Chapter 10 Biosimilarity
The final frontier

> You never really understand a person until you consider things from his point of view.
>
> **Harper Lee**

10.1 Leadership

The FDA has taken a leading role to a suggest novel analytical and objective approach to approving biosimilars pursuant to the BPCI Act of 2009. A historic snapshot points out that the Biologics Control Act was passed in 1902 to ensure purity and safety of serums, vaccines, and similar products used to prevent or treat diseases in humans, years before Congress passed the original Food and Drugs Act on June 30, 1906 (Figure 10.1). It is no wonder that the FDA has taken a major initiative over the past 107 years leading to providing a safe pathway for the approval of biological drugs coming off patent.

The term *biosimilarity* was coined after much debate, and more debates went on understanding the scope of the term. In describing it, the FDA has adopted a vocabulary that is just as interesting as it is instructional.

1. No one size fits all: The size refers to the scope of studies; the breadth and depth of studies, from the laboratory to patients, will always be molecule driven. So, do not expect the FDA to treat every application, even for the same molecule, similarly.
2. Totality of the evidence: The evidence pertains to identity, potency, safety, and purity (identity added by author). One would not do; all must conform.
3. No residual uncertainty: Residual is what is not clearly understood—there can be differences, but not those that could not be connected to potency, safety, and purity.
4. No clinically meaningful difference: *Clinically* refers to potency and safety; first correlate the CQAs to potency and safety and then justify differences.
5. Tier-based evaluation: Tiers range from not similar to fingerprint-like similar; the sponsor can maximally call its product similar. Also applies to the statistical evaluation of data, from Tier 1 to Tier 3.