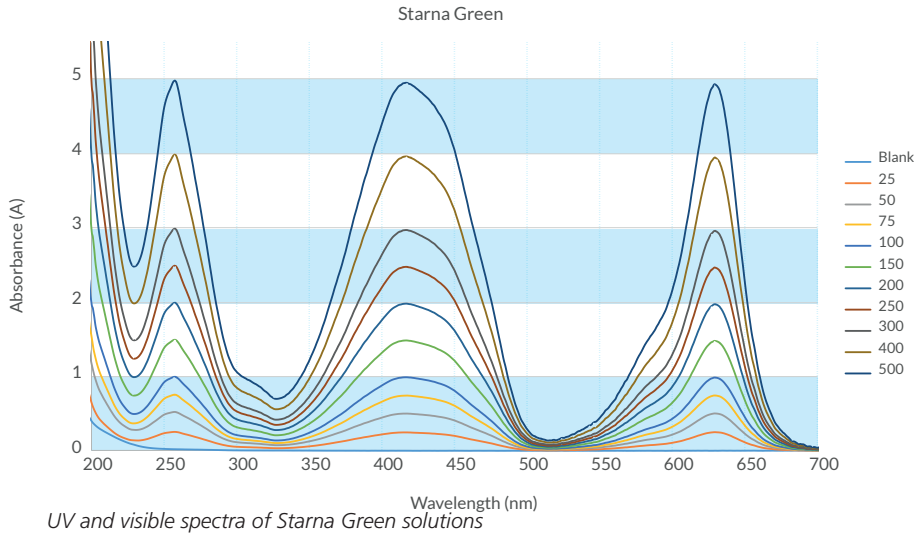
Choosing wavelength CRMs is relatively straightforward as most of them have several certified peak values over their working ranges. Absorbance CRMs require a little more thought. In the far UV, between 210 and 250 nm, nicotinic acid is the usual recommendation, but Starna Scientific's 'Deep UV' reference allows qualification down to 190 nm. At higher UV wavelengths there is more choice: the very well established potassium dichromate, the proprietary Starna Green CRM and metal-on-quartz filters. Potassium dichromate needs no introduction, but Starna Green has peaks over a wider wavelength range so may prove more generally applicable. See spectra on next page.

Metal-on-quartz filters look attractive, as they cover wavelengths from 250 nm to the near infrared, but they work partly by reflection, so stray reflections within the sample compartment could affect the measurement accuracy. Potential users should contact the manufacturer of their instrument to check its compatibility with these filters.

For stray light qualification, the EP formerly named just one stray light reference, potassium chloride solution, but both standards now list several references covering wavelengths from 190 nm to 400 nm and again a choice should be made to bracket the analytical wavelength(s).



UV spectra of potassium dichromate solutions



UV and visible spectra of Starna Green solutions

Selecting a reference material supplier

The choice of CRM supplier is as important as the choice of CRM. A filter with a calibration certificate is not necessarily a CRM! According to ISO, the International Standards Organisation, a CRM supplier should be accredited to ISO 17034:2016: General requirements for the competence of reference material producers. Another frequently cited standard is ISO/IEC 17025:2017: General requirements for the competence of testing and calibration laboratories. A fully accredited CRM supplier should be accredited to both and in any case, a proposed supplier's Schedule of Accreditation should be checked to confirm that it includes the reference material to be purchased – it may not!

Conclusions

Pharmacopoeia compliance in UV-Visible spectrophotometry can be readily achieved by following a few basic steps and selecting reference materials from a properly accredited supplier.