which provides more information about the attributes that make the process of producing biopharmaceuticals very different and more difficult from the process of making pharmaceuticals). Although it would appear that these and other differentiating attributes would greatly impact the R&D cost involved in making biopharmaceuticals versus pharmaceuticals and would thus be good reasons for the higher cost of biopharmaceuticals, economic and financial assessments have not seemed to have borne this out as of yet (DiMasi and Grabowski, 2007; DiMasi et al., 2016); see Chapter 16 for further discussion on this topic. Irrespective of what may be causing the high cost associated with biopharmaceuticals, which needs to be paid to acquire these drugs, this high cost is again placing a very heavy economic burden on those who must pay for them (Hirsch et al., 2014; McCamish and Woollett, 2011) and thus is creating an economic roadblock in getting these drugs to those who need them.

As these biopharmaceuticals start to lose their patent protection, it is hoped that the same approach of making copies (generic versions) of these drugs will provide the same economic benefits as has been achieved in the case of pharmaceuticals. Unfortunately, the attributes of biopharmaceuticals and the manner in which they are made present the manufacturer trying to make a generic (identical) copy of a biopharmaceutical with an impossible task. The reality of this situation is made apparent when it is realized that even the innovator of a biopharmaceutical cannot make its own biopharmaceutical so that every biopharmaceutical molecule in a given lot is identical. Nor can the innovator make the actual collection or distribution of different biopharmaceutical molecules that is present in a given lot identical on a lot-to-lot basis. Rather, the variation in the different forms of the biopharmaceutical that are present in a given production lot is restricted by limits or specifications associated with a collection of critical quality attributes (CQAs). These limits or specifications (which were established by the innovator in collaboration with regulators who approved them) define the allowable distribution and variation of different forms of the biopharmaceutical that can be present in any lot, so that each manufactured biopharmaceutical lot is "comparable or highly similar" on a lot-to-lot basis (Schneider, 2013). Consequently, a manufacturer trying to make a copy of a biopharmaceutical cannot possibly make an identical copy of something that itself was never identical to begin with. Thus, a copy of a biopharmaceutical cannot be called a generic (an identical copy of an innovative biopharmaceutical). Rather, it is a highly similar copy of the different forms of a biopharmaceutical that are found in the innovator's biopharmaceutical that are allowed to vary within the same (highly similar) range of limits or specifications for the same CQAs that characterize the innovator's biopharmaceutical. Nomenclature used to describe a copy of a biopharmaceutical includes several different terms such as a biosimilar, follow-on biologic, and subsequent-entry biologic (Rader, 2007), with biosimilar appearing to be by far the most common name used to describe this type of drug product.

Given the inability to make identical copies of biopharmaceuticals, in the US the availability of the abbreviated approval pathway offered via the Hatch–Waxman Act is not applicable to biopharmaceuticals. Consequently, the development of new legal regulatory legislation and scientific thinking has been required in the US (and other countries and geographical regions) to provide a process for developing copies of biopharmaceuticals through an abbreviated pathway similar to generics, as shown