BIOSIMILAR DEVELOPMENT PROCESS

There is no one size fits all approach to biosimilar product development. The goal of a biosimilar development program is to use a "totality of the evidence" approach to demonstrate biosimilarity to the reference product, not to independently establish safety and effectiveness of the proposed biosimilar.

FDA advises on scope and extent of testing during development.

DATA TO SUPPORT BIOSIMILARITY

Highly Similar

ANALYTICAL STUDIES

- Assess an array of quality characteristics using state-of-the-art technologies and multiple different tests for the same characteristic to determine if the proposed biosimilar is highly similar to the reference product
- Identify differences in quality characteristics, if any, between the reference product and proposed biosimilar
  - Examples of critical quality characteristics include structure and bioactivity
- Thoroughly evaluate the potential impact of any differences observed

Assessment of Toxicity

ANIMAL STUDIES

- Support safety decision prior to human exposure to the proposed biosimilar
- May provide additional support for demonstrating biosimilarity, but are not always needed

No Clinically Meaningful Differences

HUMAN PK AND PD STUDIES

- Compare the pharmacokinetic (exposure) and, as applicable, pharmacodynamic (response) profiles of the reference product and proposed biosimilar to support a conclusion of similar efficacy and safety
- Generally considered the most sensitive data element to support a demonstration of no clinically meaningful differences

IMMUNOGENICITY ASSESSMENT

- Compare incidence and severity of immune responses generated with the reference product and proposed biosimilar
- Generally included as part of all clinical studies

ADDITIONAL CLINICAL STUDIES

- Conducted only when residual uncertainties remain about the demonstration of no clinically meaningful differences after conducting the above-named studies
- Different from the role of Phase 3 efficacy and safety trials conducted to support traditional drug development

Experience With Reference Product

Totality of the Evidence

Biosimilarity

FDA's determination of biosimilarity is based on the totality of the evidence provided in the marketing application for FDA review. The data package in the marketing application includes an extensive analytical comparison to show that the proposed biosimilar and reference products are highly similar in structure and function. Animal, human pharmacologic, immunologic, and additional clinical data are added as needed to the analytical data in a stepwise fashion to provide the information needed to demonstrate biosimilarity.

Visit **www.FDA.gov/biosimilars** to learn more about biosimilars.

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