or partners for these small firms should they encounter problems in the development process or simply wish to sell their project. For example, among the many pharmaceutical mergers in 2014, Actavis acquired Allergan, creating a top 10 company with annual revenues of $23 billion (Loo, 2014). Small firms thus have reduced bargaining power.

An indication of the riskiness of R&D in the drug industry is the fact that only 5%–10% of the drugs that begin clinical trials will receive marketing approval from the FDA (Blackstone and Fuhr, 2012). Further, only 3 out of 10 drugs that receive FDA approval become commercial successes (Loo, 2015). Also indicative of the high risk for originators is the fact that in the past 16 years only 7 out of 103 attempts at developing a melanoma drug resulted in drug approvals. The figures for lung and brain cancer were 10 of 77 and 3 of 78, respectively (Loo, 2015).

Other factors add to the risk and uncertainty for innovators. Biologic marketing involves high cost. In fact, such costs typically rise dramatically soon after a drug is approved as the company attempts to inform potential buyers about the drug. These marketing costs (which normally are included within the sales, general, and administration category) are about equal to R&D costs (Loo, 2015). Should the drug prove unprofitable, these costs cannot normally be recouped. They are what economists refer to as sunk costs.

Also making R&D more risky is the fact that the FDA is increasingly demanding a showing of a statistically significant improvement over the standard therapy. This could increase the required sample size for clinical trials, making these trials more costly, difficult, and time consuming. Already, 85% of clinical trials face delays because of difficulties in obtaining sufficient patient recruitment (Loo, 2015).

## 16.6 PATENT PROTECTION AND EXCLUSIVITY

Encouraging biological innovation is obviously important. Patents provide 20 years of protection against competition from the date of filing for the patent. The issue is whether such protection is adequate to encourage undertaking the high cost and uncertainty of biological innovation. Since drug approval requires substantial testing and clinical trials, the actual protection is reduced substantially. Given the 8–10 years typically required for approval, actual patent protection may last around 10–12 years. One study reported that actual effective patent life for drugs is 11.7 years (Roth, 2013).

There are numerous issues with the patent system itself that raise questions about its adequacies. Critics contend that too many patents are issued, so that many are flimsy. Defending patents against infringement suits is costly, and the uncertainty about prevailing in court could undermine the incentives for innovation. The result is that the presumption of validity is reduced, encouraging patent challenges. Further adding to the uncertainties of patent litigation is the fact that patent coverage is often unclear (Roth, 2013). The patent system needs more certainty. In the generic market, the producer is making an exact copy. In the case of biosimilars, the producer is making a product that is highly similar to the reference product. In the generic case, infringement would presumably be easier to determine. This adds uncertainty to the market for both the biologic innovator and the copier, whether or not infringement is actually occurring.