biosimilar product, the EMA requires comprehensive and justified comparability studies between the biosimilar and the reference products at the quality, nonclinical, and clinical level, which are explained in detail in the EMA guidelines. The approval pathway of biosimilar products in the EU is based on case-by-case reviews, owing to the complexity and diversity of the biologic products. Therefore, besides the three general guidelines, EMA developed additional product class–specific guidelines on nonclinical and clinical studies. This approval pathway is now held up as one of the gold standards for authorizing biosimilar products.

8.2.3 North America

8.2.3.1 The United States Food and Drug Administration

For the approval of follow-on biologics in the United States, current regulations depend on whether the biological product is approved under the United States Food, Drug, and Cosmetic Act (US FD&C) or it is licensed under the United States Public Health Service Act (US PHS). For those biological drugs marketed under the PHS Act, the BPCI Act passed by the US Congress on March 23, 2010, amends the PHS Act to establish an abbreviated approval pathway for biological products that are highly similar or interchangeable with an FDA-authorized biologic drug, and gives the FDA the authority to approve follow-on biologics under new Section 351(k) of the PHS Act. Some early biological drugs, such as somatropin and insulin, were approved under the FD&C Act. In this case, biosimilar versions can receive approval for new drug applications (NDAs) under Section 505(b) (2) of the FD&C Act.

Following passage of the BPCI Act, in order to obtain input on specific issues and challenges associated with the implementation of the BPCI Act from a broad group of stakeholders, the FDA conducted a two-day public hearing on Approval Pathway for Biosimilar and Interchangeability Biological Product held on November 2–3, 2010, at the FDA office in Silver Spring, Maryland. The scientific issues covered in this public hearing included, but were not limited to, criteria and design for biosimilarity and interchangeability, comparability between manufacturing processes, patient safety and pharmacovigilance, exclusivity, and user fees.

In practice, there is a strong industrial interest and desire for the regulatory agencies to develop review standards and an approval process for biosimilars rather than an *ad hoc* case-by-case review of individual biosimilar applications. As indicated earlier, for this purpose, the FDA has established three committees to ensure consistency in the FDA's regulatory approach of follow-on biologics. The three committees are the Center for Drug Evaluation and Research (CDER)/CBER Biosimilar Implementation Committee (BIC), the CDER Biosimilar Review Committee (BRC), and the CBER Biosimilar Review Committee. The CDER/CBER BRC focus on the cross-center policy issues related to the implementation of the BPCI Act. The CDER BRC and CBER BRC are responsible for considering applicants' requests for advice about proposed development programs for biosimilar products, reviewing biologic license applications (BLAs) that are submitted under Section 351(k) of the PHS Act, and managing related issues. Thus, the review process steps of CDER BRC and CBER BRC include the following: (1) applicant submission of request for advice,