OVERVIEW OF BIOLOGICAL PRODUCTS

Biological products are a diverse category of products and are generally large, complex molecules that may not be completely defined or easily characterized. They may be produced through biotechnology in a living system (eg, microorganism, plant or animal cell) and are often more difficult to characterize than small molecule drugs. Examples of biological products include monoclonal antibodies, therapeutic proteins, cellular and gene therapy, and vaccines.

	Reference Product	Biosimilar	Interchangeable Product
Definition	A single biological product already approved by the FDA based on a full complement of safety and effectiveness data, against which a proposed biosimilar product is compared	A biological product that is highly similar to and has no clinically meaningful differences in safety, purity, and potency from an existing FDA-approved reference product, except for minor differences in clinically inactive components	A biosimilar product that meets additional requirements based on further evaluation and testing outlined by the Biologics Price Competition and Innovation Act. Expected to produce the same clinical result as the reference product in any given patient. Risk in terms of safety and reduced efficacy of alternating or switching between the products has been evaluated.
Approval Process	Submitted through the BLA process with the following requirements: • Applicant information: includes name and addresses of manufacturing facilities • Product/Manufacturing information: source material/raw material; manufacturing process and controls; formulation; facility information; contamination/cross-contamination information; environment assessment or categorical exclusion • Pre-clinical studies: safety, efficacy, and use • Clinical studies: safety, efficacy, and use • Labeling: safety, efficacy, and use	A biosimilar product application must include data demonstrating biosimilarity to the reference product, including: • Analytical studies: include structural analysis (eg, structural characteristics of the protein, post-translational modifications, and/or other potential variants) and functional assays to evaluate the pharmacologic activity of the protein (eg, potency, MOA) • Animal studies: include toxicity, PK and PD measures, and immunogenicity • Clinical studies: Human pharmacology data (PK/PD), clinical immunogenicity assessment, and clinical safety and efficacy data to demonstrate safety, purity, and potency for the condition(s) the reference product is licensed and intended to be used for	In addition to the steps for biosimilar product application, an interchangeable product must also include data demonstrating that: • The proposed interchangeable product is expected to produce the same clinical result as the reference product in any given patient, AND • For a product administered more than once to an individual, alternating or switching between the proposed interchangeable product and the reference product does not increase safety risks or decrease effectiveness compared to using the reference product without such alternation or switch
BLA Type	351(a)	351(k)	351(k)
Nonproprietary Naming	Previously includes a core name only The FDA now requires new reference products to include a unique FDA-designated four-letter suffix†. Previously approved biologics may submit a prior approval labeling supplement that include proposed suffixes.	Includes a core name (same as the reference product) attached by a hyphen to a unique FDA-designated four-letter suffix*	May include a core name and a suffix, however, FDA continues to consider the appropriate format of the suffix for interchangeable products
Prescribing	Physicians specialized in the reference product's indication can prescribe	Substitution of a biosimilar for a reference product is a matter of state pharmacy law	May be substituted for the reference product without the intervention of the prescriber

NOTES

Key: **BLA** = Biologic License Application; **FDA** = Food & Drug Administration; **MOA** = mechanism of action; **PD** = pharmacodynamics; **PK** = pharmacokinetics

* The distinguishing suffix is devoid of meaning and composed of 4 lowercase letters of which at least 3 are distinct. If the FDA does not find the proposed suffix acceptable, or the applicant does not propose suffix candidates within an appropriate time frame for FDA review, FDA may elect to assign a four-letter suffix at the time of approval.

REFERENCES

Biosimilars. U.S. Food & Drug Administration Web site. https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/biosimilars. Published February 3, 2020. Accessed March 23, 2021.

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U.S. Department of Health and Human Services Food and Drug Administration, Center for Drug Evaluation and Research (CDER), and Center for Biologics Evaluation and Research (CBER). Nonproprietary Naming of Biological Products. U.S. Food & Drug Administration Web site. https://www.fda.gov/files/drugs/published/Nonproprietary-Naming-of-Biological-Products-Guidance-for-Industry.pdf. Published January 2017. Accessed March 24, 2021.

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