substantive consideration of full study reports, the FDA advice concerning the similarity between the proposed biosimilar biological product and the reference product, and the FDA advice concerning the need for additional studies, including design and analysis.

3.3.5 BPD Type 4 meeting

A BPD Type 4 meeting is a meeting to discuss the format and the content of a biosimilar biological product application or a supplement to be submitted under Section 351(k).

3.4 Scientific considerations

3.4.1 Background

Biosimilarity is defined in Section 351(i) of the PHSA to mean that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, the purity, and the potency of the product (see Section 351(i)(2) of the PHSA). Comparative analytical data provide the foundation for a development program for a proposed biosimilar product intended for submission under Section 351(k) of the PHSA. The BPCI Act also amended the definition of biological product to include "protein (except any chemically synthesized polypeptide)."

The three pillars of establishing biosimilarity include the following:

- Analytical studies that demonstrate that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components
- Animal studies (including the assessment of toxicity)
- A clinical study or studies (including the assessment of immunogenicity and pharmacokinetics [PK] or pharmacodynamics [PD]) that are sufficient to demonstrate safety, purity, and potency in one or more appropriate conditions of use for which the reference product is licensed and intended to be used and for which licensure is sought for the biological product

3.4.2 Complexities of protein products

The three pillars for establishing biosimilarity rest on heavy scientific foundation given the complexity of protein and antibody products. The FDA has provided extensive advice on how to approach understanding this complexity and what the FDA considers to be more critical factors.