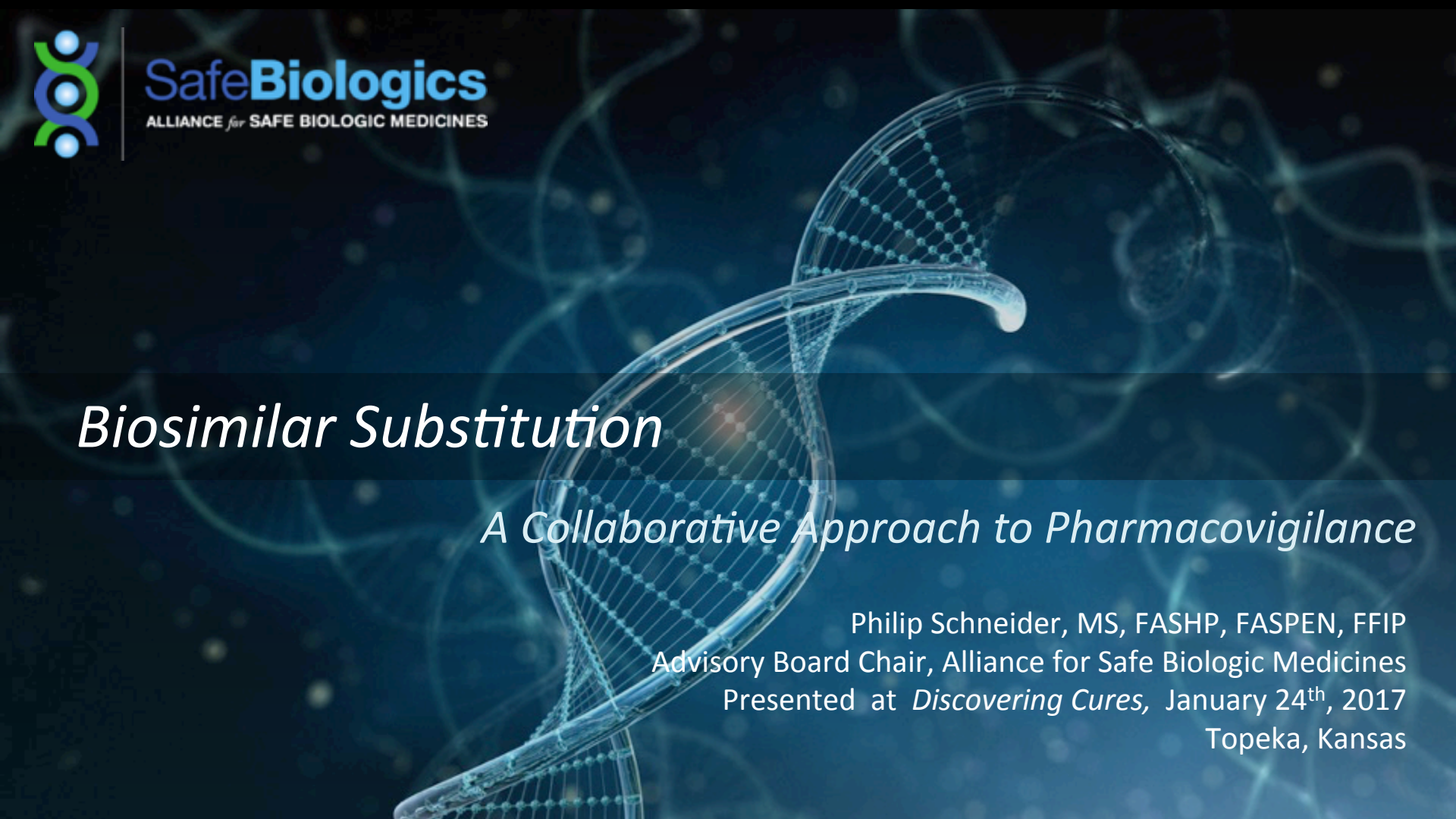

Biosimilar Substitution

A Collaborative Approach to Pharmacovigilance

Philip Schneider, MS, FASHP, FASPEN, FFIP
Advisory Board Chair, Alliance for Safe Biologic Medicines
Presented at *Discovering Cures,* January 24th, 2017
Topeka, Kansas

About The Alliance for Safe Biologic Medicines (ASBM)

Harry L. Gewanter, MD, FAAP, FACR: Chairman, pediatric rheumatologist

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- Steering Committee composed of patient and physician groups.
- Advisory Board of physicians, researchers, pharmacists, and patients.

Recap: What is a Biosimilar?

- Biosimilars are sometimes incorrectly referred to as “generic” biologics.
- However, unlike with generic copies of chemical medicines, their greater complexity and fact that they are made using living cells means biologic medicines cannot be copied exactly.
  It can only ever be “similar” to its reference biologic.
- Seemingly minor differences between biosimilar and reference can produce unexpected effects- including reduced efficacy and unwanted immune responses.
- “Interchangeable” biosimilars are those which pharmacists will potentially be able to substitute.

Interchangeability

A US-Specific higher regulatory standard to meet. More data is required.

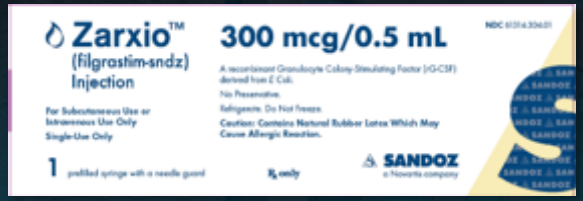
An "INTERCHANGEABLE" Biosimilar :

1) Must be **biosimilar** ("highly similar" to reference product).
2) Must have **same clinical result** expected as with reference product.
3) Must create **no additional risk to patient** when switching back and forth between itself and reference product.
4) **May be substituted for the reference product without the intervention of the prescriber.**

Nevertheless, 26 states and Puerto Rico have adopted laws requiring pharmacist-physician communication whenever biosimilar substitution is a possibility.

Four Biosimilars Approved in U.S., One Currently Available

Zarxio (filgrastim-sndz)
March 6, 2015
15% discount over reference product



Inflectra (infliximab-dyyb)
April 6, 2016
15% discount over reference product

inflectra®

Erelzi (etanercept-szzs)
August 30, 2016

Erelzi™
(etanercept-szzs)

Amjevita (adalimumab-atto)
September 27, 2016

AMJEVITA

Biosimilar Substitution

How do the EU and Canada Handle the Role of Physicians in Substitution of Biosimilars?

- The EMA advises that: "the physician should be in charge of the decision to switch between the reference and biosimilar, or vice versa."[1]
- "Health Canada does not support automatic substitution of a Subsequent Entry Biologic for its reference biologic drug and recommends that physicians make only well informed decisions regarding therapeutic interchange".[2]

1 European Medicines Agency. Questions and Answers on Biosimilar Medicines (Similar Biological Medicinal Products). London: European Medicines Agency; 2012. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Medicine_QA/2009/12/WC500020062.pdf. Accessed November 6, 2012.

2 http://www.hc-sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/seb-pbu/01-2010-seb-pbu-qa-qr-eng.php

Automatic Substitution around the World

OPPOSED by European Medicines Agency and Health Canada.

BANNED in many countries including the UK, Germany, Ireland, Spain, Sweden, Norway, and Finland.

France statutorily PERMITS in LIMITED CASES (bio-naïve patients), this policy has *never been implemented.*

Automatic Pharmacy Substitution around the World




Latin America - RANGE OF POLICIES, some physician prescribing autonomy, some do not. In those instances where physicians have "DAW" protections, enforcement is not always consistent.

Australia about to ALLOW pharmacy-level substitution of a biosimilar without physician involvement, over opposition of the Australian Rheumatology Association.

U.S. policy is evolving, but 26 states and Puerto Rico have passed laws which ALLOW "INTERCHANGEABLE" biosimilars to be substituted, providing pharmacists to communicate to physicians which product was dispensed.

Substitution Policy in the U.S.

CONGRESS

- Sets Legal definition
- Interchangeable: substitution without physician intervention

FDA

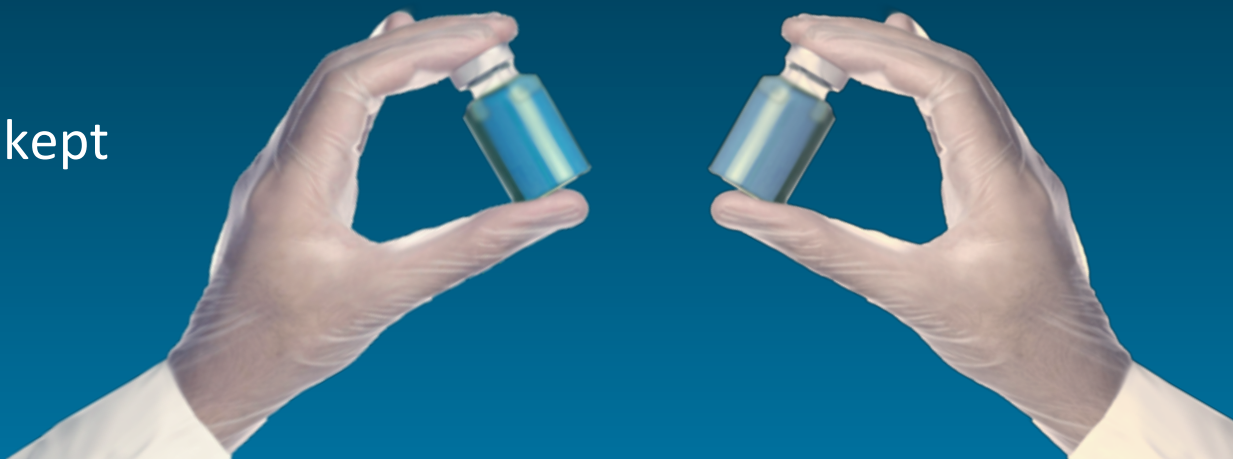
- Makes Scientific decisions
- Sets Interchangeability criteria

STATES

- Decides what pharmacists are allowed to do

Issues Surrounding Biosimilar Substitution

- Under what circumstances may a pharmacist substitute a biosimilar without the involvement of the physician?
- What communication is required between pharmacist and:
  - Physician
  - Patient
- What records must be kept of the substitution?



Why These Issues are Important

PATIENT
needs to be informed about the medicine he/she is receiving in order to make informed choices and be an effective partner in care.

REGULATORS & PHARMACISTS
Accurate patient records must be kept for pharmacovigilance/ post-market monitoring for adverse events and efficacy

PHYSICIAN
needs to be aware of what medicine patient receives to provide proper care.

PHYSICIANS & PHARMACISTS
have a responsibility to the patient and larger community to work collaboratively together- this includes clear, timely communication.

Prescriber Surveys: How Important is Communication of a Biosimilar Substitution? N=400

85% *of Canadian physicians consider it "very important" or "critical"*

77% *of EU Physicians consider it "very important" or "critical"*

80% *of US physicians consider it "very important" or "critical"*

87% *of Latin American Physicians consider it "very important" or "critical"*

Prescriber Surveys: How Important is "Dispense as Written" (DAW) Authority? (n=400)

80% *of Canadian physicians consider it "very important" or "critical" (2014)*

74% *of EU physicians consider it "very important" or "critical" (2013)*

82% *of US physicians consider it "very important" or "critical" (2012)*

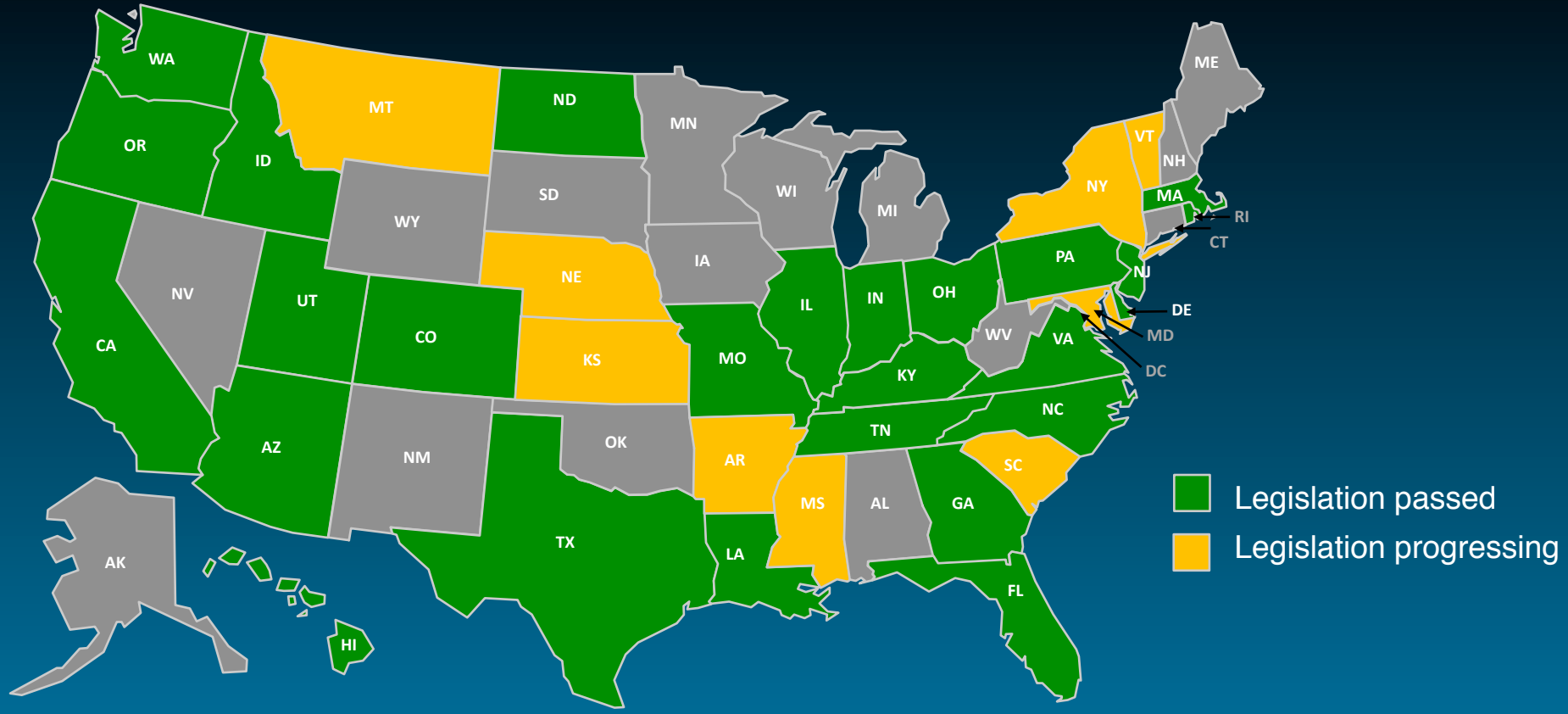
85% *of Latin American physicians consider it "very important" or "critical" (2015)*

Common Features of U.S. Substitution Laws

- Permits only substitution of "interchangeable" biosimilars.
- Require pharmacist to communicate which product – biosimilar or reference- was dispensed to patient within 5 days.
- Allow physician to specify "do not substitute", "dispense as written" or similar.
- Pharmacist to keep records for 2-5 years.

- 2013: VA, FL, OR, ND
- 2014: IN, DE, MA, ID
- 2015: TX, UT, CO, TN, GA, WA, NC, LA, IL, PR, CA, NJ
- 2016: Passed in AZ, HI, KY, MO, PA, OH. Similar bills being considered in MI, NE, NY, and elsewhere.

Physician-Pharmacist Communication Requirements by US State
January 2017



Rev. 1/22/17

Criticisms of U.S. Substitution Legislation

- Legislation premature? There are NO biosimilars in the United States marketplace.
- Premature laws create confusing patchwork of state substitution laws.
- Could legislation undermine public confidence in biosimilar medicines?

- First biosimilar approved March 6, 2015; Four approved currently. Draft Interchangeability Guidance released last week.
- Pharmacists, physicians need to work together to educate lawmakers, and create a standard for these laws that works for all.
- Physicians defaulting to "do not substitute" as only means of knowing what patient is receiving would also undermine biosimilar adoption.

Initial Resistance from Pharmacists

- Additionally, many **state pharmacy societies** had concerns that the word “notify” implied they were subservient to physicians, and preferred the word “communicate”, which implies collaboration.
- **Pharmacies** also considered the initial timeframe allotted for notification, and the length of the record-keeping provisions to be onerous.
- While helping patients and physicians, bills also **empower pharmacists** to offer lower-cost alternatives to patients without seeking authorization from physicians.
- Yet as they were made aware of the benefits the communication provisions offer to patients, they have dropped their opposition and the legislation passed.

The issue has **largely faded as an issue of debate** among the two national pharmacy societies, ASHP and APhA.

Collaboration among Pharmacists, Physicians, Manufacturers on substitution bills has resulted in improved legislation :

2013 Bill Language		2016 Bill Language
"Notification"	→	**"Communication"**
Notification **only if biosimilar substituted**	→	Communication of which biologic was was dispensed- **innovator / biosimilar**
72 hours to notify	→	**5 days** to communicate
Must retain records for **5 years**	→	Must retain records for **2 years**

Timing of Communication

- The timing of the communication process must not impose an undue burden on the pharmacist
- Communication of a substitution is after dispensing

- Must be timely enough to facilitate accurate record keeping and attribution of adverse events by the physician.

Kansas Bill: HB 2107

- A pharmacist MAY substitute a biological product for a prescribed biological product only if:
  - FDA has determined it to be interchangeable
  - Prescriber does not designate on prescription "dispense as written"
  - Patient/patient's representative receives notification of the substitution
- Pharmacist communicates to physician within 3 days which product was dispensed (except refills).
- Records must be kept for 5 years.

Physician/Pharmacist Collaboration is Key

Physicians and pharmacists should **work collaboratively** to ensure that the treating physician is aware of the exact biologic – by manufacturer – given to a patient in order to facilitate patient care and accurate attribution of any adverse events that may occurs.

Thank You For Your Attention