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European Commission
Directorate-General Health and Consumers
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Re: Nov 2012 Delegated Act on Post-Authorisation Efficacy Studies (Article 10B of Regulation (EC) No 726-2004 and Article 22B of Directive 2001/83/EC)

Dear Sir or Madam:

The following comments are submitted on behalf of Bausch + Lomb. In November 2012, the Commission posted for public consultation a reflection paper on post-authorisation efficacy studies (PAES). The paper notes that these studies are not an entirely new feature however, with the new pharmacovigilance legislation those studies would now be formally recognised. It is clarified that marketing authorisation holders can be obliged to conduct such studies by imposing that obligation as a condition to the marketing authorisation. The Commission posed several questions for input.

Bausch + Lomb is one of the best-known and most respected healthcare companies in the world. Our core businesses include contact lenses and lens care products, ophthalmic surgical devices and instruments, and ophthalmic pharmaceuticals. Founded in 1853, our company is headquartered in Rochester, N.Y., and employs more than 10,000 people worldwide. Our products are available in more than 100 countries including throughout the European Union.

In general, Bausch + Lomb supports the Commission in further exploring the application of a delegated act and appreciates the opportunity to provide the following comments on this reflection paper.

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.

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If the intent of the delegated act is to enhance regulatory clarity[1] and ensure a PAES is not liberally requested, we agree that a delegated act can provide value if criteria are explicitly described and are based on sound scientific rationale and a justified medical need. Bausch + Lomb would be concerned, however if the delegated act was applied too broadly or liberally[2]. For example, if the requirement was applied (1) to all drugs in a class without an examination of the therapeutic class (2) to gather data to explore future uses not claimed in the label or (3) to every new marketing authorization approved for a particular indication.

Bausch + Lomb recommends that a PAES be the exception rather than the norm and be required only to address gaps in knowledge about efficacy in the target population post authorisation or satisfy a specific need to further medical knowledge and improve the use of the drug (e.g., for rare diseases, life-threatening or serious conditions) for which the development program cannot address. The need to conduct additional studies must be well balanced with the need to enhance critical medical knowledge to improve the use of the authorised drug and the timelines/costs for the development of new and innovative therapies[3].

Should the delegated act move forward, Bausch + Lomb requests that in addition to the points noted in the above, the following are also clearly addressed[4].

- Ensuring there is no post-authorisation penalty imposed on pricing/reimbursement and on the clinical positioning of the drug due to a requested PAES.

- Clarify a timeframe for when a PAES may appropriately be requested particularly, if the requirement may potentially be viewed as an "open door" to require these types of studies any time post authorisation[5].

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[1] To enhance critical medical knowledge to improve the use of the drug particularly in rare diseases, life-threatening or serious conditions for which the development program cannot address or to ensure a consistent process to negotiate the need and timing for a PAES

[2] The Regulation (EU) No1235/2010 (4.1.b) states, "to conduct a post-authorisation efficacy study when the understanding of the disease or the clinical methodology indicate that previous efficacy evaluations might have to be revised significantly."

[3] Reference is made to ICH E5, "Requirements for extensive duplication of clinical evaluation for every compound can delay the availability of new therapies and unnecessarily waste drug development resources."

[4] Or appropriately cross-reference to existing guidelines

- Consistent with Regulation (EU) No1235/2010[6] , include a clearly defined process for negotiation if the marketing authorisation holder believes the study may not be necessary or, the timing to conduct the study is not appropriate[7].

Consultation item No 2: Do you have any comments *"efficacy vs. effectiveness"* Do you agree that generally speaking post-authorisation efficacy studies should focus on generating efficacy data?

Generally speaking, the PAES should focus on generating effectiveness data since the knowledge that will be gathered will be more useful to prescribing physicians in a real-life setting. While the reflection paper states that the use of "effectiveness" has been inconsistent in the EU[8], it also states "effectiveness is normally used to describe the benefits of a treatment under real-life conditions…." which is consistent with the effectiveness definition used by the EU High Level Pharmaceutical Forum. Conditions to marketing authorisation may warrant an efficacy study[9] however, information gathered once efficacy has been established is generally in a real-world setting[10].

Consultation item No 3: Referring to the different types of studies, please comment on the seven different situations described ….?

As noted in response to consultation item No. 1, a PAES be the exception rather than the norm and be required only to address gaps in knowledge about efficacy in the target population post authorisation or satisfy a specific need to further medical knowledge and improve the use of the drug (e.g., for rare diseases, life-threatening or serious conditions) for which the development program cannot address. The need to conduct additional studies must be well balanced with the need to enhance critical medical knowledge to improve the use of the authorised

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[5] For example, 5.4 Studies in the context of the European standard of care, particularly if the standard of care is off-label

[6] Regulation (EU) No1235/2010 (prior to 4.2) states, "The imposition … shall be duly justified" and (4.2) "The Agency shall provide the marketing authorisation holder with an opportunity to present written observations within a time limit which shall specify,…."

[7] Page 8 states, "Post-authorisation efficacy studies should only be imposed if the reasonable assumption that the results they produce will help to answer in an objective…"

[8] And, "effectiveness is not directly referred to in the EU pharmaceutical legislation, at least not in the context of the evaluation of the benefits of a medicinal product."

[9] For example, 5.1 Studies aimed at determining clinical outcome following initial assessment based on surrogate endpoints

[10] For example, 5.3 Studies in sub-populations,5.7 Studies in everyday medical practice

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drug and timelines/costs for the development of new and innovative therapies. Given that the most appropriate active comparator might vary from Member State to Member State, safeguards are recommended so that manufacturers would not be expected to undertake multiple trials.

Bausch + Lomb appreciates the opportunity to provide these comments and recommendations.

Sincerely,

Kimberly Belsky
Bausch + Lomb
Executive Director, Policy and Communication
Global Regulatory Affairs – Pharmaceuticals