clinical development activity for a generic is greatly reduced or potentially even eliminated (see Figure 2.1B).

This reduction or elimination of clinical work, coupled with the elimination of the normal long and precarious drug discovery process, greatly reduces the time and cost of developing and commercializing a generic. The success of this activity enables the generic manufacturer to charge the end user and/or payer of its generic a much lower price than what the innovator charges, while still being able to make a reasonable profit. The end result is that those who use and/or pay for the original drug could now pay the lower price for effectively the same drug (generic version) in preference to the more costly innovator's drug. As a result, the business of making generic drugs has been an overwhelming success not only as a new business, but more importantly as a way to provide a major cost saving to those who need and pay for these drugs.

This success is validated in the US by the fact that in 2009 (Kozlowski et al., 2011) over 75% of the pharmaceutical prescription drugs sold were generic versions, which increased to 86% in 2014 (Hirsch et al., 2014) resulting in drug price reductions relative to the original drug of 77%–90% (FDA, 2015a; Hirsch et al., 2014; Kozlowski et al., 2011; Sarpatwari et al., 2015). Consequently, the US health care system saved over $158 billion in 2010 (FDA, 2015a) and $193 billion in 2011, which, when summed over various time periods, have been reported to total savings of about $1.1 trillion for 2002–2011 (GPhA, 2012) or $1.5 trillion for 2005–2015 (Sarpatwari et al., 2015). It is this cost saving that is the real success story and intended purpose of generics, which has greatly reduced the economic burden placed on government agencies and other third-party payers of health insurance who are the major payers, along with the patients who use these drugs. Indeed, by achieving this remarkable cost reduction, these life-saving and life-enhancing drugs have become more readily available to a much wider population of individuals who would not have otherwise enjoyed their benefit.

Nevertheless, the landscape of drug development in the last three decades has undergone great changes in terms of the nature of the type of drugs that are now being developed to achieve even greater life-improving outcomes. This major paradigm change has been fueled by the applied application of knowledge gained through the scientific breakthroughs in the various areas of molecular biology, biochemistry, and other related and peripheral areas of science that have led to development of an entirely new class of drugs. These new drugs are called biopharmaceuticals and are predominately proteins (note: although biopharmaceuticals can be composed of other biological materials, e.g., nucleic acids and carbohydrates, all further discussions in this chapter referencing biopharmaceuticals will be concerned specifically with protein biopharmaceuticals).

Although biopharmaceuticals represent a great improvement in our ability to provide much more effective and highly targeted therapeutic agents, unfortunately they are generally felt to come associated with a much higher cost in their development and manufacturing (Blackstone and Fuhr, 2012; Ventola, 2013). This higher cost has been associated with their much greater complexity and consequently the much more challenging task of producing and characterizing them, especially from a physicochemical prospective. Properties of these new drugs that create this complexity and