LC/UV-DAD FOR IDENTIFICATION TESTING IN BP MONOGRAPHS

We are seeking views from stakeholders on a proposal to include LC/UV-DAD (Diode Array Detection), also known as a photo-diode array (PDA) detection, as a routine identification test option in BP monographs.

Background

BP monographs are designed for products that are manufactured within the quality framework for medicinal products. When applied within this framework, the identification test (or tests) in the monograph is intended to confirm that the drug product contains the drug substance on the label, or that a drug substance is what it claims to be.

The minimum number of tests to provide assurance of identity are used; for this reason, IR is the preferred method, if suitable, as the resulting spectra are highly discriminatory. If an IR test is not suitable, then a combination of less discriminatory tests is used; for example, a chromatographic test together with UV spectrophotometric method or a combination of chromatographic tests where the mechanisms of separation are different.

The individual aspects of LC/UV-DAD are already routinely applied in compendial methods for identification. UV-DAD can capture the spectrum of absorbance across the whole UV range of the detector, instead of absorbance at a specified wavelength or wavelengths, for components eluting from the LC column. The output of LC/UV-DAD is comparable to the combined results of light absorbance and peak comparison pair of identification tests in current published monographs, for example in the BP monograph for Furosemide Injection.

Proposed change

We are proposing that LC/UV-DAD is used as one of the routine identification tests in BP finished product monographs; considered as a potential test option alongside IR, TLC, UV spectrophotometry and chromatographic peak comparison tests. IR spectra are more discriminatory than UV spectra and therefore IR will remain the identification of choice for BP monographs. The ability of LC/UV-DAD to separate components in a mixture means this technique is often suitable where IR is not. This test is most likely to appear in monographs for more complex formulations (e.g. multi-active preparations and oral solutions/ suspensions) and low strength products.

Reasons for change

- The BP have received several monograph development method submissions from different stakeholders which use LC/UV-DAD as an identification test.
- This technology is well established, understood and accepted by industry and regulators.
- ICH guidelines recognised the use of diode-array detectors to assess peak purity in ICH Q2 (R1), Validation of Analytical Procedures: Methodology in 1996 and section 3.2.2 (New Drug Products, Identification) of ICH Q6A.
- The component functions of this technique (peak comparison to a standard in LC assay methods and UV light absorbance spectral comparison) are already used as compendial identification methods.

We anticipate the following benefits to BP users through the adoption of this test for identification purposes:

- Simpler analysis and greater efficiency when carrying out identification testing of complex formulations and low strength products;
- Improved identification specificity for some complex formulations/low strength products;
- Alignment with industry practice, registered methods and regulatory expectations.

Planned adoption in the BP

The target adoption of LC/UV-DAD for identification tests is from the BP 2022 onwards, subject to the comments received in response to this consultation and endorsement of the recommendation by BP Commission.

The separate principles (LC and UV) are described in Appendix II and III of the BP and due to the maturity of this technology and ease of use/interpretation of results, no additional guidance has been drafted for inclusion in the Supplementary Chapters. Draft wording to show how LC/UV-DAD might be included in monographs can be found in the box below.

IDENTIFICATION
In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210-400 nm:

the UV spectrum of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

In addition to this more general consultation, BP users will have the opportunity to comment on the specific monographs where a LC/UV-DAD identification test is proposed, prior to publication of the new or revised monograph(s). In this draft monograph review period (1 July – 30 September 2020), LC/UV-DAD identification tests are proposed for:

- Metformin and Sitagliptin Tablets
- Metformin and Sitagliptin Prolonged-release Tablets

- Clenbuterol Granules (BP Vet)
- Clenbuterol Oral Solution (BP Vet)

Consultation questions

Your comments are welcomed on the following questions, along with any other comments that you feel are relevant to this consultation:

1. Do you support the proposal to adopt LC/UV-DAD as one of the routine identification tests in BP finished product monographs?

2. What benefits and challenges would you experience if LC/UV-DAD is introduced into BP monographs for identification testing?

3. What could the BP do to mitigate any challenges? For example, by providing additional guidance or adjusting implementation timings.

How to respond

Please send your comments by email to bpcom@mhra.gov.uk with the subject 'LC/UV-DAD for identification'.

Please tell us a little about who you are, so that we can put your comments in to context:

Job title:
Company / Organisation:
Sector: Industry / Regulator / Academia
Industry sub-sectors: Innovator / Generics / Contract Organisation / Trade Association
QC / QA / Compendial Affairs/ Regulatory Affairs / R&D

The deadline for comments is 30 September 2020.

Outcomes and feedback

Following a review of the stakeholder comments we receive and discussion by the BP Commission, the outcome of the consultation will be published on the BP website. You can subscribe to email alerts from the BP to receive updates on our activities.