

Change proposal response: Moving to fully numerical limits 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.

This response document contains:

1. Report summary
2. Key themes from the responses
3. Outcomes
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Report summary

The BP sought views from stakeholders on a proposal to begin a process of moving to fully numerical limits in related substances tests, where determined using LC or GC, in monographs developed by the BP for medicinal substances and products. The change proposal recognised that alignment with ICH Q3A(R2) and Q3B(R2) guidance to present related substances results numerically would be beneficial for BP users.

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.

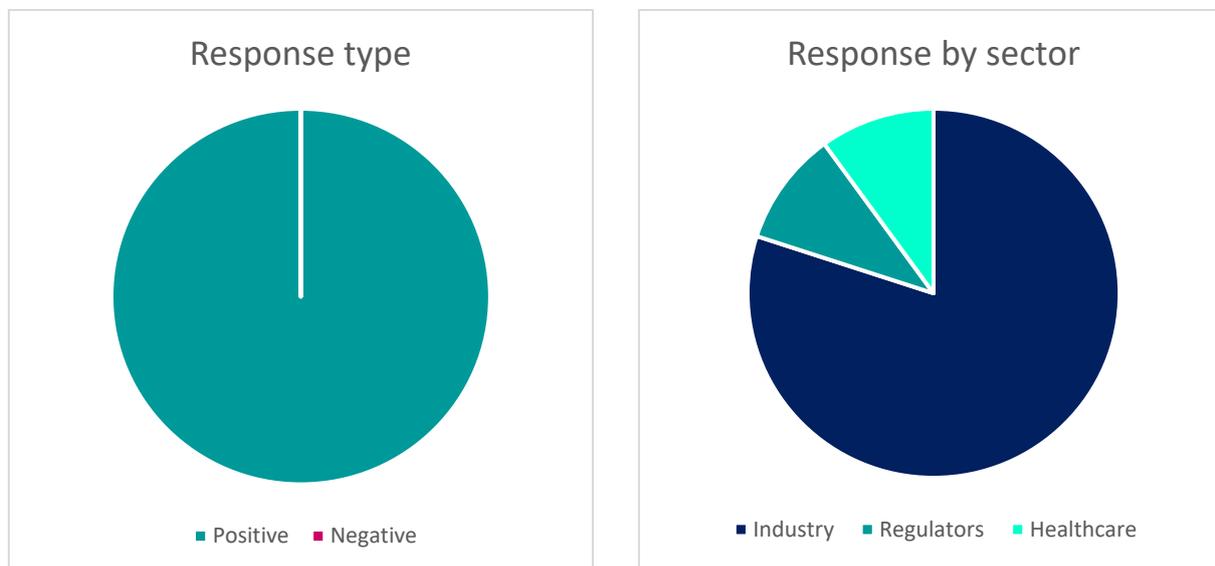
Responses were received from a range of important BP stakeholders including pharmaceutical manufacturers, regulatory bodies and the healthcare sector. The responses were reviewed and presented to BP Commission in November 2020, as shown below.



The responses we received to this change proposal were unanimously in favour of the move to fully numerical limits. As a result, BP users can expect to see these introduced in monographs from BP 2023 onwards.

1. Key themes from the responses

1.1 Response overview



The responses from stakeholders fully supported the implementation of fully numerical related substances limits in BP monographs.

1.2 Benefits identified by BP users

Easier adoption of BP methods Stakeholders told us that numerical results allow them to monitor trends across batches, so adoption of numerical limits in BP tests would make it easier to use BP methods for routine impurity testing. BP users will also be able to see a clear indication of the validated range, making it easier to identify verification and/or additional validation requirements that are needed to adopt the method for routine use for their products.

Alignment Stakeholders told us that introducing numerical limits in BP monographs would be aligned with their current practices. Therefore, that this change would facilitate transfer and comparison of specifications established under ICH and allow easier determination of compliance with the BP. Alignment with other compendia was also seen as beneficial.

Clarity and transparency Several stakeholders highlighted that the introduction of numerical limits would improve the clarity and transparency of BP monographs, making the limits easier to understand for regulatory functions as well as analysts.

1.3 Potential challenges faced by BP users

Speed of implementation Some responses highlighted that it could be challenging if a large number of monographs were revised to introduce this change concurrently. This was due to additional activities that would be needed to review and implement any changes required.

1.4 Requested mitigation steps

Guidance Stakeholders asked for information and guidance to support this change, ranging from wider communication of the background to the change and implementation time, to providing clearer guidance on what verification should be carried out before performing a BP related substances method and how to calculate results.

Time Gradual, informed introduction of numerical limits was seen as beneficial to BP users. This would allow time for BP users to carry out any additional activities needed to ensure product compliance was maintained.

2. Outcomes

Proposal adopted Based on the positive response to this change proposal, the BP will introduce fully numerical limits into related substances and individual impurities tests in monographs from BP 2023 onwards. Stakeholders said that, as this change would align with the approach already taken by most manufacturers, this should not present a significant challenge to them.

Gradual introduction A clear message from stakeholders, that gradual introduction of fully numerical limits into related substances tests would mitigate a potential challenge due to a change in compliance checking activity, has been heard. Numerical limits will be introduced in a phased approach to individual monographs over time. Numerical limits will only be introduced where appropriate data is available and is reviewed by BP Expert Advisory Groups.

Informed introduction Stakeholders will have the opportunity to submit comments on each monograph where quantitative limits are introduced. 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].

Guidance Additional guidance will be included in the Supplementary Chapters of the BP 2023 to support BP users as this change is introduced into monographs. The '[How to use the BP](#)' guide will also be updated to reflect the change in approach to related substances limits.

3. Implementation

The changes will be introduced on a gradual basis into new and revised monographs, where data supporting the change is available. Monographs where this change is being introduced will be available on the BP website for comment prior to publication in the BP. BP users can expect to see fully numerical limits introduced into BP related substances tests from BP 2023 onwards.

Additional guidance for BP users will be provided in BP 2023 Supplementary Chapters and a revision of the 'How to use the BP guide'.

We will continue to listen to our stakeholders as this change 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.