equivalence trials (Chow and Liu, 2004). To facilitate the proper interpretation of the study results, it is important to show that the trial has assay sensitivity. A trial of poor quality is likely to lack assay sensitivity and may lead to an erroneous conclusion of equivalence of the biosimilar to the RBD (Snapinn, 2000). Another important consideration in the interpretation of the study results is the constancy assumption, as previously discussed (Chow and Liu, 2004). Verification of the assumption can be difficult and typically requires the external validation of the results of the current trial relative to historical trials with the RBD.

9.5 CONCLUSIONS

The extrapolation of indications is the leveraging of safety and efficacy data from clinical studies in one indication to support the authorization of other indications in which the biosimilar has not been studied but for which the reference product is authorized. After review of all quality data, nonclinical data, and PK/PD study/ies and clinical trial(s), a biosimilar product may or may not be authorized for all routes of administration, doses, and indications for which the reference product is authorized. The biosimilar guidance documents from regulatory authorities for biosimilars indicate that it may be possible to extrapolate clinical data to other indications (in which the biosimilar has not been studied) where rationales are sufficiently persuasive. The decision to extrapolate should be based primarily on the demonstration of similarity through extensive comparability studies that compare the physicochemical attributes and the biological activity between the biosimilar and reference product.

The clinical development for biosimilars consists of complex processes associated with regulatory and scientific issues. A biosimilar has to demonstrate that its structure and function(s) are (highly) similar to the reference product prior to conducting clinical trials in sensitive populations. Extrapolation of indications is possible when the appropriate data and rationales are provided. However, extrapolation would be unlikely if there is evidence that an observed difference may impact a mechanism that could be important in the treatment of an indication to which extrapolation is required. Based on the same dataset, regulatory agencies may render different regulatory decisions; this is the same as for any other therapeutic product. Further dialogue and harmonization among regulatory agencies on their decision making should be considered as experience with the scientific and regulatory issues related to biosimilars increases.

Recently, a new amendment to the Food and Drugs Act, Bill C-17, also called Vanessa's law, has provided the regulator with added authorities such that it is now possible to take a lifecycle approach to the regulation of any drug product in Canada, including biosimilars.

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