Safeguarding public health

MHRA

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18 February 2013

THE UK GOVERNMENT'S RESPONSE TO THE EUROPEAN COMMISSION PCPAES/12/01 – PUBLIC CONSULTATION ON PAES

Dear Sir / Madam,

Please find attached the MHRA's response to the European Commission's delegated act on post-authorisation efficacy studies.

Yours sincerely,

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Head of EU, International and Strategy

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MHRA

THE UK GOVERNMENT'S RESPONSE TO DELEGATED ACT ON POST-AUTHORISATION EFFICACY STUDIES

Consultation item No 1: Do you think that a delegated act on the situations in which a post-authorisation efficacy study may be required will be of added value and that the Commission should consider bringing forward a draft delegated act? Please provide reasons for your opinion.

The UK Government considers that a document that provides clear regulatory and scientific guidance on the circumstances of when a PAES maybe required will be beneficial to both regulators and industry. However, it is considered that the scientific and methodological aspects of the proposed act should be addressed more fully in separate guidance documents drafted from the relevant EMA committees.

Two approaches to PAES are noted;
1. 'enable the assessment of efficacy of medicinal products for human use in everyday medical practice / where concerns relating to some aspects of the efficacy of the medicinal product are identified and can be resolved only after the medicinal product has been marketed'
2. 'when the understanding of the disease or the clinical methodology indicate that previous efficacy evaluations might have to be revised significantly'.

More clarity regarding the specific circumstances of when PAES may be required under each approach would be helpful.

Consultation item No 2: Do you have any comments on the above? Do you agree that generally speaking post-authorisation efficacy studies should focus on generating efficacy data?

We agree PAES should have a primary focus on generating efficacy data (efficacy includes whether a medicinal product is effective in clinical practice). PAES should not lead to the premature granting of marketing authorisations. We support the tone of the paper that randomised trials represent the highest standards of evidence for treatment comparisons (it is also true that they are not always feasible).

There appears to be an explicit link in the document between PAES, the collection of real life data and reimbursement decisions. Reimbursement decisions are not relevant to medicines legislation and the considerations are outside the scope of the proposed delegated act.

Consultation item No 3: Please comment on the seven different situations described above. Do you agree that in these situations, a competent authority may ask for a post authorisation efficacy study? Are there any other situations not covered by points 5.1 to 5.7 in which it would also be justified to oblige a marketing authorisation holder to conduct an efficacy study? If this is the case, could you please elaborate on these situations and, if possible, give specific examples to underpin the need?

There is a general support for the situations described in points 5.1 to 5.7. However, it is recognised that there may be additional circumstances, as yet unforeseen, and a point 5.8 should be included which allows for PAES to be requested on a case by case basis, in light of benefit risk concerns.

In relation to point 5.5, the scope should be broadened to the following: Studies linked to a change in the understanding of the standard of care for the disease and/or the benefit risk of the medicinal product

The circumstances under which it is appropriate to carryout a non-randomised study for any of the situations listed must be carefully considered and should be more explicitly stated. Under 5.1, continuation of an ongoing RCT is not a reflected option. This may be appropriate and highlights the limitations of the paper in terms of the methodological aspects of 'collecting more data', which should be addressed by further guidance from relevant EMA committees.

Consultation item No 4: Do you have any comments on the above?

The scientific and methodological aspects of the proposed act, including comments on Trial Design, should be addressed in separate comprehensive guidance documents, drafted by the relevant EMA committees.

The statement that advances in statistical methods allow the possibility of performing unbiased analysis of data coming from everyday medical practice should be supported by good evidence.

Consultation item No 5: Please feel free to raise any other issues or make any comments which have not been addressed in the consultation items above.

The consultation document highlights the importance of the use of accurate terminology and definitions (for example, the definition of a pragmatic trial).

The concept of a 'large simple trial', maintaining the benefits of randomisation while restricting the inclusion/ exclusion criteria and follow-up to better reflect clinical practice has not be considered. Large simple trials and standard randomised controlled trials have a place in the post-authorisation setting.

The intention of PAES should be clarified in the context of the move towards adaptive licensing.