Biosimilars: Pathway to the Marketplace

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February 2008

Published in the 2008 Contact Canada Canadian Biotechnology Guide

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Since many patents for innovative biologics will expire in the next few years, interest in the development of "generic" biologics (more appropriately called "biosimilars") is increasing. Biosimilars are large complex molecules that are not bioequivalent to the innovator products, thus there is need for a legal and regulatory approval framework for these products distinct from the traditional generic approval pathway. It is not possible for biosimilar manufacturers to make identical copies, in part due to different cell lines, manufacturing processes, conditions, materials and formulations as compared to innovator products. As well, animal models are not sufficiently predictive of immunogenicity in humans. Clinical trial data is required for biosimilars though they do rely partly on clinical trial data generated by innovators.

The European Commission ("EC") has approved biosimilars for human growth hormone, epoetin alfa and epoetin zeta. The US FDA has approved a human growth hormone biosimilar. No biosimilars have been approved in Canada.

The EC has established legislation and guidelines on similar biological medicinal products. The guidelines state that "comparability studies are needed to generate evidence substantiating the similar nature, in terms of quality, safety and efficacy, of the new similar biological medicinal product and the chosen reference medicinal product"[1]. The EC's European Medicines Agency (EMEA) also has guidelines directed to quality, non-clinical, and clinical aspects for similar biological medicinal products[2]. The EMEA requires that studies "should demonstrate that there are no meaningful differences between the biosimilar and the biological reference medicines in terms of safety and efficacy"[3].

The US FDA noted that its approval for the human growth hormone biosimilar did not create a pathway for other follow-on products, and that new legislation would be required to create a biosimilar regulatory approval system. The US Senate and House have been drafting bills for approving biosimilar and interchangeable biological products, which include provisions regarding data required to demonstrate biosimilarity, interchangeability, periods of exclusivity and patent resolution. Although efforts are in progress, it is not clear when the US will implement legislation.

Health Canada has not yet publicly announced a legal or regulatory framework for biosimilar approval. In July 2006, Health Canada issued a fact sheet on subsequent entry biologics (SEBs; i.e. biosimilars) which stated that the Biologics and Genetics Therapies Directorate (BGTD) was in the process of developing a framework concerning regulatory, legal and scientific issues. In June 2007, a similar message was reiterated in a meeting between BIOTECanada and BGTD.

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[1] http://www.emea.europa.eu/pdfs/human/biosimilar/043704en.pdf

[2] http://www.emea.europa.eu/pdfs/human/biosimilar/4934805en.pdf;http://www.emea.europa.eu/pdfs/human/biosimilar/4283205en.pdf

[3] http://www.emea.europa.eu/pdfs/human/pcwp/7456206en.pdf

Market entry of biosimilars may provide products at a reduced cost to patients and drug payers. However, the overriding issue of concern is patient safety in using biosimilars. Innovators must also be provided with incentive to continue developing life-saving biologics. Thus, legal and regulatory frameworks need to be instituted to address these issues. The challenge is in drafting legislation that is acceptable to both innovators and biosimilar manufacturers. Given that biosimilars have only recently been approved in Europe, long-term safety data is not yet available, such as information regarding immunogenicity.