

# BIOSIMILARS: What health care providers need to know

## Section 1: The Biosimilar Development Process

### The Biosimilar Development Process



#### Data to Support Biosimilarity

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.

#### Highly Similar



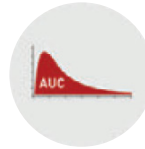
Analytical Studies

#### Toxicity Tests



Animal Studies

#### No clinically meaningful difference



Human PK & PD Studies



Immunogenicity Assessment



Additional Clinical Studies

<https://www.fda.gov/files/drugs/published/Biosimilar-Development-Process.pdf>

### Biosimilars Price Competition and Innovation Act (BPCIA)

Legislation to drive cost savings is the biggest factor driving biosimilar development

The BPCIA was established in 2009 to create an **abbreviated licensure pathway** for biological products that are demonstrated to be **“biosimilar”** to or **“interchangeable”** with an FDA-licensed biological product.

[fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/ucm216146.pdf](https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/ucm216146.pdf)

### Distinctions between Generics and Biosimilars

	Generics	Biosimilars
<b>QA</b>	-50 QA tests done before possible approval	-250 QA tests done before possible approval
<b>Development</b>	about 3 years	about 7-8 years
<b>Manufacturing</b>	Bioequivalent/identical to reference product and replicable in different laboratories	Same complex amino acid sequence as reference biologic. Unique, living cell line with possible post-translational modification.
<b>Interchangeability</b>	Interchangeable/Automatic substitution	No interchangeability or automatic substitution. Best with new starts or sustained remission+stable dosing.
<b>Immunogenicity</b>	Reactions not easily attributable to product	Reactions may be attributable to both product- and host-related factors
<b>Cost Savings</b>	80-90% discount over reference product	20-30% discount over reference product

### Regulatory Requisites Associated with Biosimilars

#### Pharmacokinetics

**what the body does to a drug**  
(Absorption, distribution, metabolism, and excretion (ADME))

For biosimilars, highly similar PK or PD alone is generally insufficient to establish “bioequivalence,” as they are large & complex proteins with unique manufacturing processes

#### Pharmacodynamics

**what the drug does to the body**  
(biochemical and physiologic effects)

#### Extrapolation

Clinical trials in one indication used as rationale for clinical use in other indications for which the originator biological product is approved. Requires appropriate scientific justification.

#### Interchangeability

Additional requirements to show that the biosimilar produces the same clinical result as the reference product in any given patient. The safety and efficacy of switching will also have been evaluated.

#### Pharmacovigilance

Post-marketing monitoring, detecting and prevention of adverse events or drug-related problems. Clinical trials are usually too small to detect rarer AEs, especially if duration is limited.

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## Section 3: Biosimilars in Clinical Practice

### Scenarios for/against Biosimilar use

#### Positioning biosimilars in clinical practice within IBD treatment paradigms

<b>Adalimumab/infliximab naïve patients (new start)</b>	Same indications and dosing as RP agents
<b>Sustained remission plus stable dosing of adalimumab/infliximab</b>	Could use biosimilar if more cost-effective*
<b>Drug holiday with history of response</b>	Could use biosimilar in re-challenge
<b>Loss of response to adalimumab/infliximab</b>	If attributed to high titer, do not switch
<b>Clinically significant antibodies present to adalimumab/infliximab</b>	Do not use biosimilar
<b>Primary non-response to adalimumab/infliximab</b>	Do not use biosimilar
<b>Patient at high-risk for disease flare/stable dose not identified</b>	Do not switch to biosimilar
<b>Patient has a high-risk condition (e.g. pregnancy)</b>	Do not switch to biosimilar

\*Consider checking IFX levels/antibodies before biosimilar switch to identify patients at greater risk of flaring or non-response