SafeBiologics
ALLIANCE *for* SAFE BIOLOGIC MEDICINES

A Collaborative Approach to Pharmacovigilance: The Physician's Perspective

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Endocrinologist
Chairman, the Alliance for Safe Biologic Medicines

Presented at "*Ensuring Access to Safe Biosimilars: Policy Developments and Emerging Challenges*"
Washington, DC
Feb. 25, 2014

Collaborative Approach: Communication Between Physician and Pharmacist is Key to Good Pharmacovigilance.

Physician concerns when using drugs:

- **Quality:** Will the drug be safe and effective?
- **Interchangeability:** What data are necessary to establish this?
- **Substitution:** When? By whom?
- **Naming:** Should biosimilars have distinguishable names?

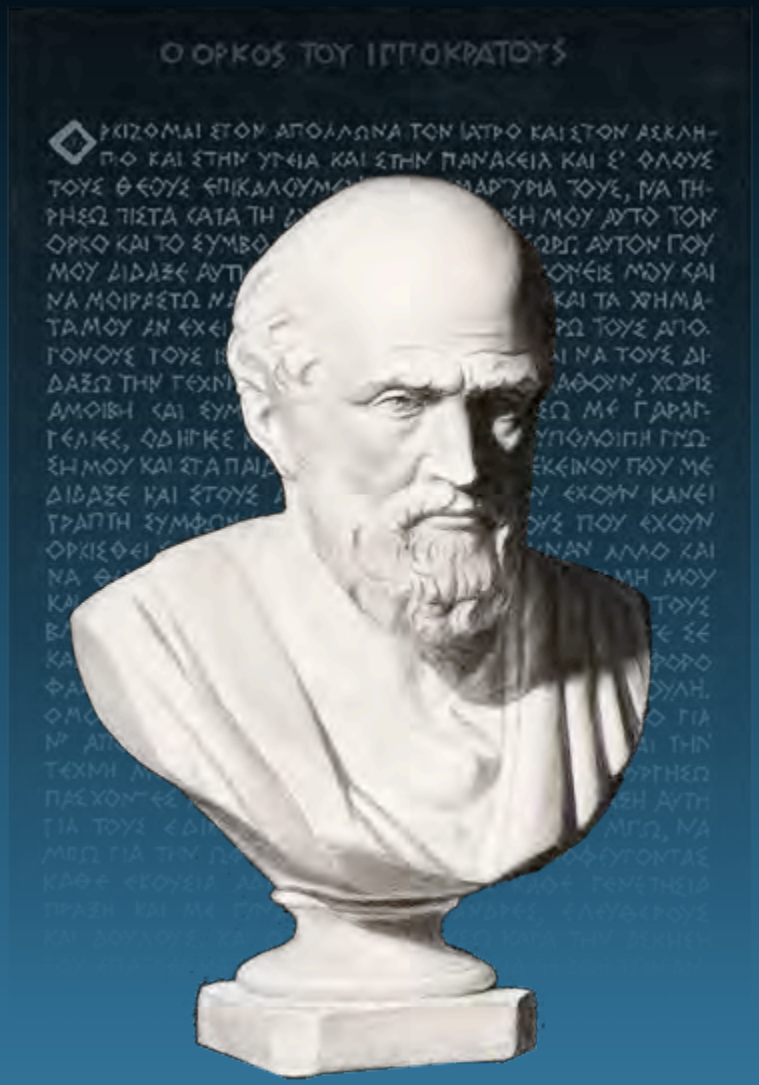
ASBM Prescriber Surveys

ASBM has conducted two surveys that examine the perspectives of the physicians who prescribe biologics.

- *U.S. Prescriber Survey (September 2012) 376 Physicians*
- *E.U. Prescriber Survey (November 2013) 470 Physicians*

A Physician's Guiding Principles

- Patient safety is paramount.
- Information is power: the more we know, the better for patients.
- Data is required to ensure confidence.



Hippocratic Oath: "first, do no harm"

Physicians and Pharmacists Must Know What the Patient Receives.

Review: Biologic vs. Chemical Medicines

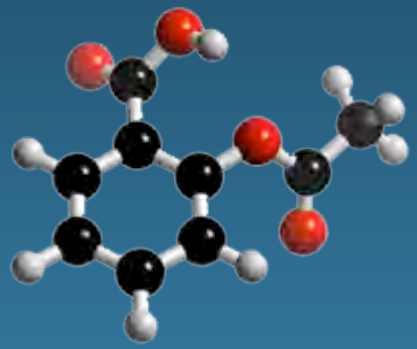
SIZE: significantly larger

STRUCTURE: more complex

STABILITY: susceptible to light, heat, denaturing / degradation

SENSITIVITY: small manufacturing changes can cause AE's

DRIFT: can change with time



Confusion can result with identical naming…

Eprex® (**epoetin alfa**)

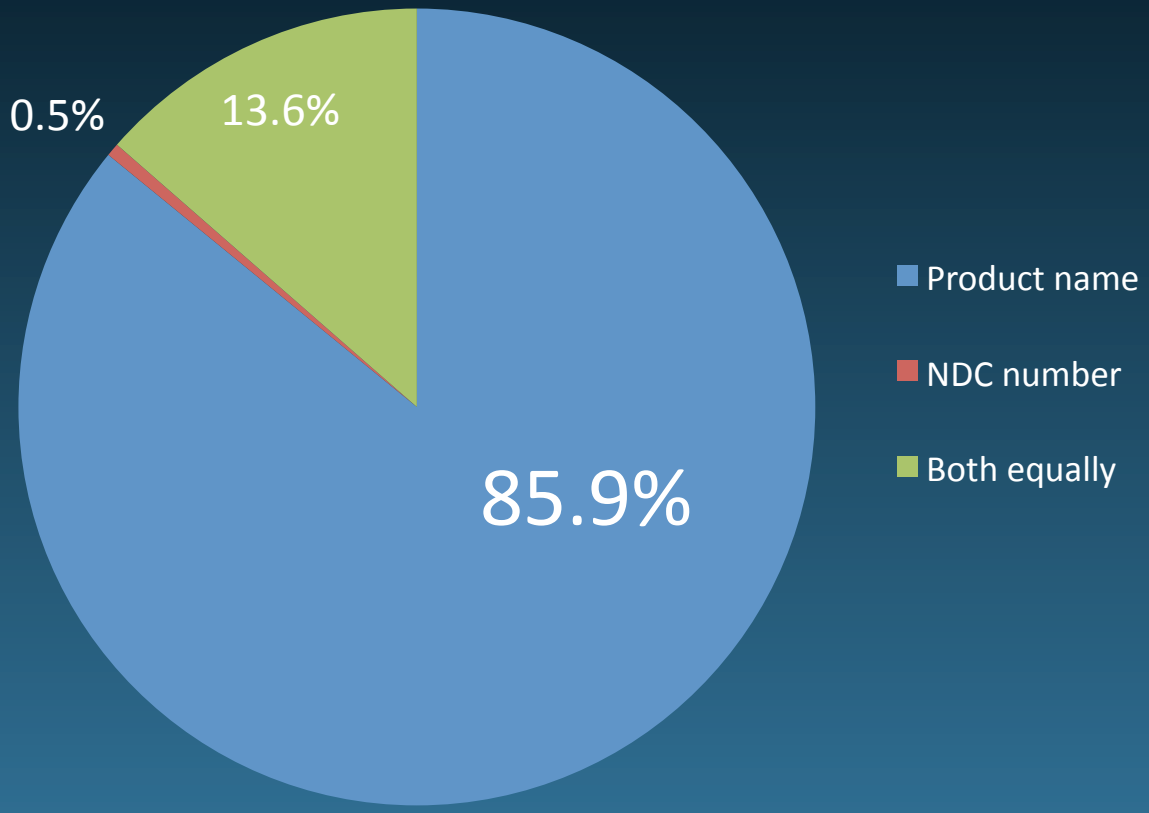
Binocrit™ (**epoetin alfa**)

Abseamed (**epoetin alfa**)

Epoetin alfa Hexal (**epoetin alfa**)

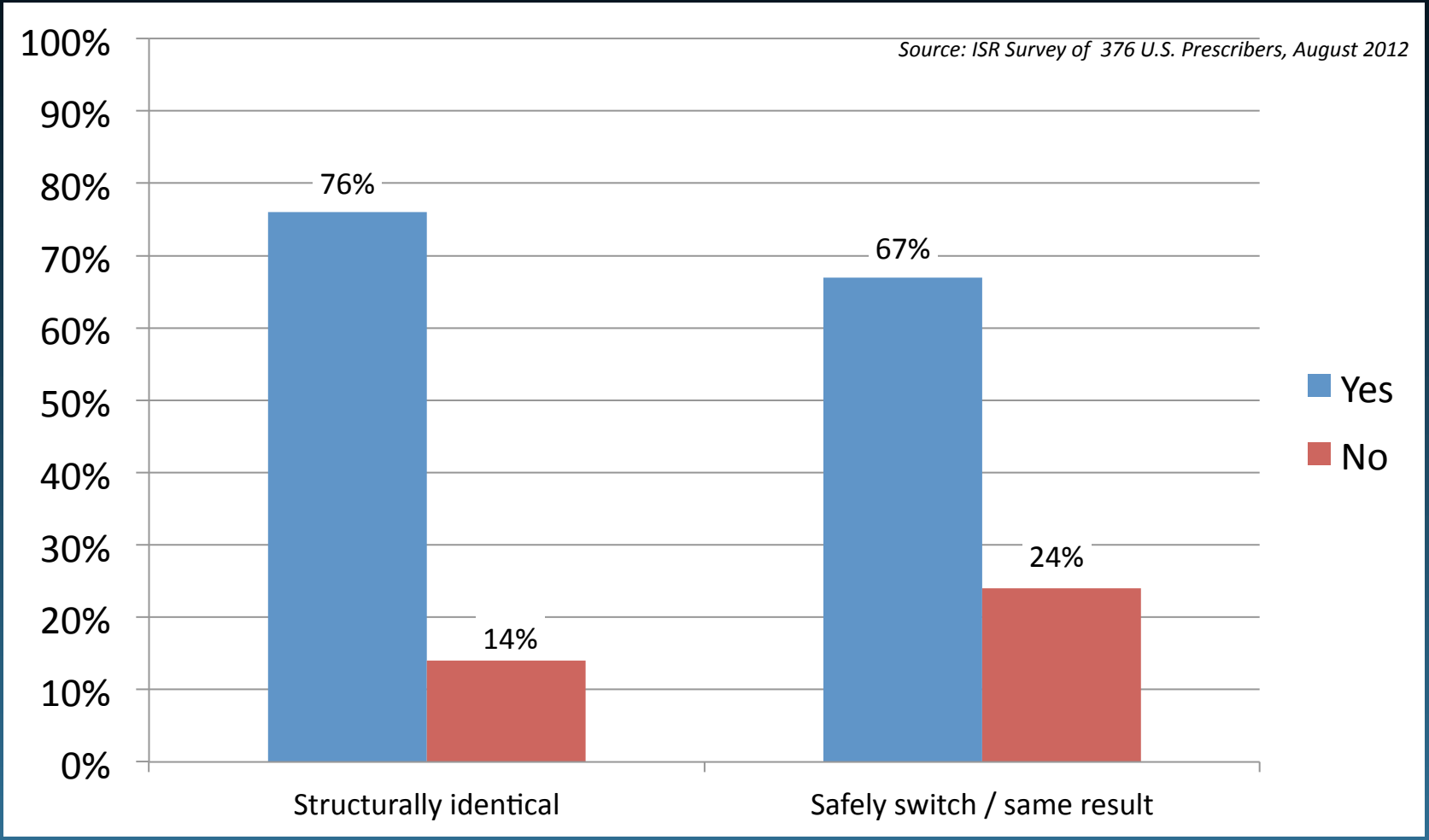
IF ONE OF THESE GENERATES AN ADVERSE EFFECT IN THE PATIENT, WILL THE DOCTOR KNOW WHICH ONE?

Names or numbers? A strong majority (86%) of physicians prefer using product names for identifying adverse events



Source: ISR Survey of 376 U.S. Prescribers, August 2012

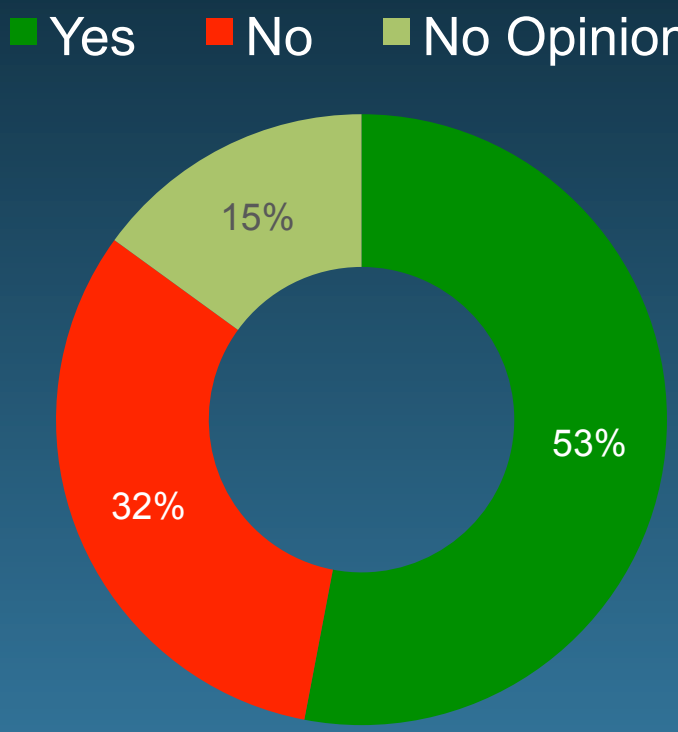
What U.S. Physicians think Identical Naming means…



Identical names, even with extensive patient and physician education, would result in inappropriate substitution.

European Prescriber Survey Results: Non-proprietary name implications – Structurally Identical?

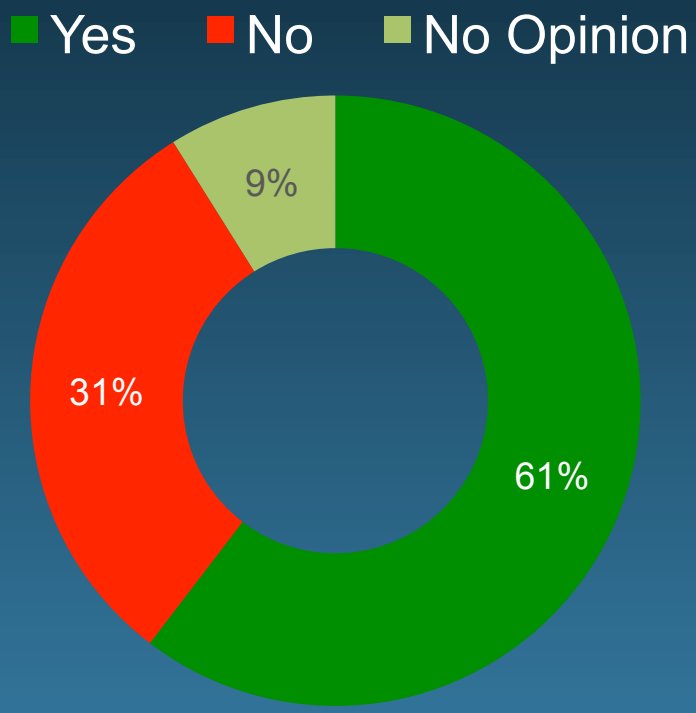
"If two medicines have the same non-proprietary scientific name, does this suggest to you or imply that the medicines are structurally identical?" (N=470)



Industry Standard Research Survey of 470 Prescribers in Europe, 2013

European Prescriber Survey Results: Non-proprietary name implications – Approval

"If two medicines have the same non-proprietary scientific name, does this suggest to you or imply that the medicines are approved for the same indications?" (N=470)



Industry Standard Research Survey of 470 Prescribers in Europe, 2013

Manufacturers must be transparent

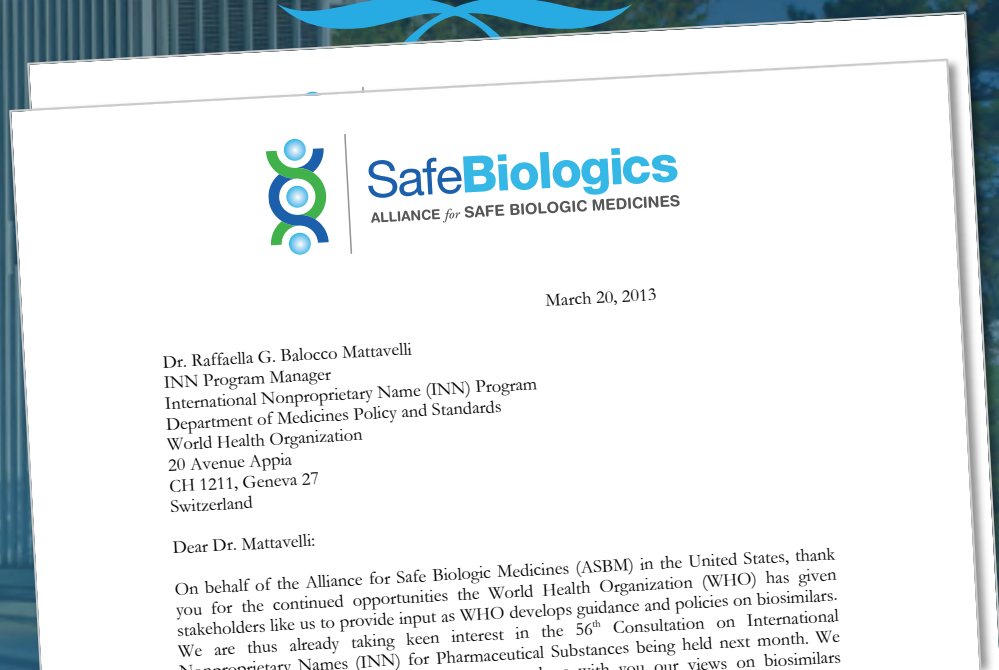
- **Track and trace** of biologics is more challenging than with chemical drugs. Adverse impact may go unrecognized in patients for months.
- **Patient response** must be traced to the correct manufacturer's product.
- **Multiple means of product identification** avoid a single point of information failure.
- **Unique naming** provides transparency and helps differentiate **products for observing and reporting adverse events.**
- Patients and their caregivers are the **last line of defense - unique names ensure that they can accurately identify the product.**

ASBM Sent Letters to WHO in Advance of 56th and 57th Consultations on International Nonproprietary Names (INN) and Presented at the INN Open Session for Stakeholders – October 22, 2013

"Product naming is an important element of biologic safety. We firmly advocate that all biologics should receive **distinct non-proprietary names** to ensure products will be distinctly identified **to facilitate accurate attribution of adverse events.**

The non-proprietary name of a reference product and product/s biosimilar to it, should have a **common, shared root** but have distinct and **differentiating prefixes or suffixes** as a means of facilitating clear adverse event reporting.

Furthermore, as we have expressed in the past to FDA, we believe that instituting a system of **unique names** for biologic medicines will achieve the common goal of enhancing access to life-changing therapies, while also **protecting the safety of the patients we represent**."



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March 20, 2013

Dr. Raffaella G. Balocco Mattavelli
INN Program Manager
International Nonproprietary Name (INN) Program
Department of Medicines Policy and Standards
World Health Organization
20 Avenue Appia
CH 1211, Geneva 27
Switzerland

Dear Dr. Mattavelli:

On behalf of the Alliance for Safe Biologic Medicines (ASBM) in the United States, thank you for the continued opportunities the World Health Organization (WHO) has given stakeholders like us to provide input as WHO develops guidance and policies on biosimilars. We are thus already taking keen interest in the 56th Consultation on International Nonproprietary Names (INN) for Pharmaceutical Substances being held next month. We

WHO Solution: The Unique Global Biological Qualifier (BQ)

October 22, 2013
Proposed at the 57th Consultation on International Nonproprietary Names:

- A global coding system of random letters assigned to biosimilar by INN Secretariat to ensure unambiguous identification.
- Would require voluntary cooperation, avoiding assignment of non-unified qualifiers by individual regulatory bodies.
- Proposal has the support of representatives from Japan and Australia, which have or are developing their own BQ standards, but expressed willingness to conform with the global standard.
- Unclear whether EMA will support a BQ

✓ World Health Organization

✓ pmda JAPAN

✓ Australian Government
Department of Health
Therapeutic Goods Administration

✗ EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Safe Substitution of Biosimilars

Congress defined 2 different levels of biosimilar.

BIOSIMILARS:

- HIGHLY Similar

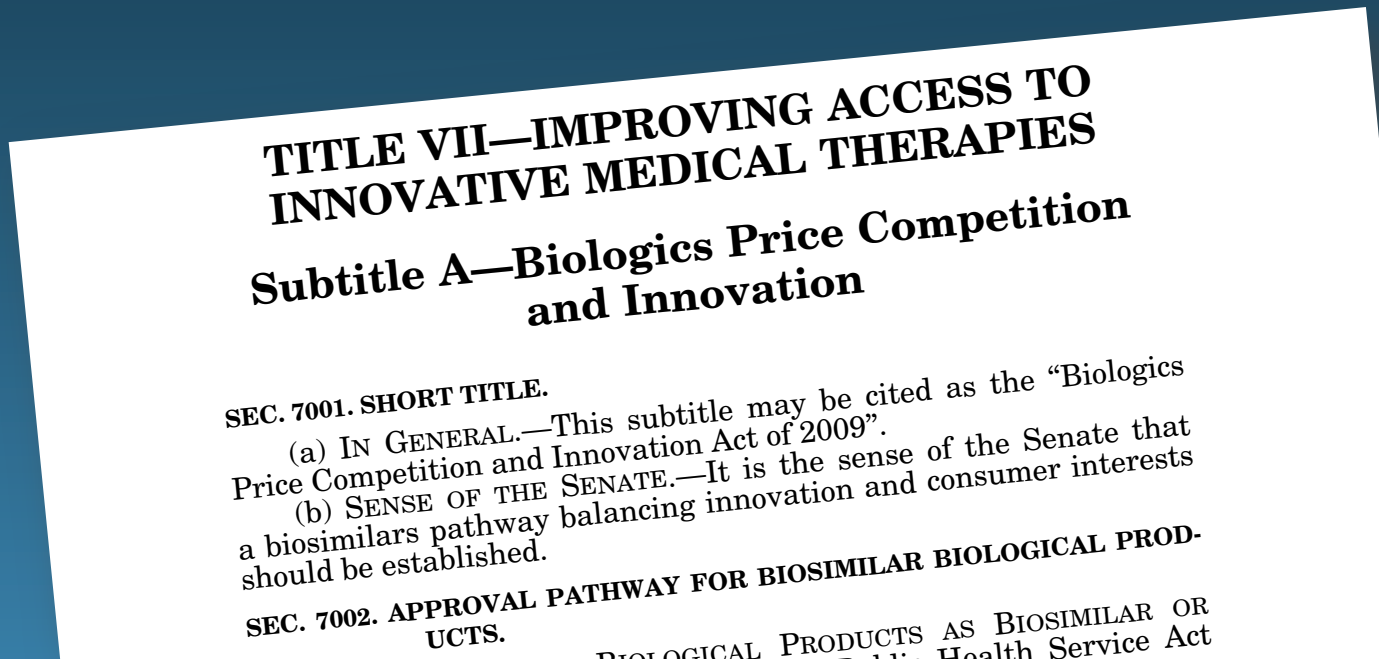
INTERCHANGEABLE BIOSIMILARS:

- HIGHLY Similar
- SAME EFFECT is EXPECTED in ANY given PATIENT
- NO ADDED RISK from switching

What Does The Law Say About Interchangeability?

Biologics Price Competition and Innovation Act,
Section (351)(i)(3)

‘‘(3) The term ‘interchangeable’ or ‘interchangeability’… means that the **biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.**



TITLE VII—IMPROVING ACCESS TO INNOVATIVE MEDICAL THERAPIES

Subtitle A—Biologics Price Competition and Innovation

SEC. 7001. SHORT TITLE.

(a) IN GENERAL.—This subtitle may be cited as the “Biologics Price Competition and Innovation Act of 2009”.

(b) SENSE OF THE SENATE.—It is the sense of the Senate that a biosimilars pathway balancing innovation and consumer interests should be established.

SEC. 7002. APPROVAL PATHWAY FOR BIOSIMILAR BIOLOGICAL PRODUCTS.

BIOLOGICAL PRODUCTS AS BIOSIMILAR OR
Health Service Act

Who decides if substitution is allowed?

CONGRESS
- Legal definition
- Interchangeable: substitution without physician intervention

FDA
- Scientific decision
- Interchangeable criteria

STATES
- Application
- Decide what pharmacists are allowed to do

What is "Automatic Substitution"?

1) Prescriber writes a prescription

2) Pharmacist is allowed, or required, by state law to provide a different medicine to the patient without consulting prescriber

In fact, today NO EUROPEAN COUNTRY, OR CANADA ALLOWS Automatic Substitution:

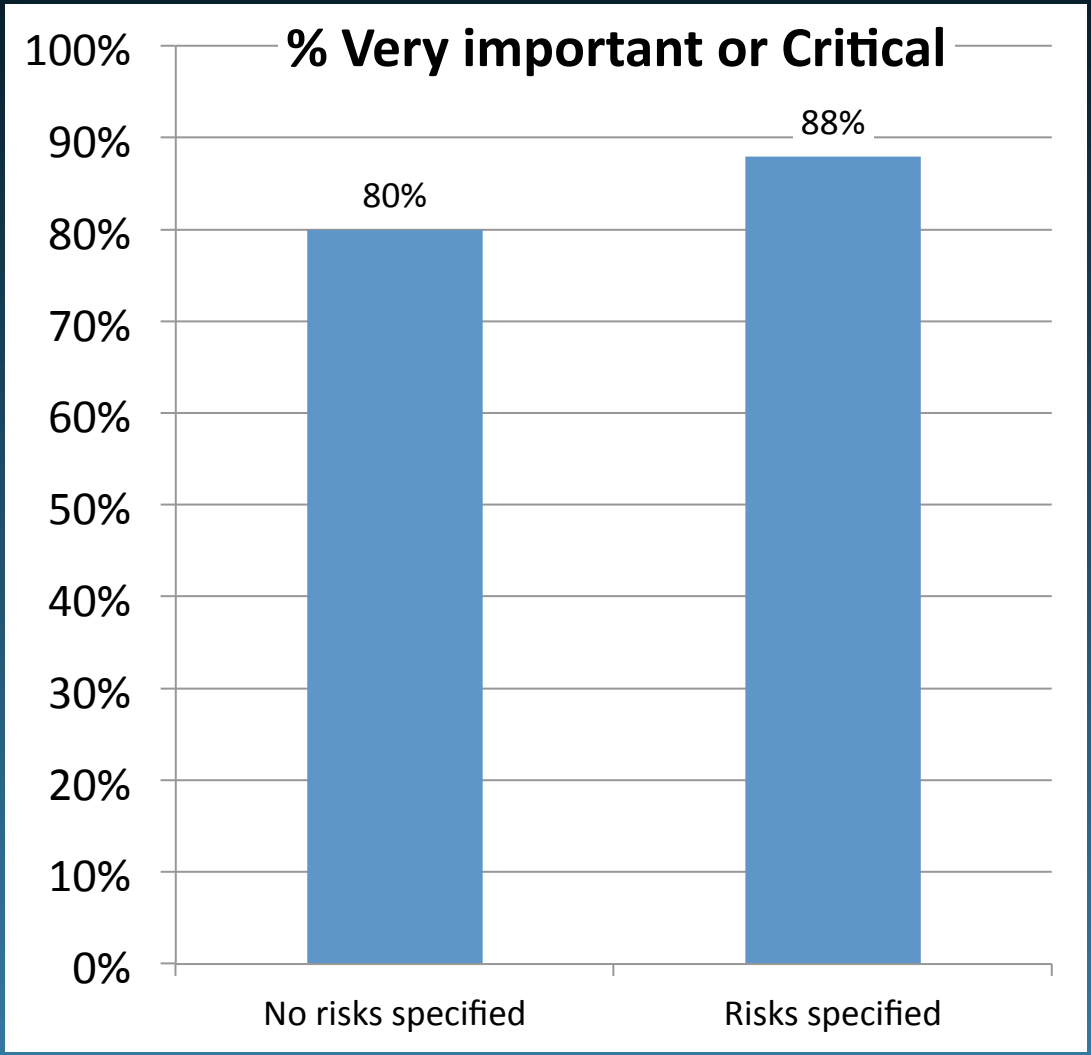
What do Clinicians Say about Biologic Substitution?

U.S. Survey Results: Importance of Notification of Medication Switching: With and Without Known Risks

Question: How important would it be for you to be notified by the pharmacist that your patient has received a biologic other than the one you prescribed

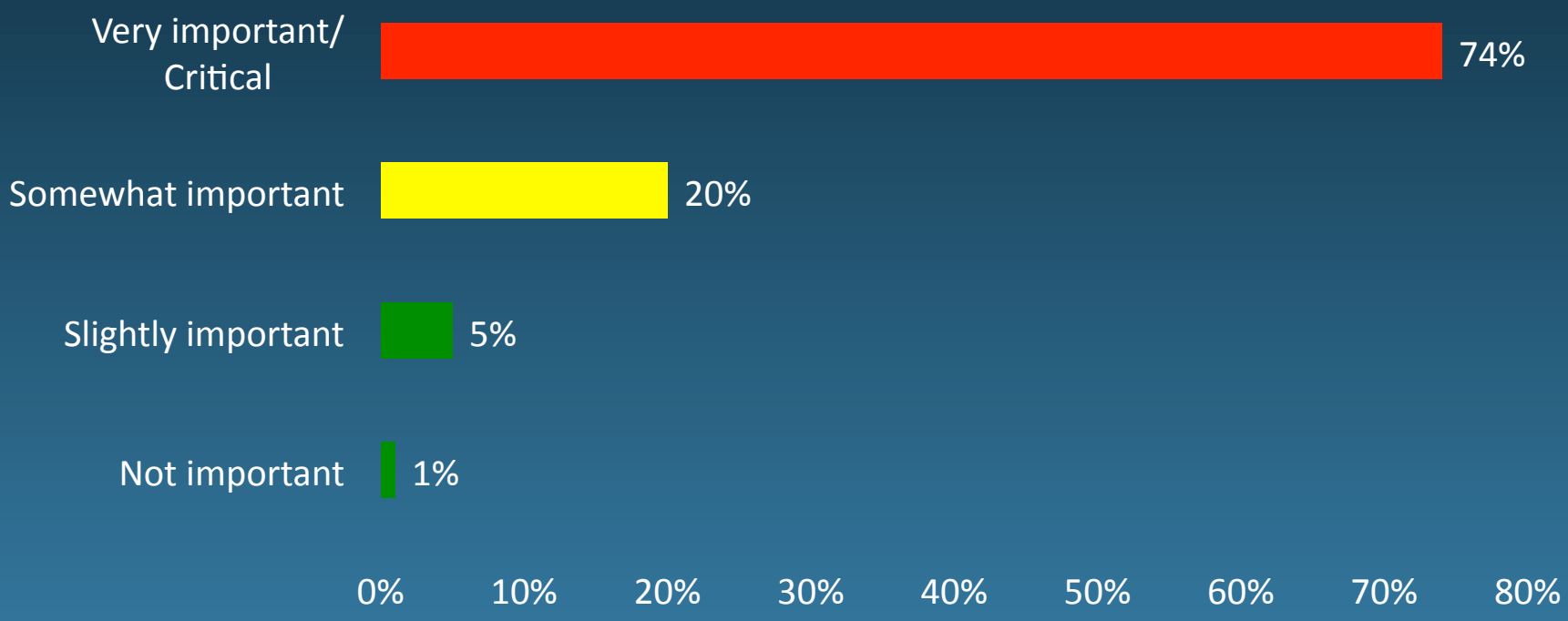
…if you were aware that the product **could cause an unwanted immune response** in some patients or that **small differences between brands could have clinical implications for patients?**

Survey of 376 physicians who prescribe biologics



European Prescriber Survey Results: Importance of DAW Authority

"In a situation where substitution by a pharmacist was an option in your country, how important would it be to you to have the authority to designate a biologic medicine as 'DISPENSE AS WRITTEN' or 'DO NOT SUBSTITUTE'?" (N=470)



Industry Standard Research Survey of 470 Prescribers in Europe, 2013

Early Indications From States

- Concerns about a lack of uniformity and patchwork approach.
- Cost pressures great.
- Likely there will be some states where PHYSICIANS WILL NOT BE NOTIFIED after a substitution has occurred.

Standard-Examiner

Biosimilar drug bill clears hurdle

02/20/2013

SALT LAKE CITY — A local lawmaker's push to help facilitate the introduction of biosimilar drugs to the Utah market has cleared a key committee hurdle. SB 78, sponsored by Sen. Stuart Adams, R-Layton, received a favorable recommendation in a Senate committee Wednesday and now advances to the Senate for further review.

Herald-Tribune

'Biosimilar' drug bill passes

By Lloyd Dunkelberger, Herald-Tribune
/ Tuesday, February 19, 2013

TALLAHASSEE- The battle over biosimilar drugs moved ahead today in the Florida House, as the Health Quality Subcommittee approved a bill that would create standards for using a new wave of pharmaceutical products that are expected to gain in popularity in the next few years.

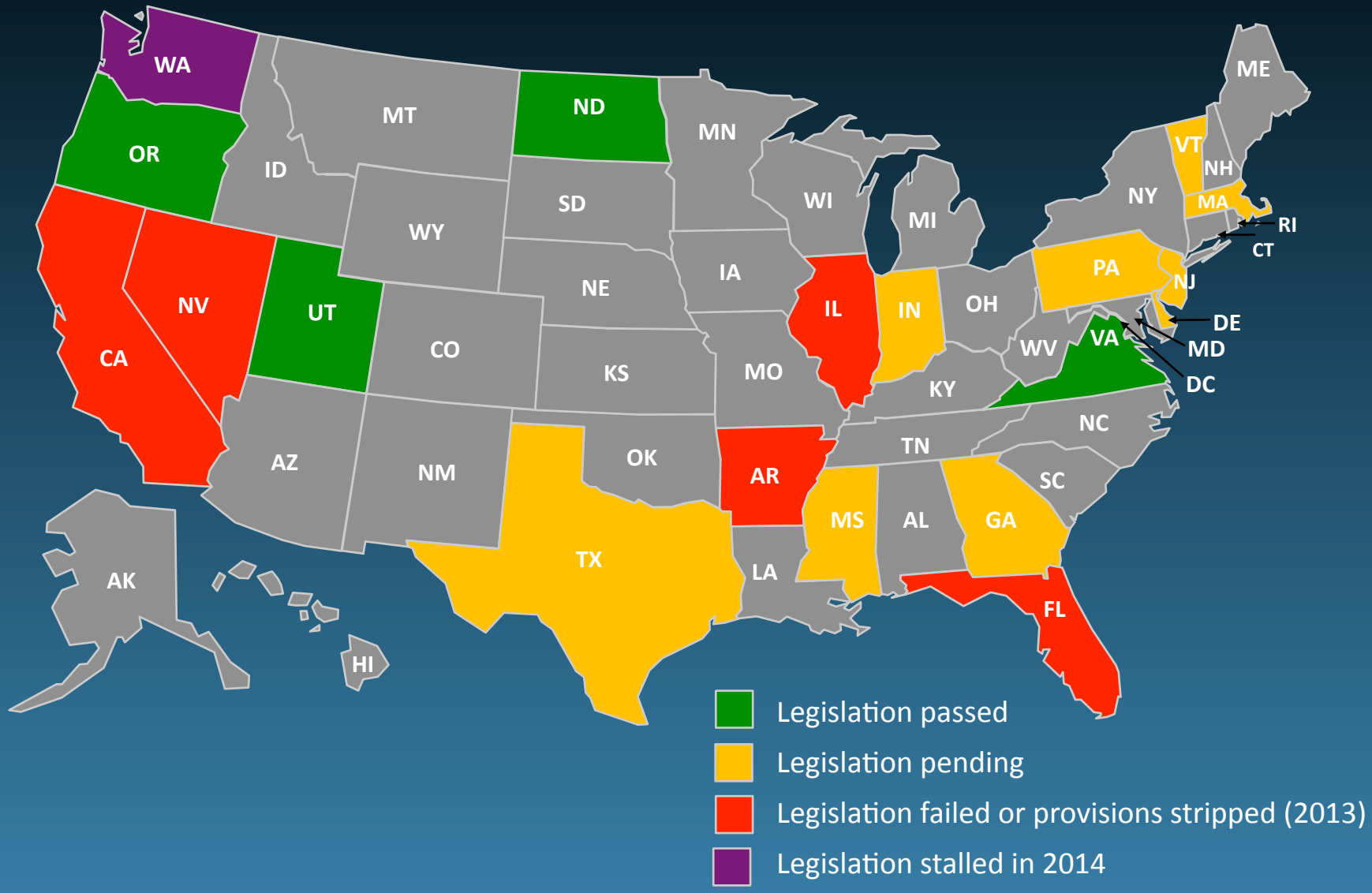
Richmond Times-Dispatch

Gewanter: Legislation would protect patients taking complex meds

Thursday, January 24, 2013 12:00 am
BY HARRY GEWANTER

The treatment of many serious and chronic medical conditions has been changed dramatically by a class of cutting-edge medications called "biologics." These medications have produced clinical miracles for thousands of children and adults with arthritis, psoriasis, inflammatory bowel disease, multiple sclerosis, cancers and other diseases. Instead of facing death or significant disability, biologics have changed the course of these diseases and allowed patients to continue to work, attend school and have a more typical life.

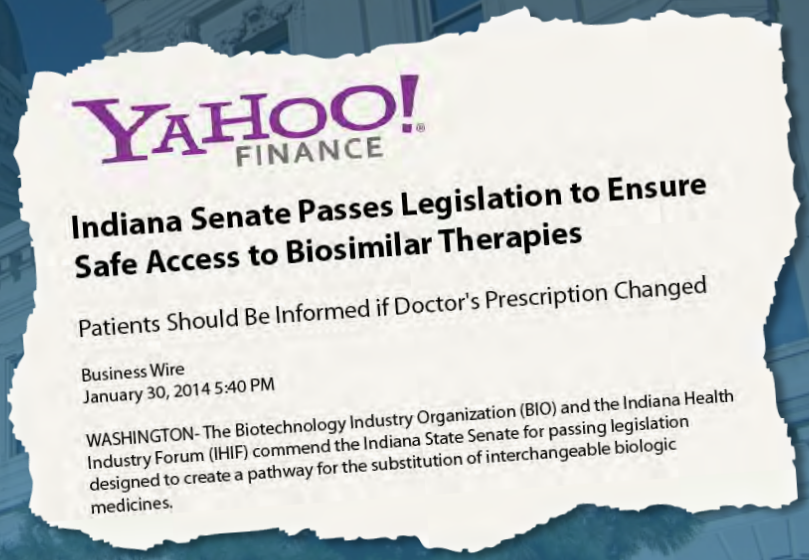
Physician Notification Provisions as of 2/25/2014



January 2014: Indiana Senate Passes Substitution Legislation

S.B. 262 likely being voted on as early as <u>today.</u>

- Pharmacist "MAY Substitute" ONLY IF Physician indicates "may substitute" on prescription
- Pharmacist MUST inform customer of substitution
- Pharmacist has 10 DAYS to communicate with physician after substitution



YAHOO! FINANCE

Indiana Senate Passes Legislation to Ensure Safe Access to Biosimilar Therapies

Patients Should Be Informed if Doctor's Prescription Changed

Business Wire
January 30, 2014 5:40 PM

WASHINGTON- The Biotechnology Industry Organization (BIO) and the Indiana Health Industry Forum (IHIF) commend the Indiana State Senate for passing legislation designed to create a pathway for the substitution of interchangeable biologic medicines.

Changes in Legislation Between 2013 and 2014

Increasing support for these provisions as a result of a dialogue between physicians, industry and pharmacists:

2013 Bill Language		2014 Bill Language
"Notification"	→	"Communication"
72 hours to notify	→	10 days to communicate
Must retain records for 5 years	→	Must retain records for 2 years

Previously Opposed, Now Supporting

Several generic manufacturers who previously opposed now support these provisions, including:

- Actavis
- Hospira
- Sandoz

InsideHealthPolicy
An Inside Washington news service

February 14, 2014

Latest News

Four Companies Kept Out Of GPhA Discussions On State Biosimilar Strategy

Four Generic Pharmaceutical Association member companies that disagree with the association's stance on state biosimilar legislation will be asked to leave a working group meeting while other companies discuss state-level strategy, according to an internal GPhA email obtained by FDA Week.

February 2014: Washington Substitution Legislation Stalls

Despite progress, an obvious need for further education remains.

H.B. 2326 was not brought up by majority in time to be considered this session.

- Physician must indicate either “DISPENSE AS WRITTEN” or “SUBSTITUTION PERMITTED” on prescription
- MANDATORY substitution (Pharmacist “SHALL substitute” UNLESS patient requests brand name)
- Label shall contain name of biosimilar and its manufacturer
- 10 DAYS to note in patient record the name product substituted and its manufacturer, OR notify physician
- Records retained for 2 years

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