

# Substituting Interchangeable Biological Products

## (Note)

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### **Background:**

Biological products are a growing class of medicines available to treat disease. Biological products differ from traditional drugs in a few key ways. Biologics are manufactured in living cells, while drugs are manufactured through a chemical process. Many biologics are produced using recombinant DNA technology. Biologics are large, complex molecules, while chemical drugs are much smaller molecules.

A generic drug, a substitute to a brand-name drug developed through a chemical process, is approved by the FDA when analysis demonstrates the same active ingredient, strength, dosage form and route of administration as the brand-name drug. The generic drug becomes available on the market after the patent for the brand-name drug expires. Generic drugs are less expensive. Pharmaceutical companies say the price differential is because the brand-name drugs' costs must recover companies' research and development costs.

Biosimilars, interchangeable biologicals and follow-on biologics are the names given to the "generic" versions of brand-name biologics. These substitutes will not be identical to the brand-name biologic due to the complexity of the manufacturing process. According to a 2014 research report prepared for the Connecticut legislature, the difference in price between generic (chemical) drugs and the brand-name reference drug can be as high as 80 percent. However, the development and approval process costs for a biosimilar are much higher and the difference in price between the original biologic and the biosimilar typically ranges from 15 to 30 percent. At least 14 biosimilars are currently approved for use in the European Union.

The FDA was authorized to approve an expedited pathway for biosimilars and interchangeable biologicals in March 2010 when the Biologics Price Competition and Innovation Act of 2009 was included in the Affordable Care Act. The law provides a 12-year patent protection period for brand-name biologics. While draft guidance for the expedited pathway has been released by the FDA, no final guidance has been approved, nor have any biosimilars been approved for sale in the United States.

Even after an interchangeable biological is approved by the FDA, it must meet additional requirements to be considered "interchangeable." The FDA must determine that the biosimilar can be expected to produce the same clinical result as the brand-name product in any patient and that it has similar safety risks as the brand-name product. At the point that the FDA deems a biosimilar interchangeable, state law will govern how substitutions will be allowed. The first FDA approval was announced March 6, 2015.

### **Biosimilar State Laws: First Round in 2013-14**

In anticipation of FDA approval of interchangeable biologicals, eight states--Delaware, Florida, Indiana, Massachusetts, North Dakota, Oregon, Utah and Virginia--passed bills in 2013 and 2014 to regulate the substitution of biosimilars for brand-name biologics by pharmacists. In California, a bill was passed in the 2013 session but was vetoed by Gov. Jerry Brown. At least 11 other states have considered bills on biosimilar substitution but failed to approve them.

All eight enacted bills restrict substitution to FDA-approved interchangeable biosimilars. Seven of the eight states provide that a pharmacist or assistant can make a substitution unless the prescribing authority indicates a prohibition against substitution. The Indiana law reverses the substitution assumption and allows substitution if the prescribing authority specifically authorizes it. Virginia's law specifically provides that the substitution is not allowed if the patient "insists" on the brand-name biologic. The Utah law requires that the purchaser specifically requests or consents to the substitution.

All states require notice to the patient, or the person receiving the medication, of the substitution of a biosimilar for the name-brand prescribed. The Virginia law, the first in nation to be adopted, requires the label indicate the biosimilar name and manufacturer, and if substituted, the brand-name biologic. Delaware also requires the name of the biosimilar on the label.

All states require the pharmacist provide notice to the prescribing authority of a substitution. Indiana adds that that the prescribing authority also be provided the name of the substitution and the manufacturer. Florida's notification is limited to certain classes of pharmacies placing notice in electronic records.

Record keeping requirements vary across the eight states, from not less than one year to not less than five years for the pharmacies. Indiana, North Dakota, Massachusetts and Virginia also mandate record keeping for the prescribing authority. Utah specifies that the pharmacy record include the name of the substitution and the manufacturer.

Utah's law is the only one that specifies that it applies to out-of-state mail order pharmacies. Delaware, Florida and Indiana require that the state boards of pharmacy maintain on their public websites a listing of FDA approved interchangeable biosimilars.

Certain provisions of the early laws in Utah and Virginia were set to sunset May 1 and July 1, 2015, respectively. Utah subsequently amended its law in 2015 removing the sunset provision altogether. Virginia provisions requiring pharmacists making a substitution to notify the prescriber within five days did sunset on July 1, 2015, as did the requirement that the pharmacist notify a patient of the retail cost of both the prescribed biologic and the interchangeable biosimilar. The Oregon law sunset the physician (prescribing authority) notification provision Jan. 1, 2016.

### **State Laws Adopted in 2015**

In 2015, 11 states passed legislation addressing interchangeable biological products. Utah amended its 2013 law, removing the sunset set for 2015. Eighteen states and Puerto Rico have passed laws to regulate the substitution of interchangeable biologics. One state, Idaho, made changes to its Board of Pharmacy regulations, bypassing legislation.

In 2014, the leading companies involved in biologic, biosimilar and interchangeable biologics met and agreed to principles related to pharmacist-prescriber communication provisions in state legislation. Eighteen manufacturers of biologics have currently signed on as members of the biosimilar coalition. The principles agreed to are:

- State pharmacy laws should be updated to enable pharmacy substitution of only interchangeable biologics, as approved by the FDA.
- In settings where interoperable electronic health records, or EHR, are in place, entry by the pharmacist of the biologic product dispensed shall satisfy requirements for pharmacist-prescriber communication.
- In instances where EHR are not yet available, the pharmacist shall communicate the dispensing of a biologic product to the prescriber, using any prevailing means, provided that communication shall **not** be required where:
  - There is no FDA-approved interchangeable biologic for the product prescribed; or
  - A refill prescription is not changed from the product originally dispensed.
- Other provisions related to the dispensing of a biologic product shall replicate state law pertaining to small molecule products, including that the patient is aware of the medicine they receive, physicians retain dispense-as-written authority and pharmacy records are retained.

## Substituting Interchangeable Biological Products

Bill / Law	Signed by Governor	Prescribing authority approval / prohibition of biosimilar substitution	Notice of biosimilar substitution to patient	Notice of biosimilar substitution to prescribing authority	Record keeping requirements	Sunset	Other
<a href="#">Virginia HB 1422</a>	First adopted 3/16/2013	Can substitute unless prescribing authority indicate "brand medically necessary" <b>or</b> patient insists on brand	Yes; label with substitution and manufacturer, and if substituted, label as such with brand name	Pharmacist must notify prescribing authority.	Pharmacy and prescribing authority for not less than 2 years	7/1/2015: Notifying prescriber; notifying patient of retail cost comparison	
<a href="#">North Dakota SB 2190</a>	3/29/2013	Can substitute unless prescribing authority indicates prohibition	Yes	Pharmacist must notify prescribing authority	Pharmacy and prescribing authority keep records not less than 5 years		
<a href="#">Utah SB 78</a>	4/1/2013	Can substitute unless prescribing authority indicates prohibition <b>and</b> the purchaser specifically requests or consents to the substitute	Yes	Pharmacist must notify prescribing authority	Name of substitution and manufacturer on file copy	5/15/2015	Applies to out-of-state mail service pharmacies
<a href="#">Florida HB 365</a>	5/31/2013	Can substitute unless prescribing authority indicates prohibition	Yes	In certain class of pharmacies, enter into electronic medical record	Pharmacy keeps records not less than 2 years		Requires Board of Pharmacy to maintain website listing of FDA-approved substitutions
<a href="#">Oregon SB 460</a>	6/6/2013	Can substitute unless prescribing authority indicates prohibition	Yes	Pharmacist must notify prescribing authority	Pharmacy keeps records not less than 3 years	Physician notification sunsets 1/1/2016	Requires Board of Pharmacy to maintain website listing of FDA-approved substitutions
<a href="#">Indiana SB 262</a>	3/25/2014	Prescribing authority has indicated "may substitute"	Yes	Notice of name and manufacturer of substitution to prescribing authority	As already required under law (2 years for pharmacy and 7 years for prescribing authority)		Requires Board of Pharmacy to maintain website listing of FDA-approved substitutions
<a href="#">Delaware Senate Substitute 1 for SB 118</a>	5/28/2014	Can substitute unless prescribing authority indicates prohibition	Yes	Pharmacist must notify prescribing authority			Requires Board of Pharmacy to maintain website listing of FDA-approved substitutions
<a href="#">Massachusetts H 3734</a>	6/24/2014	Can substitute unless prescribing authority indicates prohibition	Yes	Pharmacist must notify prescribing authority	Pharmacy, prescribing authority and administering practitioner no less than 1 year		

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<a href="#">Utah HB 279</a>	3/27/2015				Within 5 business days, name of product and manufacturer (electronic and/or other mediums)	Removes 5/15/2015 sunset	Amends 2013 law. Deletes “biosimilar” and defines “interchangeable biological product”
<a href="#">Colorado SB 71</a>	4/3/2015	Can substitute if FDA has determined biological product is interchangeable and if practitioner has not indicated that the prescription must be dispensed as written	No	Pharmacist must notify prescribing authority	Within a reasonable amount of time in an electronic system, the name of the product and manufacturer; pharmacy must keep records for 2 years		Board must maintain on website link to FDA resource that identifies all approved interchangeable biological products
<a href="#">Tennessee SB 984</a>	5/4/2015	Can substitute unless the prescriber indicates intent to dispense as written	Yes, noting the substitution on the prescription label	Specific product provided to the patient, including the name of the product and the manufacturer	Within reasonable time, electronic prescribing technology or a pharmacy record that is electronically accessible by the prescriber. Otherwise, the pharmacist shall use facsimile, telephone, electronic transmission, or other prevailing means		The board of pharmacy shall maintain a link on its web site to the current list of all biological products determined by the FDA to be interchangeable biological products.
<a href="#">Georgia SB 51</a>	5/6/2015	May substitute when there is an interchangeable biological product. If a practitioner prescribes a biological product by its nonproprietary name, the pharmacist shall dispense the lowest retail priced interchangeable biological product in stock. A patient may instruct the pharmacist not to substitute an interchangeable biological product.	Yes, on prescription label, state the fact there has been a substitution and disclose the identity and manufacturer of the dispensed product	Yes, product name and manufacturer	Must communicate with prescriber of the product by entry of record on an electronic med recs system within 48 hours		The board shall maintain a link on its website to the current list of all biological products determined by the FDA to be interchangeable with a specific biological product.

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<a href="#">Washington SB 5935</a>	5/11/2015	Can substitute unless the prescribed biological product is requested by the patient or the patient's representative	Yes	Yes	Within five business days following the dispensing of a biological product, either the name of the product and the manufacturer or the FDA code.		The pharmacy quality assurance commission shall maintain a link on its website to the current list of all biological products determined by the FDA as interchangeable.  Pharmacies must post sign that substitution is allowed with consent of physician.
<a href="#">North Carolina HB 195</a>	5/21/2015	Can dispense prescription of interchangeable biological product if it meets the following: manufacturer/distributor's names are on the label of the package, manufactured in accordance with good manufacturing practices, manufacturer has adequate provisions for drug recall and return of outdated drugs	Yes, on prescription label	Must communicate by electronic medical records	Within a reasonable time following dispensing		Board of Pharmacy must maintain web link to FDA list of approved interchangeable biological products
<a href="#">Texas HB 751</a>	6/19/2015	Can dispense biological product as long as it costs less than the prescribed drug or product. Must inform patient there is a less expensive product available, ask patient to choose between the biological product.	Yes, record on the prescription form and prescription label.	Yes. Not required if there is no interchangeable product or if a refill is not changed from the product dispensed on the prior filling	No later than the third business day after dispensing	Section 5 about communication regarding dispensed biological product expires 9/1/2019.	Board shall link to FDA list of approved interchangeable biological products.
<a href="#">Louisiana HB 319</a>	7/1/2015	Can substitute unless prescribing authority indicates prohibition	No	Yes, unless there is no interchangeable equivalent biological product approved by FDA	No later than 5 business days after dispensing by any means of communication		*This bill only addresses notifying the prescriber

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<a href="#">Illinois SB 455</a>	7/30/2015	Can be substituted if drug is deemed interchangeable by FDA, if the prescribing physician does not indicate that substitution is prohibited, if the pharmacy informs the patient of the substitution	Yes	Yes	No later than 5 business days after dispensing by electronic records; records to be maintained for 5 years		The Dept. shall maintain a link on its website to the current list of all biological products determined by the FDA to be interchangeable with a specific biological product.
<a href="#">California SB 671</a>	10/6/2015	Approved, only if biological product selected is not the same or of lesser cost than the prescribed product. Cannot substitute if prescriber does not indicate a substitution cannot be made.	Yes	Yes, electronically accessible record	No later than 5 business days after dispensing by electronic records		California State Board of Pharmacy shall link to FDA list of approved interchangeable biological products.
<a href="#">New Jersey AB 2477</a>	11/9/2015	Allowed, only if authorized prescriber indicates there should be no substitution, if it's determined by FDA to be interchangeable or equivalent	Yes, recorded on prescription label	Yes, including name of product and manufacturer	No later than 5 business days after dispensing		Every pharmacy or drug store selling biological products shall post sign no smaller than 12" x 12" at the entrance disclosing that upon request, consumer is told of the price savings for a substitution