4.2.18 Animal data

Animal toxicity data are useful when uncertainties remain about the safety of the proposed product prior to initiating clinical studies.

- The scope and the extent of animal toxicity studies will depend on publicly available information and/or data submitted in the biosimilar application regarding the reference product and the proposed biosimilar product, and the extent of known similarities or differences between the two.
- A comparison of PK/PD in an animal model may be useful.

4.2.19 Clinical studies

The nature and the scope of clinical studies will depend on the extent of residual uncertainty about the biosimilarity of the two products after conducting extensive structural and functional characterizations and, where relevant, animal studies.

4.2.20 Type of clinical data

- As a scientific matter, the FDA expects an adequate clinical PK, and PD if relevant, comparison between the proposed biosimilar product and the reference product.
- As a scientific matter, at least one clinical study that includes a comparison of the immunogenicity of the proposed and reference products will be generally expected.
- As a scientific matter, a comparative clinical study will be necessary to support a demonstration of biosimilarity if there are residual uncertainties about whether there are clinically meaningful differences between the proposed and reference products based on structural and functional characterizations, animal testing, human PK and PD data, and clinical immunogenicity assessment.

4.2.21 Comparative human PK and PD data

- Demonstrate PK (and PD) similarity.
- Assess clinically meaningful differences between the proposed biosimilar and the reference products.
- PK and/or PD is generally considered the most sensitive clinical study/assay in which to assess for differences, should they exist.
- Support a demonstration of biosimilarity with the assumption that similar exposure (and PD response) provides similar efficacy and safety (i.e., an exposure–response relationship exists).
- Clinical PK data generally will be expected; PD data are desirable (case-by-case consideration).