9.1 INTRODUCTION

Since the approval of the first biosimilar, Omnitrope, by the European Medical Agency in 2006 (EMA, 2006), biosimilars have been authorized in many jurisdictions, including Australia, Canada, Japan, Korea, the US, and many other countries. Subsequent-entry biologic (SEB) is the Canadian term used for a biosimilar that enters the market subsequent to a Canadian biological drug (the reference product) previously authorized in Canada. For the purpose of marketing authorization, a biosimilar relies in part on prior information in the public domain regarding safety and efficacy deemed relevant due to the demonstration of similarity to the reference biologic drug (RBD).

Similarity to the RBD in terms of quality characteristics, biological activity, toxicity, and clinical safety and efficacy can be demonstrated through comprehensive comparability exercises between the biosimilar and the RBD. The side-by-side structural and functional characterization of the biosimilar and the RBD to demonstrate similarity is the foundation of the biosimilar development program. Extrapolation of indications is an established scientific and regulatory process adopted by many regulatory agencies based on clinical data generated in one or two indications (Health Canada, 2010; EMA, 2015; FDA, 2015). Before extrapolation can be considered, biosimilar sponsors must present convincing and compelling similarity data to regulatory agencies. The totality of evidence collected from all comparative studies ultimately determines the marketing authorization of a biosimilar and its authorized indications.

The first biosimilar authorized in Canada was Sandoz's biosimilar growth hormone, Omnitrope, in 2009 (Klein, 2011). To date, Health Canada has issued Notices of Compliance (NOC) for three biosimilars within the product classes of human growth hormone and tumor necrosis factor (TNF)-inhibitor, for use in Canada (see Table 9.1).

TABLE 9.1
Health Canada Authorized Subsequent Entry Biologics/Biosimilars

Product Name	Active Substance	Therapeutic Area	Authorization Date
Omnitrope	Somatropin	Growth hormone deficiency in adults and children	April 20, 2009
Remsima	Infliximab	Ankylosing spondylitis Psoriatic arthritis Psoriasis Rheumatoid arthritis	January 15, 2014
Inflectra	Infliximab	Ankylosing spondylitis Psoriatic arthritis Psoriasis Rheumatoid arthritis	January 15, 2014
Omnitrope	Somatropin	Small for gestational age Small for gestational age Turner syndrome	May 8, 2015