Fuhr, 2013). Entrants into biosimilars are likely to be large, biological originators for other reference products.

Marketing costs could be substantial, especially in the early days of biosimilars, as producers have to educate providers and patients about the quality of their products. This means that the biosimilar is likely to have to devote substantial resources to attain buyer acceptance. However, since many biologics are infused, the buyers are physicians or hospitals, so that marketing efforts may be less than expected. On the other hand, originators may have long-term contracts with large buyers that could impede entry of biosimilars.

Moreover, because biosimilars are not exact copies, presently their approval requires clinical trials, whereas for generics or small-molecule drugs, no clinical trials are required. These trials can be quite expensive. A study found that 85% of clinical trials were already being delayed because of difficulties in obtaining sufficient patient recruitment (Loo, 2015). Also, with the large number of biosimilars being developed for each reference product, it will become even more difficult to recruit volunteers for clinical trials, which increases the time and cost to complete clinical trials.

Patients on reference biologics that may be treating life-saving diseases could be understandably reluctant to participate in a clinical trial. However, those who cannot afford the biologics may be willing to participate. Moreover, obtaining the reference product could be quite costly. For example, a study involving 1500 patients receiving a biologic like Soliris would have a $200 million cost in 2015 if the study requires 3 months of treatments. The calculation is only meant to suggest the possible cost of clinical trials for biosimilar entrants. Also, the originators may be reluctant to sell their product to potential competitors.

Another entry barrier factor that makes entry difficult is the uncertainty about the success of the biosimilar. In part, this is because of the large number of companies planning to enter the market with biosimilars or improved versions of the reference product, biobetters. For example, in 2011 it was reported that companies were developing 21 biosimilars and 12 biobetters for Herceptin and 21 biosimilars and 13 biobetters for Rituxan (Blackstone and Fuhr, 2013).

The highly similar but not identical nature of the biosimilar makes obtaining interchangeability status difficult. The lack of interchangeability will preclude automatic substitution at the pharmacy level. Physicians will then have to authorize substitution. Given the possible problems, including the risk of immunogenicity and possible resulting legal actions, physicians may be reluctant to authorize substitutes. Another cost that biosimilars will incur is that of postmarketing surveillance. Increasingly, the FDA is requiring such efforts, and biosimilars would seem to be particularly susceptible to such a requirement.

16.12 PATENT DANCE

Biosimilars also face patent issues. The BPCIA includes detailed requirements for patent disclosures by both the biosimilar applicant and the innovator. This, as noted in an earlier chapter, has been referred to as the patent dance. Within 20 days of its application being accepted by the FDA, the biosimilar shall provide its application