Chapter 2 The biosimilar landscape

In the landscape of extinction, precision is next to godliness.
Samuel Beckett

2.1 Background

Biopharmaceutical products constitute the newest category of products that will soon expand to constitute more than two-thirds of all new drugs over the next 20 years. Given the types of diseases and conditions, both rare and common, treated by biopharmaceutical products, which include cancer, diabetes, anemia, rheumatoid arthritis, multiple sclerosis, and many more to come, this category of products is indeed unique, the commercial returns astronomical and the service to humankind provided by lower-cost alternates to licensed biopharmaceuticals, biosimilars, unparalleled.

In 1902, Congress passed the Biologics Control Act, which applied to "any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention and cure of diseases of man" and required the licensure of facilities making these products. Over the next hundred plus years, Congress expanded this list of covered products to include, among other things, vaccines, blood, blood products, allergenic products, and proteins (except chemically synthesized polypeptides) and their analogs. Despite these amendments, Congress never defined the listed terms and, in particular, never defined *analogous*, so the scope of the biological product definition remained unclear. The overlapping definition of *drug* added to this complexity. The Food and Drugs Act of 1906 and the Federal Food, Drug, and Cosmetic Act of 1938 (FDCA) broadly define *drug* to include, among other things, substances intended for use in the cure, the mitigation, or the prevention of disease, and the latter statute mandated the submission of a nondisclosure agreement (NDA) before the marketing of a drug. Although these *drug* definitions encompassed many biologics, the statutes did not provide concrete parameters for distinguishing nonbiological drugs from biological products. In 1944, when Congress revised and codified the 1902 Public Health Service Act (PHSA), it clarified that the NDA requirement did not apply to biologics, but it did not elucidate the scope of the biological product definition. Regulators attempted to fill this gap by promulgating regulatory definitions of virus, therapeutic serum, toxin, antitoxin, and analogous product. For example, the 1947 regulations, which are essentially similar to the current ordinance, defined products analogous to a toxin or antitoxin