

TABLE 2.1
Comparison of Key Attributes of a Pharmaceutical (Generic) and Biopharmaceutical (Biosimilar) That Make Them Different in Terms of Physicochemical Analysis

Attribute	Pharmaceutical (Generic)	Biopharmaceutical (Biosimilar)
Size and chemical complexity (primary structure)	Small drugs having a single unique structure with a small number of different chemical targets capable of giving rise typically to a small number of covalent altered forms of the drug with no or altered drug activity.	Very large drugs made of a large number of different chemical targets capable of giving rise to many different covalent forms of the drug. These drugs also require the intricate folding of their main structural element, the polypeptide chain(s), which is stabilized via a collection of weak noncovalent bonds (or weak secondary bonds). Alteration of these noncovalent bonds can give rise to alterations in this folding providing the opportunity for generating additional drug forms with different chemical properties and biological activity. Consequently these drugs tend to be a very heterogeneous collection of highly similar drugs having the same or similar drug activity, but some forms may have altered or no drug activity.
Mode of synthesis	Direct chemical synthesis using simple well controlled raw materials that requires a limited number of chemical reaction steps that can overall be well monitored and controlled.	A synthesis process that is totally dependent on the use of living cells resulting in the following: (1) exposure of the drug to an enormous array of enzymatic and chemical reactions called posttranslational modifications (PTMs) within the cell resulting in a very heterogeneous drug product with many variant forms and (2) to a very difficult drug manufacturing problem due to the intrinsic complexity of cells requiring a very wide range of factors to be controlled that are highly sensitive to small changes (e.g., raw materials—complex growth media, growth conditions, container surfaces).

(Continued)