

Chapter 5 Biopharmaceutical tools

Technology is nothing. What's important is that you have faith in people, that they're basically good and smart, and if you give them tools, they'll do wonderful things with them.

Steve Jobs

5.1 Background

In the 1980s, when the Hatch–Waxman law came for generic drugs, the biological products were excluded, simply because it was then inconceivable how a similarity could be established, since in most cases, the true structure and composition of many biological products had not been established with certainty; the age of recombinant manufacturing and sophisticated analytics had not yet ushered in, and, as a result, all these drugs were excluded from the generic pathway of approval. Today's analytical instruments can be millions of times more sensitive than what was available just a couple of decades ago.

The biopharmaceutical tools used to characterize stand-alone biologics (that form the subject of 351[a] filing) and the tools used to establish analytical and functional similarities for biosimilars (that form the subject of 351[k] filing) also take a different qualification. The choice of biopharmaceutical tools to establish identity, purity, safety, and potency for biosimilars requires an orthogonal approach since the exact structure that is responsible for the mode of action (MoA) may not always be apparent. It is for this reason that understanding the FDA's stance on biosimilarity requires a review of available biopharmaceutical tools and their appropriate deployment. There has been a recent expansion of analytical tools that now comprise several novel approaches that may be used to provide additional confidence in the similarity of biological products. This chapter is not intended as a primer for analytical methodologies, only their specific use to demonstrate biosimilarity.

5.1.1 The tools

There are numerous analytical methods to evaluate the safety, purity, and potency profiles of a biosimilar, among which are circular dichroism (CD), nuclear magnetic resonance (NMR), immunological tests (ELISA, immunoprecipitation, biosensors, etc.), biological activity from in vitro