

# WHAT DO I NEED TO KNOW ABOUT BIOSIMILARS?

## INTERCHANGEABILITY AND SUBSTITUTION

### BIOLOGIC AND BIOSIMILAR MEDICINES

Biologic medicines are large, complex molecules that are made in living cells, grown in a laboratory. Some examples include vaccines and therapeutic proteins that help your body to fight illnesses such as cancer and arthritis.

Biosimilars are replicas of biologic medicines. However, exact copies of biologic medicines are not possible. Biologics are made in living cells, and because of this, there will always be small differences between a biosimilar and the biologic medicine it is based on. Testing biosimilars in patients as part of a clinical trial is very important in evaluating whether these small differences have any effect on the way the medicine works in the body. The extreme complexity and large molecular size of biologic medicines mean that even minor differences between two similar biologics can cause unexpected reactions in patients, including unwanted immune reactions.

### WHAT IS INTERCHANGEABILITY?

Interchangeability is a standard established by the FDA. To receive regulatory approval as an interchangeable biosimilar, a higher level of evidence is required than that needed to prove biosimilarity.

First, a sponsor must first demonstrate biosimilarity.

And then, prove that it produces

the same effects in a patient when substituted for the originator product- without any additional risks. If a biosimilar receives an interchangeability designation, it can be substituted at the pharmacy without the intervention of the prescribing physician.

The FDA have established this higher standard for approval because of the potential of biologics to cause immune reactions in the body.

For example, a patient that is clinically stable on a biologic, may be switched to a biosimilar. The small differences between the biologic and the biosimilar may cause an immune reaction in the body that may stop the patient from responding properly to both the biosimilar AND the original biologic, leaving them with no treatment options. It is the role of regulatory authorities to make sure that this possibility is evaluated and eliminated before a biosimilar can be approved as an interchangeable.

The specific data requirements to receive regulatory approval for interchangeability are still being determined by the FDA.



## WHAT IS AUTOMATIC SUBSTITUTION?

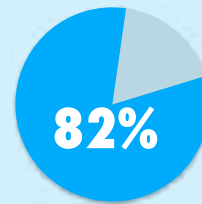
This is the substitution of the originator biologic with the biosimilar by the pharmacist without the intervention of the prescribing physician. **With patient safety in mind, ASBM supports the following principles related to automatic substitution:**

1. Only interchangeable biosimilars should ever be substituted.
2. In the event of a substitution, the pharmacist dispensing the medicine communicates to the physician prescribing the medicine the specific biologic that was dispensed to the patient, who is also notified of the substitution. The result is that everyone involved in patient care knows exactly the medication that the patient received. This allows for the appropriate monitoring of a patient's response to treatment, as well as close tracking of adverse events, and accurate attribution of any problems to the correct product.
3. Physicians retain the right to prevent a substitution they consider inappropriate for their patient by writing 'dispense as written' or "do not substitute" on the prescription.

## Physicians Want to Know Which Medicine Their Patient Receives...



of Biologic Prescribers consider **COMMUNICATION** of a **BIOSIMILAR SUBSTITUTION** "Very Important" or "Critical"



of Biologic Prescribers consider the ability to write "**DISPENSE AS WRITTEN**" or "**DO NOT SUBSTITUTE**" to be "Very Important" or "Critical"

Source: 2015 ASBM Survey of 400 U.S. biologic prescribers. All ASBM surveys available at [www.safebiologics.org](http://www.safebiologics.org)

## IN THE US, AUTOMATIC SUBSTITUTION IS GOVERNED BY THE INDIVIDUAL STATES

As of March 2016, 19 U.S. states and one territory have passed legislation permitting automatic substitution. These include California, Colorado, Delaware, Florida, Georgia, Idaho, Illinois, Indiana, Louisiana, Massachusetts, New Jersey, North Carolina, North Dakota, Oregon, Tennessee, Texas, Utah, Virginia, Washington, and Puerto Rico.

All but one have included requirements for clear and timely pharmacist-physician communication and record-keeping in the event of a substitution. Currently, 20 additional states are considering legislation on this topic. Learn about your State's automatic substitution policy by visiting [www.safebiologics.org](http://www.safebiologics.org).

## AUTOMATIC SUBSTITUTION AROUND THE WORLD

Pharmacy-level substitution is not supported by the European Medicines Agency or Health Canada. Many countries have banned the practice, including UK, Germany, Ireland, Spain, Sweden, Norway, and Finland.

France legally permits it in limited cases but has been unable to implement this policy. Australia is poised to become the only advanced nation to allow automatic substitution. As of March 2016, only Venezuela permits the practice.

*The Alliance for Safe Biologic Medicines is a diverse group of stakeholders including physicians, pharmacists, patients, researchers, and manufacturers of both biologics and biosimilars. ASBM is an organization focused on promoting the use of biologic medicines, while ensuring their safety and efficacy.*

Learn more at [www.safebiologics.org](http://www.safebiologics.org).



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ALLIANCE for SAFE BIOLOGIC MEDICINES

