Any remaining concerns about safety (due to the reduced clinical experience with the biosimilar at the time of marketing authorization) and pharmacovigilance are discussed next.

15.5.2 Pharmacovigilance and Traceability

Extrapolation of clinical safety has also been an issue heavily discussed after the marketing authorization of biosimilars. Even though safety is assessed throughout the clinical development program of the biosimilar (PK/PD and pivotal clinical efficacy studies), it is recognized that this safety database is limited (i.e., insufficient to identify rare adverse effects) when they have been approved. Therefore, clinical safety of biosimilars must be monitored closely on an ongoing basis during the post-approval phase, including continued benefit–risk assessment (Ebbers et al., 2012). The objective of the preauthorization comparative safety data is the identification of any new signal not previously identified with the originator medicine, and the extent and type of safety data and duration of the study will depend on the adverse events known for the reference product. Any possible safety concerns that may result from a different manufacturing process from that of the reference product, especially those related to infusion-related reactions and immunogenicity, should be described in the risk management plan and should be monitored closely on an ongoing basis during the postmarketing phase. This approach follows the same rationale as applied from any other biological medicinal product on the market when changes are introduced in its manufacturing process. Long-term postmarketing data are a requirement for both originators and biosimilars and have allowed the identification of rare safety signals—for example, cases of pure red cell aplasia in patients treated with epoetin or progressive multifocal leukoencephalopathy (PML) in patients with multiple sclerosis treated with (natalizumab) or in patients with psoriasis treated with efalizumab (Ruiz and Calvo, 2011).

In general, immunogenicity should be studied before marketing authorization application and using the same principles as described earlier for the clinical safety approach.

After a 10-year experience in the EU no special safety concerns have been identified for biosimilars. However, it is necessary to have a continuous surveillance system as for all biological medicinal products. A good pharmacovigilance system relies on good traceability in order to unequivocally identify the specific medicinal product and precise batch number causing an adverse effect. This equally applies to innovators and biosimilars. Further measures have been proposed recently to improve the traceability of similar biotherapeutic products, such as adding a biological qualifier (BQ) to the international nonproprietary names (INNs), as proposed by the WHO (2014). Adding this four random letter code to the name of the active ingredient would not enhance traceability and could even cause more confusion when reporting adverse events (as it would result in additional information to register and it does not identify the specific batch). The commercial name of the product and batch number, as described in the current legislation, if properly reported, should be enough and any measures to facilitate or improve recording of these critical data would be welcome.