the costly RP has unfortunately placed on those who must pay for them, which, if achieved, should also increase the distribution of these drugs to those who need them but cannot afford them.

On the one hand, the key to a biosimilar's regulatory approval is dependent on the successful demonstration of biosimilarity—that the biosimilar is a highly similar copy of its corresponding RP with no meaningful difference in terms of safety, purity, and potency. On the other hand, the key to a biosimilar's commercial success can only be realized by achieving the following: (1) the ability to make biosimilars at a low enough cost so that they can be commercially offered to those who need them and must pay for them at a price significantly low enough in comparison to the corresponding RP (the subject matter of Chapter 16), so that these biosimilars will be purchased over the more costly RP (and over any residual lingering concerns about biosimilar's potential greater risk relative to that of the RP) and (2) the ability to offer the biosimilar at a price that will also provides a profit to the biosimilar manufacturer to justify its investment in this endeavor. Clearly, if *both* of these critical milestones are not achieved, we will have accomplished little and wasted much in diverting and squandering precious resources from the opportunities of finding new and improved drugs (especially for unmet health needs). At the same time, we will have lost a great opportunity for lowering the cost of health care and improving our ability to get these drugs to those who need them.

In tackling the subject matter of biosimilarity in this chapter, the author has dealt solely with the part of the biosimilarity exercise that is concerned with demonstrating biosimilarity from a structural perspective. In taking on this task, the author has discussed the associated scientific challenges and the impressive array of analytical tools and their capabilities that are available to assess the scientific attributes required to establish biosimilarity. Nevertheless, as noted by the FDA "Despite improvements in the analytical techniques, current analytical methodology may not be able to detect or characterize all relevant structural and functional differences between two products" (FDA, 2015d). This potential shortcoming is due to the small and subtle nature of structural differences in biopharmaceuticals that can make a significant difference in the performance of this class of drugs (as mentioned in Section 2.11) that can vary in importance from one biopharmaceutical to another (e.g., deamination for one biopharmaceutical may be an issue, while deamination in an entirely different biopharmaceutical may not). Hence, any structural difference observed through the use of our powerful analytical toolbox can be a potential source of concern. Unfortunately, as we increase our analytical power, we will likely also increase our ability to detect differences that may or may not be important. Coupling all this with the very subjective terminology concerning a biosimilar's successful milestone marker that is defined by the phrase "highly similar" only brings more uncertainty into play as to what a biosimilar manufacturer exactly needs to assure regulators that any observed difference between its biosimilar and the corresponding RP does not constitute a point of uncertainty (concerning a clinical meaningful difference) that will stand in the way of the biosimilar's approval. As a result, a biosimilar manufacturer needs to work closely with regulators early on in its biosimilar development program to get a clear picture as to what structural, functional, and even clinical data regulators will want to see (especially after the biosimilar manufacturer presents