2.1 INTRODUCTION

In general, once the patent protection of a product expires, others have the legal opportunity to freely copy (manufacture) and sell the same product that previously was only allowed to be made and sold by its innovator. However, in the case of making and selling a copy of an innovator's (original) drug, a regulated approval process is required. In the United States (US), until the mid-1980s, the approval process required was effectively the same lengthy and costly regulated approval process needed to obtain the approval of the original drug (see Figure 2.1A), but without the need to conduct drug discovery activities. This situation was a significant impediment to making a copy of a drug that could be sold at a much lower price. However, in 1984 with passage of the Hatch–Waxman Act (also known more formally as the Drug Price Competition and Patent Term Restoration Act of 1984), the requirements for obtaining regulatory approval for making and selling a copy of an innovator's drug, specifically for innovative small-molecule drugs called pharmaceuticals, greatly changed (Frank, 2007). Of great importance in passage of this Act is the availability of a significantly abbreviated approval pathway that greatly reduces the time and cost involved in making a copy of a drug by reducing or eliminating the need for clinical work (see Figure 2.1A vs. 2.1B). Key to being able to use this abbreviated approval pathway is the critical outcome of demonstrating that the structure of the drug copy (called a generic) is an *identical* copy of the structure of the innovator's drug. At the heart of this work are the analytical physical and chemical (physicochemical) data submitted to regulatory agencies to support this *structural identity*, along with data showing the comparability of these materials in terms of purity, bioequivalence, and stability.

For pharmaceuticals whose size in terms of molecular weight (MW) is typically only a few hundred Daltons (Da), the availability of appropriate analytical physicochemical tools [such as nuclear magnetic resonance (NMR), mass spectrometry (MS), Fourier transform infrared (FTIR), spectroscopy, chromatography, and electrophoresis] can, with very high fidelity, confirm the structural identity between an