Re: *MHRA Guidance on the Licensing of Biosimilar Products*

Dear Sir or Madam,

Thank you for the opportunity to provide comments on the recently published MHRA guidance on the licensing of biosimilar products.

The Alliance for Safe Biologic Medicines (ASBM) is a diverse group of stakeholders including physicians, pharmacists, patients, researchers, and manufacturers of both biologics and biosimilars. ASBM is an organization focused on promoting the use of biologic medicines. However, we believe that the ultimate goal of biosimilar medicines is to find a balance between producing economical drugs for our patients, while actively promoting the paramount importance of patient safety.

Based on this principle, ASBM offers the following comments regarding the totality of evidence required to support a biosimilar designation, interchangeability, and pharmacovigilance.

A. Lack of Requirement for in vivo Studies in Animals

In reference to the relevant content for showing comparability between the biosimilar and the reference product, MHRA has indicated that:

> *No in vivo studies from animals are requested as these are not relevant for showing comparability between a biosimilar candidate and its RP: this includes pharmacodynamic studies, kinetic studies and toxicity studies.*

ASBM believes that results from animal studies are a valuable component of the totality of evidence generated during the development of a biosimilar. Unless there is no animal species that can provide pharmacologically relevant data for the product, results from animal toxicity studies may be used to support the safety evaluation of the proposed biosimilar and more generally to support the demonstration of biosimilarity between the proposed product and the reference product. While animal studies may not be warranted in all circumstances, ASBM believes they are useful when uncertainties remain about the safety of a proposed product following an extensive structural and functional characterization.

B. Changes in Requirement for a Comparative Efficacy Trial in Most Cases

The MHRA guidance has also indicated that:

> *In most cases, a comparative efficacy trial is not considered necessary.*

Given that it is not possible to create a structurally identical copy of a reference product, ASBM believes that a comparative clinical study will generally be warranted to rule out the existence of any clinically meaningful differences between the proposed biosimilar and the reference product. While there are cases in which a comparative efficacy trial is not warranted (i.e., when structure, physicochemical characteristics, and biologic activity can be well characterized and clinically relevant PD parameters are available), we believe this will be a minority of biosimilar products and recommend the language in the guidelines be amended to state,

> *In **some** cases, a comparative efficacy trial is not considered necessary*

C. Traceability

Regarding traceability, MHRA states that:

> *A key requirement for pharmacovigilance of biosimilars is the need to ensure continuous product and batch traceability in clinical use to support detection of any important safety issues that may be product- or batch- specific.*
>
> *Accurate traceability of biosimilars by brand name and batch number must be assured in the post-marketing setting. The importance and method of traceability needs to be highlighted in the product information and on the product packaging or labelling as appropriate.*
>
> *Traceability should be fully integrated in the healthcare settings, for example electronic data recording and record linkage etc.*

ASBM is aligned with MHRA's position on traceability. ASBM believes that the overall goal of post-marketing pharmacovigilance plans is to accurately and promptly trace a patient's adverse event to a particular product, manufacturer and lot number. Proper labeling, product tracking and an operational system of reporting and attributing adverse events are all components of a well-functioning pharmacovigilance program.

D. Interchangeability and Substitution

Regarding interchangeability and substitution, MHRA has stated the following:

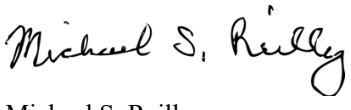
> *Once a biosimilar is authorised, it is considered interchangeable with the RP, which means that a prescriber can choose the biosimilar over the RP (or vice versa) and expect to achieve the same therapeutic effect.*
>
> *The decision rests with the prescriber in consultation with the patient, who needs to be aware of the brand name of the product received.*
>
> *Substitution at the pharmacy level without consulting the prescriber is not permitted for biological medicines, including biosimilars.*

In the US, interchangeable biosimilars have met a higher regulatory standard in that it has been shown they can be safely switched back and forth with the originator product, without any additional risk to the patient. ASBM, and many others in the clinical community, believe that to gain approval as an interchangeable biosimilar, there should be strong scientific and clinical rationale to use the interchangeable biosimilar in all the diseases for which the original biologic is approved.

Around the world, substitution decisions are largely handled at the local government level; in the US, the decision of whether a biosimilar is substitutable is made at the state level. In Canada, this decision is made at the provincial level, while within the European Union, the decision is made by individual Member States. ASBM believes that patients and their physician should remain in control of their treatment decisions, rather than an insurer, government, pharmacy, or other third party. We support MHRA's position on the prohibition of automatic substitution.

Thank you for the opportunity to comment on this important guidance.

Sincerely,



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