manufacturing process, and efficacy. For a given domain such as PK, the proposal is briefly described as follows:

Step 1: Assess biosimilarity based on a prespecified criterion;
Step 2: Calculate the probability of reproducibility;
Step 3: Claim "success" if the probability of reproducibility is larger than p_0.

As a result, an overall biosimilarity index across domains can be developed as follows:

Step 1: Obtain p_i, the probability of reproducibility for the ith domain, $i = 1, \ldots, K$;
Step 2: Define the biosimilarity index $p = \sum_{i=1}^{K} w_i p_i$ where w_i is the weight for the ith domain;
Step 3: Claim global biosimilarity if $p > p_0$ where p_0 is a prespecified value.

The statistical properties of Chow's proposed biosimilarity index are currently evaluated through simulations.

1.3.9 Remarks

Current methods for the assessment of bioequivalence for drug products with identical active ingredients are not applicable to biosimilars due to fundamental differences. The assessment of biosimilarity between a biosimilar and the reference product in terms of surrogate endpoints (e.g., pharmacokinetic parameters and/or pharmacodynamic responses) requires the establishment of the Fundamental Biosimilarity Assumption in order to bridge the surrogate endpoints and/or biomarker data to clinical safety and efficacy.

Under the established Fundamental Biosimilarity Assumption and the selected biosimilarity criteria, it is also recommended that appropriate statistical methods (e.g., comparing distributions and the development of the biosimilarity index) be developed under valid study designs for achieving the study objectives (e.g., the establishment of biosimilarity at specific domains or drug interchangeability) with a desired statistical inference (e.g., power or confidence interval). To ensure the success of studies conducted for the assessment of biosimilarity, regulatory guidelines/guidances need to be developed. Product-specific guidelines/guidances published by the EMA have been criticized for not having standards. Although product-specific guidelines/guidances do not help to establish standards for the assessment of biosimilarity of biosimilars, they do provide the opportunity for accumulating valuable experience/information for establishing standards in the future. Thus, several numerical studies could be pursued, including simulations, meta-analysis, and/or sensitivity analysis, in order to (1) provide a better understanding of these product-specific guidelines/guidances and (2) check the validity of the established Fundamental Biosimilarity Assumption, which is the legal basis for assessing biosimilarity.