

# Biosimilars

## Exploring the history, science, and progress

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**BACKGROUND:** Biosimilars provide opportunities for improving healthcare access and outcomes and reducing overall healthcare costs for patients with cancer.

**OBJECTIVES:** The purpose of this article is to explore the history of biosimilars, regulatory pathways, and barriers to biosimilar approval. This article also aims to describe the patient and clinician barriers to biosimilars use and the progress that has been achieved since the first biosimilar approval in Europe in 2006 and in the United States in 2015.

**METHODS:** A literature search was conducted to retrieve articles that are highly relevant to the history of biosimilars development and regulatory pathways in the United States, Europe, Asia, and Canada. Patient and clinician perspectives on safety issues and concerns regarding immunogenicity and bioequivalence that limit use of biosimilars are also included.

**FINDINGS:** Patient and provider concerns regarding immunologic patient safety issues, such as immunogenicity, lack of comparability, and low biosimilarity, still exist. The clinical safety, efficacy, and tolerability of biosimilars are among the top concerns in patients, prescribers, and clinicians.

### KEYWORDS

biologics; biosimilars; comparability; safety; efficacy; tolerability; immunogenicity

### DIGITAL OBJECT IDENTIFIER

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**ALL BIOSIMILARS ARE BIOLOGICS, WHICH ARE MEDICINES** derived from living systems that may be sourced from nature or produced using recombinant techniques, also known as “genetically engineered” or “biotech” products (McCamish & Woollett, 2012). The recombinant products are the initial candidates for biosimilars in the United States and Europe, and they include simple replacement hormones (e.g., recombinant human insulin, growth hormones) or large complex molecules with extensive post-translational modifications (defined as any alteration that occurs after synthesis of the protein chain) (e.g., monoclonal antibodies [Mabs]) (Goldsmith, Kuhlmann, & Covic, 2007; Thill, 2015). The concept of biosimilars is based on a high level of scientific credibility, the quality of regulatory decision making, and public trust for safety and efficacy (Schiestl, Zabransky, & Sörgel, 2017).

Biologics have revolutionized the treatment and management of many malignant diseases, such as cancer (Atkins, 1997; Carbone, 1990; Fernandes et al., 2018; Holdsworth, Gan, & Kitching, 2016; Nepom, 2002; Nowak, Lake, Kindler, & Robinson, 2002; Rott & Mrowietz, 2005). Biosimilars provide opportunities for improving healthcare access and outcomes and reducing overall healthcare costs (Bridges et al., 2018; McCamish & Woollett, 2012; McCamish, Yoon, & McKay, 2016; Mulcahy, Hlávka, & Case, 2017; Nabhan & Feinberg, 2017; Woollett, 2012). However, several regulatory and cost barriers to biosimilar approval exist, as do patient and clinician barriers to biosimilar use (Beck et al., 2017; Bennett et al., 2014; Jacobs, Singh, Sewell, Al-Sabbagh, & Shane, 2016; Tanabe, Sugimoto, & Fujimoto, 2015; van Overbeeke, De Beleyr, de Hoon, Westhovens, & Huys, 2017).

## Background

### Biologics

Precursors of biologics began in Europe with the work of pioneering scientists in the 1800s. In Germany, Robert Koch investigated and isolated organisms responsible for cholera (Koch, 1884) and tuberculosis (Koch, 1891), and Louis Pasteur developed the first vaccine for fowl against chicken cholera in the latter part of the 19th century (Pasteur, 1881). The United States soon followed the growing science of immunology and biologic therapies, with Theobald Smith and Daniel E. Salmon pioneering heat-killed vaccines against hog cholera (Salmon, 1886). During the 20th century, new vaccines and antitoxins were developed that offered preventive and curative options for some of the most dreaded diseases afflicting mankind, including diphtheria and tetanus (Poland & Barrett, 2009; U.S. Food and Drug Administration [FDA], 2002).

Under the Biologics Control Act of 1902, the United States accelerated what Europe has pioneered, with state and national laboratories initially