Pfizer

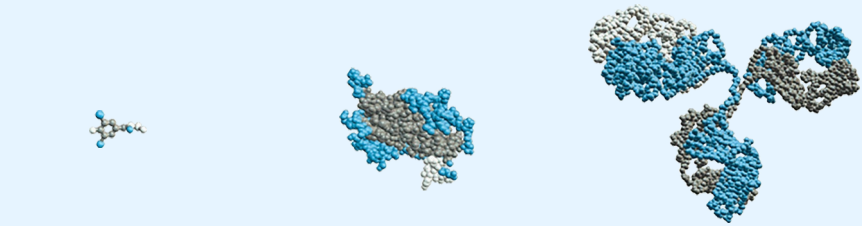
Important Facts

Healthcare Professionals Should Know About Biosimilars

Biosimilars: Defining Characteristics

Biosimilars are highly similar versions of reference biologics, with no clinically meaningful differences in terms of safety, purity, and potency.[1]

Biologics, including biosimilars, are more complex than small molecules.[2-5]

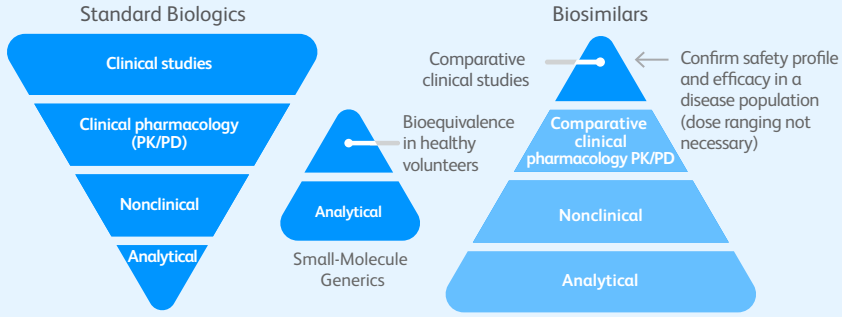


While small-molecule generics are chemically synthesized, biosimilars (and reference biologics) are created in living cells and require significant expertise and state-of-the-art technology to manufacture and produce.[3,6]

Development of Biosimilars

Providing a change in thinking from how reference biologics are evaluated, the US Food and Drug Administration (FDA) evaluates biosimilars based on a totality-of-evidence approach.[1,7,8]

DEVELOPMENTAL PATHWAYS[7-11]



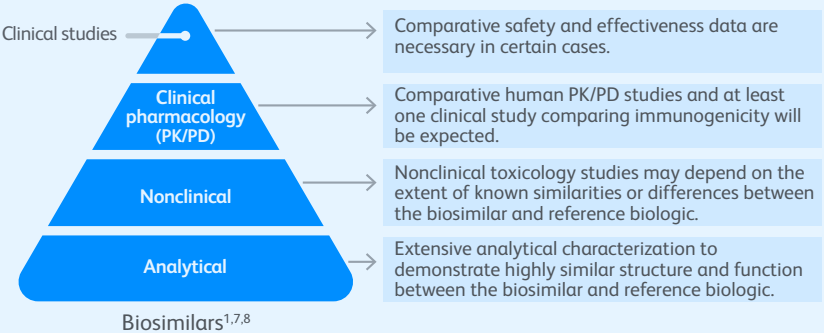
PK, pharmacokinetic; PD, pharmacodynamic.

The goal of biosimilar development is to demonstrate that there are no clinically meaningful differences between the proposed biosimilar and the reference biologic—not to reestablish the clinical benefit of the reference biologic.[1]

The Totality of Evidence

The FDA approval process evaluates the totality of evidence to ensure biosimilar quality, efficacy, and safety.[1]

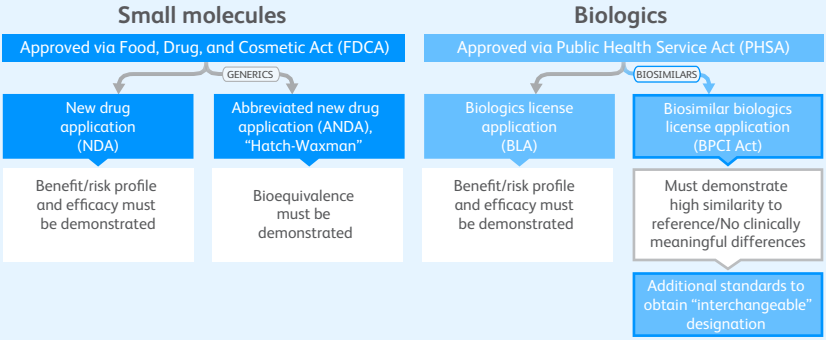
THE TOTALITY OF EVIDENCE: A STEPWISE APPROACH[1]



Approval Pathway for Biosimilars

Biosimilars may be approved through an abbreviated licensure pathway if high similarity with a reference product is established.[1]

STANDARD AND ABBREVIATED PATHWAYS FOR DRUG APPROVAL IN THE UNITED STATES[1,11-16]



Development of a biosimilar requires substantial time and financial investment.[17]

A biosimilar may involve a time investment of 5 to 9 years or more and cost more than $100 million to develop (not including regulatory fees),[17,18] whereas development of a traditional generic may take up to 2 years and cost $1 million to $4 million.[19,20]

Extrapolation: A Scientific and Regulatory Principle

After biosimilarity is determined, extrapolation enables potential licensure of a biosimilar across indications approved for the reference biologic.[1,21-23]

SCIENTIFIC JUSTIFICATION IS REQUIRED IN EACH INDICATION NOT STUDIED CLINICALLY [1,24-26]

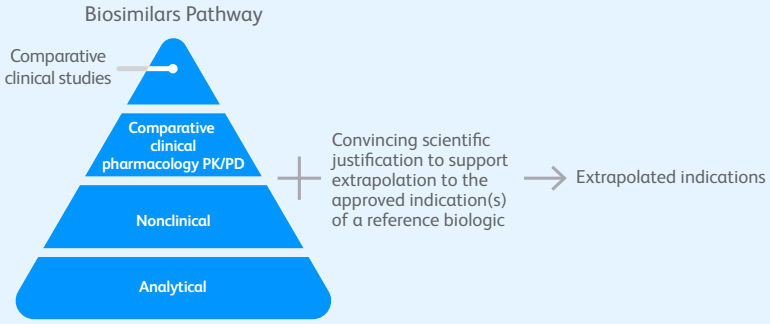


Image adapted from FDA Overview of Regulatory Guidance for Biosimilars 2019.

Biosimilar extrapolation occurs from the reference biologic to the biosimilar, when scientifically justified, based on all available data—not from the indication(s) studied with the biosimilar to other indications[25]

Extrapolation is not automatic—scientific justification in each indication not clinically studied is organized around 4 key aspects that are considered by the FDA.[1]

KEY FDA CONSIDERATIONS FOR EXTRAPOLATION[1]

MECHANISM OF ACTION
- Experience with the reference biologic can help define the mechanism of action (MOA) and functional moieties in each indication

PK AND BIODISTRIBUTION
- PD measures may provide important MOA information

IMMUNOGENICITY
- Differences that may exist in each patient population

EXPECTED TOXICITIES
- Differences that may exist in each indication and patient population

Scientific justification combines experience with the reference biologic and the totality of evidence.[1,27-29]

SCIENTIFIC JUSTIFICATION FOR EXTRAPOLATION[1,27-29]

EXPERIENCE WITH THE REFERENCE BIOLOGIC

- **Building on the high structural similarity** between the 2 products, **experience with the reference biologic** helps provide an understanding of the 4 key FDA considerations

SUPPORT FROM THE TOTALITY OF EVIDENCE

- **Structural studies and in vitro models** demonstrating **functional similarity across potential MOAs**
- Clinical data that **address differences between indications**
- Clinical data that may be compared to **existing evidence with the reference biologic**

The rationale for extrapolation is to[21,24,30]

- Avoid unnecessary clinical studies
- Reduce development costs
- Allow for reallocation of resources

An Interchangeability Designation Requires a Biosimilar to Meet Additional Standards[15,31]

According to the FDA, products designated interchangeable may be substituted at the pharmacy level for the reference biologic without the intervention of the prescribing healthcare provider.

To be designated interchangeable, the biologic product

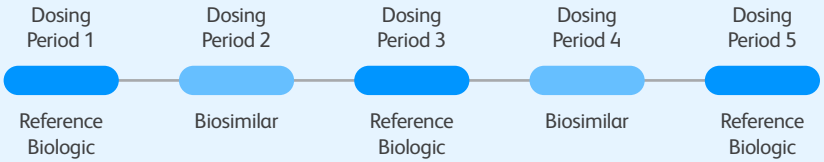
- Must be biosimilar to the reference biologic
- Must be expected to produce the same clinical result as the reference biologic in any given patient

For a biological product administered more than once, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference biologic is not greater than the risk of using the reference biologic without such alternation or switch.

The interchangeability designation

An interchangeability designation considers the potential for alternation (multiple switches) between a biosimilar and reference biologic without physician intervention.[15,31]

ALTERNATION



On July 28, 2021, the US FDA approved the first interchangeable biosimilar, an insulin product[32]

Potential Value of Biosimilars

Biologics have been used successfully to treat many life-threatening and chronic diseases. Between 2008 and 2020, biologics have grown from 13 % to 25 % of new FDA approvals.[33-35]

The potential cost savings from biosimilars to healthcare systems may be substantial.[36,37]

ESTIMATED REDUCTION IN DIRECT SPENDING ON BIOLOGIC DRUGS IN THE UNITED STATES FROM 2020 THROUGH 2024[36]

Up to $104 billion

Biosimilars may provide multiple benefits to the US healthcare system.[38-40]

POTENTIAL OF BIOSIMILARS FOR PATIENTS, PAYERS, AND PROVIDERS[38-40]

Additional treatment choices at potentially lower cost to the healthcare system

Offer a variety of therapeutic options

Possible savings to the healthcare system

Biosimilars may provide potential financial flexibility to practices[36,37,41]

- Reduced drug spending on biologics may lead to potential cost savings
- Savings may provide reallocation of funds for other important projects
- Helps meet cost targets

How Biosimilars May Help Bring Value to Some Patients

Biosimilars may improve access to biologics

Biosimilars have the potential to make a **positive impact on some patients** and the healthcare system by offering additional treatment choices and reduced costs. These savings to the healthcare system may enable more patients to have access to biologics.[38,40-42]

Biosimilars may help reduce the costs of biologic medicines

There are currently **approved biosimilar** options covering 3 oncology therapeutic antibodies and 3 supportive care agents.[43,44]

Biosimilar alternatives in oncology and supportive care are available for 4 of the most costly medical benefit drugs for patients with commercial insurance or Medicare.[43,45]

Biosimilars in oncology and supportive care have had **greater and more rapid uptake** than other biosimilars, and the biosimilar oncology therapeutic antibodies are tracking toward nearly **60% market uptake** in the first 2 years of availability.[36]

Increased biosimilar competition has led to **decreased price for every therapeutic agent** in oncology and supportive care where biosimilars are available.[36,46]

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