

Executive Summary

The first generation of biological drugs, which have introduced many revolutionary treatments to life-threatening and rare illnesses, is currently facing patent expiration. As a result, research-based and generics pharmaceutical companies alike are pursuing the opportunity to develop “generic” substitutes to original biologics, which are also known as biosimilars.

Yet the field of biosimilars presents several important challenges – safety, regulatory, legal and economic – which are the topic of discussion across the globe. Most of these discussions stem from the idea that, unlike the relatively straightforward process of introducing a generic equivalent to an original drug based on a new chemical entity (NCE), the process of introducing a biosimilar to an original biological drug is far more complex.

With this in mind, the purpose of this paper is to examine the various challenges that biosimilars raise, particularly with regards to the regulatory framework, commercial opportunities, intellectual property rights (IPRs) and most importantly of all, to public safety.

The paper examines several discussions related to safety and regulatory issues, including the amount of clinical studies that should be required as part of the testing and approval process, as well as whether the biosimilar should be considered “automatically” interchangeable with the original biologic.

Discussions surrounding the commercial implications of biosimilars are also considered. In particular, given the complexity of biological drugs, which will only continue to grow with the next generation, the paper notes that the existing and future biosimilar players may include both some of the largest generics companies and some research-based companies. Overall, it is suggested that the biologics market may see fewer biosimilar competitors as well as a smaller gap in prices between biosimilars and original biologics.

Furthermore, the paper examines debates surrounding intellectual property (IP) issues, especially concerning patent protection and data exclusivity. Patent-related discussions include the potential for biosimilar companies to “design around” relevant patents of original biologics, with the result that patent protection may not be as robust for biological drugs as they are for NCE-based drugs, as well as the importance of streamlining the resolution of patent disputes, based on the idea that they will become more complicated with biosimilars. Debates related to data exclusivity, which has tended to be a hot topic especially in the US, mainly concern the appropriate length of data exclusivity, as well as whether to afford exclusivity to biosimilar companies, given that they will probably be required to submit their own clinical data.

In the midst of these and other discussions surrounding biosimilars, several countries and regions have created - or are in the process of creating - regulatory pathways that seek to address the various debates. This paper takes four of the most relevant pathways, namely the EU, WHO, Canada and the US (where legislation is still

under way), as case studies and evaluates in particular whether these pathways have resolved the safety and IP dilemmas discussed in the previous section.

With regard to safety issues, the paper finds that submitting the results from at least one or two clinical trials relating to the new biosimilar seems to be the standard among almost all of the cases. With regard to the issue of “interchangeability” (i.e. the possibility of providing the patient with a biosimilar substitute to the original biologic drug), most countries seem to ban this practice altogether (i.e. Germany, Sweden, Spain and the Netherlands). Alternatively, some countries, such as Canada, recommend rigorous scientific and clinical data before the decision is taken.

In summary, the paper presents the following policy considerations for future biosimilar frameworks:

- 1) Legislation should require a baseline scientific comparison of the biosimilar with the original drug.
- 2) Based on the differences identified in the scientific comparison with the original biologic, the legislation should identify the level of clinical data that will be needed to evaluate and approve the biosimilar.
- 3) Legislation should call for post-marketing safety studies in order to monitor any potential differences in safety and efficacy between the biosimilar and original drug that become apparent once a biosimilar enters the market.
- 4) Legislation should define the standard and criteria for interchangeability of the biosimilar with the original drug.
- 5) Finally, legislation should provide sufficient incentives to research-based companies via IP protection. It should ensure that patent protection is not eroded with the entry of biosimilars. If appropriate, the term of data exclusivity may be extended. Furthermore, authorities will need to consider the incentives for biosimilar companies and evaluate whether some amount of data exclusivity for biosimilars will be necessary to attract investment, especially given that the cost will probably be higher than with generic drugs.

The above recommendations should allow more clarity and predictability for those wishing to enter the market as well as providing enhanced scientific rigour, in the interests of patients.