need to be treated with a biosimilar product if it is available; otherwise the treatment is not reimbursed. But patients already treated with a brand-name biological have the right to continue receiving the same biological brand. Consequently, the prescribability, but not the interchangeability, of biosimilar products is recommended.

Even though it has been reported that there has been some experience in Europe with switching (Ebbers et al., 2012), it needs to be stressed that adequate data are scarce. The studies reported so far suffer from a number of important drawbacks. First, all studies referred to in Ebbers et al. (2012) deal with epoetins, G-CSFs, or human growth hormones. These are relatively small biologicals characterized as having low immunogenicity. Second, most of these studies have included a small number of patients or volunteers, had a short duration, and investigated a switch in only one direction. Therefore, these data do not reflect potential clinical practice. Third, some of these studies did not study switches related to biosimilars but rather switches between different originator molecules. Fourth, the majority of these studies were designed to evaluate comparable efficacy, and thus most if not all were strongly underpowered to detect changes in safety profiles upon switching. In addition, any postapproval data analysis is also not valid for drawing firm conclusions on the safety of switching since such databases (1) are not set up to detect adverse events specifically related to switches at an individual level and (2) typically suffer from underreporting.

Currently, the Norwegian Medicines Agency is encouraging a substitution culture and has initiated a clinical study to investigate the safety and efficacy of switching between IFX (Remicade) and the biosimilar Remsima in patients with rheumatoid arthritis, spondyloarthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease, and chronic plaque psoriasis (NOR-SWITCH study, 2015). The primary endpoint of the NOR-SWITCH study is the occurrence of disease worsening in the indications being studied. However these endpoints cannot actually be analyzed together, and the sample size in each disease is underpowered to show a difference if it exists (Declerck et al., 2015).

In France, a new law (but yet to be implemented by decree) states that pharmacists will be legally permitted to substitute a biosimilar for the prescribed reference biological medicine as long as the prescribing physician has not marked the prescription as "nonsubstitutable" (Allen & Overy, 2014). Importantly, substitution will be allowed only for treatment-naïve patients. It could therefore be noted that the law actually considers the "replacement" of the reference drug by a biosimilar product (i.e., their parallel prescribability) and not their substitution (i.e., within-subject switching) as understood by the European Consensus Group. If the pharmacist decides to substitute/replace a biosimilar for the prescribed biological, the brand name of the dispensed product should be written on the prescription and the prescribing physician should be informed in order to maintain an accurate medical record.

10.6 CONCLUDING REMARKS

Regulatory approval of both small-molecule generics and biological biosimilars means directly an agreement only that they are prescribable—that is, that the drug products may be provided to naïve patients who have not taken the drug until this point in any form.