Figure 10.1 The U.S. Post Office recognized the 1906 Act as a landmark of the 20th century when it released this stamp, the design of which was based on a 19th-century patent medicine trading card.

10.2 Biosimilarity

This is the final judgmental call by the FDA, not by the sponsor, and it is based on the FDA, not the sponsor, to conclude that CQAs are highly similar. The sponsor can only label its submission as *similar*, and not claim it to be highly similar.

Biosimilarity is a description that a sponsor candidate product is indeed biosimilar. Note that *biosimilarity* means "biological response similarity," not "biological products that are similar." There is a fine defining line here. To assure that the biological response is similar, the sponsor has to demonstrate on a formal tier basis that starts with analytical and functional characterization of the biosimilar candidate, followed by any safety evaluations in nonclinical setting, where possible, and the required clinical pharmacology evaluation, at least at the level of PK and additionally, PD, where possible. For example, the FDA will require both PK and PD studies in healthy subjects for filgrastim, but only a PK study for adalimumab in healthy subjects, since the latter does not have a PD model in healthy subjects.

Clinical trials in patients are different from the trials conducted for new molecules. The focus in conducting patient trials of biosimilars is intended to demonstrate equivalent effectiveness (not efficacy) and safety. Figure 10.1 shows the interrelationship of these two attributes to the expectation of the FDA for new biologics. Note the subtle difference between effectiveness and efficacy. The efficacy of the products has already been established; the biosimilar sponsor is required to prove equal effectiveness if potency and content can be proven to be equivalent using analytical and functional similarity and, where a PD model does not exist, in limited trials in one sensitive indication.

The safety is proven in analytical and functional similarity testing and in clinical pharmacology studies or in the studies planned for demonstrating equivalent effectiveness (Figure 10.2).