



INTERNATIONAL GENERIC AND
BIOSIMILAR MEDICINES ASSOCIATION

February 11, 2019

Division of Dockets Management (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061

Re: Docket No. FDA-2011-D-0611; IGBA Comments on FDA’s Questions and Answers on Biosimilar Development and the BPCI Act (Revision 1)

The International Generic and Biosimilar Medicines Association (IGBA) representing member associations from the USA (AAM), Canada (CGPA), South Africa (GBMSA), India (IPA), Jordan (JAPM), Japan (JGA), Europe (Medicines for Europe) and Taiwan (TGPA), as well as associate member associations from Australia (GBMA), Brazil (ProGenericos), Mexico (AMEGI) and Saudi Arabia (NCPI), very much welcomes the U.S. Food and Drug Administration (FDA) prioritizing ongoing efforts to improve the efficiency of the biosimilar and interchangeable product development and approval process as well as highly appreciates the development of new policies to improve the availability, competitiveness and adoption of biosimilars as affordable alternatives to originator (reference) biological products. We thank you for providing us with the opportunity to comment via this consultation and wish to comment on the “Questions and Answers on Biosimilar Development and the BPCI Act (Revision 1)”. We believe that seeking to improve access to quality medicines worldwide and to promote the quality, safety and efficacy of biosimilar medicines is of utmost importance.

IGBA previously submitted a Reflection Paper on the Waiving of Bridging Studies¹ in which we proposed a new international biosimilars framework allowing bridging studies to be waived in specific circumstances based on core scientific and regulatory principles established for current products. To that end, below, please find our specific comments to “Q. 1.8. Can a sponsor use comparative animal or clinical data with a non-U.S.-licensed product to support a demonstration that the proposed product is biosimilar to the reference product? [Updated/Retained in Final December 2018]”:

The updated response to this question nicely lists the relevant considerations for the use of non-U.S.-licensed product, and also includes the concept that a PK bridge can be waived if scientifically justified. However, we interpret the wording of the Q&A in a way that a PK bridge is typically required and represents the norm rather than the exception to justify the use of a non-U.S.-licensed product as the comparator for one or more of the comparative analysis of reference biologic and proposed biosimilar. This notion in the final Q&A to enforce the requirement for a clinical PK bridging study to enable the use of non-U.S.-licensed

¹ IGBA Reflection Paper on waiving bridging studies for biosimilar medicines applications. Submitted to FDA September 2018. Available online at: <https://bit.ly/2I5G7Hi>.





reference product in comparative clinical trials is in conflict with FDA's commitment in the Biosimilar Action Plan² to evaluate ways to facilitate the increased use of non-U.S.-licensed comparator products in certain studies to support an application under section 351(k).

We are concerned that the wording of the Q&A may create a bias of the FDA biosimilar review process towards a default requirement for a PK bridge even in cases where all considerations as listed in the answer of Q.I.8. result in the conclusion that the non-U.S.-licensed is in fact of the same quality and representative of the U.S.-licensed reference product. This requirement therefore adds unnecessary development steps and costs for biosimilar products. We recommend FDA to prospectively work to avoid such a bias so that a PK bridge should become the exception rather than the norm and is conducted only in cases where uncertainties remain after the evaluation of the analytical bridging study and publicly available information. This "exceptional PK bridge" would facilitate the development of lower-cost, safe and effective biosimilars and interchangeable biological products and increase competition and affordability of biological therapeutics consistent with the goals of the BPCIA.

Our prime recommendation is to amend the final Q&A, as proposed below. If this is not possible in the short term, we urge FDA to ensure by internal processes that a PK bridge is seen as an exceptional requirement in the routine biosimilar review process rather than the norm.

Proposed changes to Q.I.8.:

"However, as a scientific matter, analytical studies and **in exceptional cases** a ~~at least one~~ clinical pharmacokinetic (PK) study ~~and, which may, if appropriate, at least one~~ **include** pharmacodynamic (PD) **endpoints** study, intended to support a demonstration of biosimilarity must include an adequate comparison of the proposed biosimilar product directly with the U.S.-licensed reference unless it can be scientifically justified that such a study is not needed.

"As a scientific matter, the type of bridging data needed will always include data from analytical studies (e.g., structural and functional data) that directly compare all three products (i.e., the proposed biosimilar product, the U.S.-licensed reference product, and the non-U.S.-licensed comparator product), and ~~is likely to~~ **if absolutely needed**, will also include bridging clinical PK and/or PD study data for all three products."

Thank you for your time and consideration of these comments.

Best,

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About IGBA

The International Generic and Biosimilar Medicines Association (IGBA) was founded to strengthen cooperation between associations representing manufacturers of generic and biosimilar medicines from around the world. The IGBA is at the forefront of preserving sustainable competition within our industry, by stimulating competitiveness and innovation in the pharmaceutical sector; thereby, ensuring millions of patients around the world have access to high quality, pro-competitive medicines. For more details see the IGBA website at: www.igbamedicines.org.

² FDA Biosimilars Action Plan (July 1, 2018),
<https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM613761.pdf>