Change proposal response: LC/UV-DAD for identification testing in BP monographs

Introduction

The BP wishes to thank all stakeholders for contributing views on the change proposal. The continued cooperation and participation of our stakeholders ensures that the development and improvement of our monographs supports the needs of all users, and that we continue to maintain robust, high quality standards for pharmaceutical substances and medicinal products in the interest of protecting public health.

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1. Report summary

The BP sought 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. The change proposal acknowledged a significant increase in LC/UV-DAD identification test proposals submitted to the BP, the adoption of LC/UV-DAD for identification in other compendia, the maturity of the technology, and it's acceptance by regulators, industry and recognition in ICH guidelines.

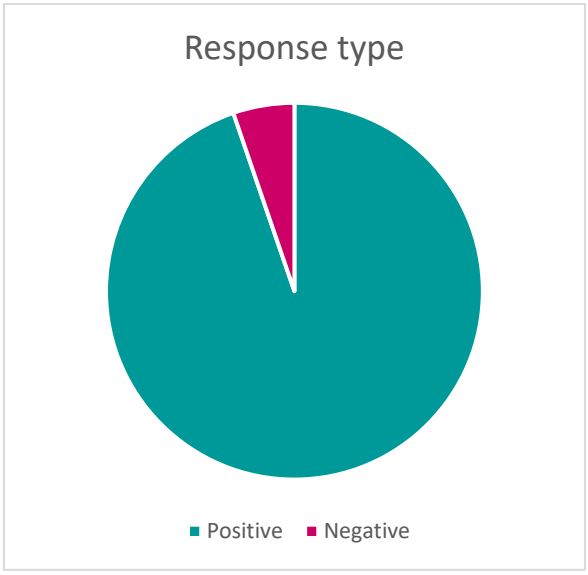
The change proposal was made available on the BP website between 1 July and 30 September 2020. The purpose was to seek views from BP users, understand the benefits and challenges that users may experience if the change was adopted and how we could support users if the change proposal was adopted.

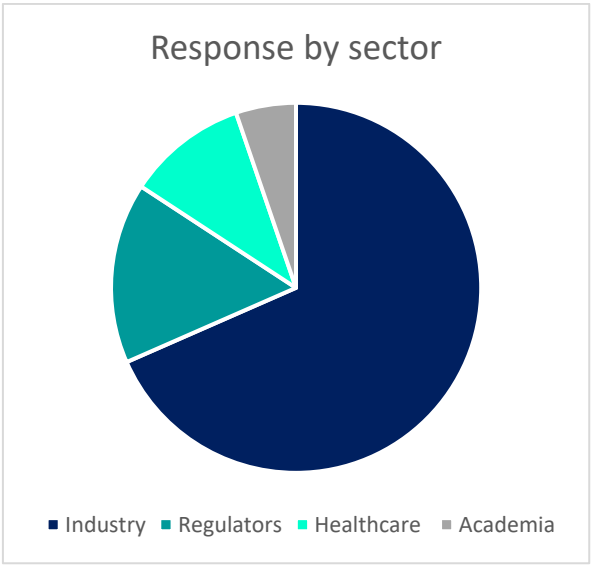
Responses were received from a range of valued stakeholders including pharmaceutical manufacturers; regulatory bodies; academia/researchers; and the healthcare sector. The responses were reviewed by the BP's New Analytical Technologies ad-hoc working group and the recommendations presented to BP Commission in November 2020, as shown below.

The responses we received to this change proposal were broadly in favour of the inclusion of LC/UV-DAD as a routine identification test option for BP monographs. As a result, BP users can expect to see LC/UV-DAD identification tests in some monographs from BP 2022 onwards.

2. Key themes from the responses

2.1 Response overview





The responses demonstrated broad support for introducing this identification test option into BP monographs.

2.2 Benefits identified by BP users

Efficiency Responses highlighted that adopting LC/UV-DAD could reduce the number of methods and equipment types needed to test compliance while maintaining the same level of assurance for product identification. Adopting this as a routine identification test option can offer time and resource efficiencies without compromising the quality of the result.

Widely accepted and adopted Several responses supported adoption of this test as it is a well-established technique, widely accepted by regulators and adopted in industry. It has been found to be robust and reliable in routine use.

Alignment The ease of demonstrating compliance when test methodologies are aligned with registered methods and other compendia was seen as beneficial. LC/UV-DAD identification tests are widely used in approved registered methods and have been adopted in monographs of the European Pharmacopoeia (Ph Eur), United States Pharmacopeia (USP) and International Pharmacopoeia (Ph Int).

2.3 Potential challenges faced by BP users

Equipment upgrade costs Some responses acknowledged that as diode array LC detectors cost more than single wavelength or variable wavelength LC detectors, availability of the instrumentation within laboratories may present a challenge for some stakeholders.

DAD detector sensitivity A few responses noted that DAD detectors are normally less sensitive than single wavelength detectors. Although this would not present an issue for the identification and assay test, it was noted that there may be detector sensitivity challenges where the assay and related substances methods were also harmonised.

2.4 Requested mitigation steps

Time Gradual, informed introduction of LC/UV-DAD identification tests was seen as beneficial to BP users. This would allow sufficient time to carry out any additional activities needed to implement changes, and for phased upgrading of equipment.

User flexibility Alternative test options, particularly where an existing monograph would be revised to include a LC/UV-DAD identification test would be welcomed by users. This would allow for user flexibility in which identification test to use.

Guidance Provision of user guidance was another common theme, although there was no strong trend identified in the type of guidance requested. Example UV spectra, acceptance criteria and specific detector parameters were highlighted in the responses as helpful to users.

3. Outcomes

Proposal adopted Based on the predominantly positive responses to this change proposal, the BP will introduce LC/UV-DAD identification tests into monographs as one potential identification test option; and considered for suitability alongside IR, TLC, UV spectrophotometry and chromatographic peak comparison tests. The ability of LC/UV-DAD to separate components in a mixture means this technique may be suitable where IR is not. This type of test is most likely to, although not exclusively, be included in monographs for more complex formulations, for example, multi-active preparations, oral solutions/suspensions and low strength products.

Gradual introduction A clear message from stakeholders, that gradual introduction of LC/UV-DAD identification tests into monographs will mitigate a potential challenge due to instrument availability, has been heard. IR will remain the identification test of choice in BP monographs. LC/UV-DAD identification tests will be evaluated in the same way as any other analytical test included in BP monographs (see BP Supplementary Chapter III for information on monograph development processes). The potential for impact on other tests will also be considered, such as sensitivity in related substances methods, when the test method is harmonised with the assay. Taking this approach, introduction will be at a measured pace.

Informed introduction Stakeholders will have the opportunity to submit comments on each monograph where LC/UV-DAD is proposed as an identification test. New and revised draft monographs are made available on the BP website for 3 month comment periods each year [1 January to 31 March; 1 April to 30 June; 1 July to 30 September and 1 October to 31 December].

User flexibility Use of alternative methods is permitted by the General Notices of the BP. To support user flexibility, the 2 identification acceptance criteria will be written as discrete requirements to facilitate substitution of one requirement by alternative methodology, should a BP user demonstrate that the substituted method is suitable.

Guidance The UV spectra of the drug substances will be taken into account when LC/UV-DAD is considered as an identification test. The spectra should ideally be reasonably characteristic i.e. show some absorbance at wavelengths > 220 nm. Example UV spectra, where available, will be included in the example test results section of the BP website, which can also be accessed via the 'More resources' section of monographs in the online BP publication.

4. Implementation

The positive response to this change proposal means that LC/UV-DAD identification tests will be considered alongside other identification test options for inclusion in BP monographs. Adoption of the test is subject to the assessment and Expert Advisory Group approval processes applied to all BP monographs. BP users can expect to see LC/UV-DAD identification tests in appearing in some of our monographs from BP 2022 onwards.

We will continue to listen to our stakeholders as this test is introduced to ensure that the mitigation steps we have proposed are working, and that any additional support our users may need is available. Please get in touch with us by email, bpcom@mhra.gov.uk, if you think we can provide further advice or support.