SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES

# *Increasing Physician Confidence in Biosimilars*

Harry L. Gewanter, MD, FAAP, FACR
Chairman, Alliance for Safe Biologic Medicines (ASBM)
www.safebiologics.org

7th Latin American Forum on Biosimilars (2017)
8th Brazilian Forum on Biosimilars
Brasilia, Brasil
June 28-29, 2019

# ***Disclosures***

I have no relevant financial disclosures.

# *Overview*

- Who is ASBM and What Do We Do?
- Barriers to Biosimilar Acceptance
- What Concerns Physicians About Biosimilars
- How We Can Use Global Physician Surveys to Increase Confidence in Biosimilars
- Suggestions for Building Physician Confidence

# *Who is ASBM and What do We Do?*

# *The Alliance for Safe Biologic Medicines (ASBM)*

ASBM is an organization consisting of patient, physician, research and manufacturing organizations devoted to promoting the safe introduction and monitoring of biosimilar medications

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

# *The Alliance for Safe Biologic Medicines (ASBM)*

## ASBM Leadership

Harry L. Gewanter, MD, FAAP, FACR
Chairman
Pediatric Rheumatologist

Philip Schneider, MS, FASHP
Advisory Board Chair
Associate Dean, University of Arizona College of Pharmacy

Michael Reilly, Esq.
Executive Director
michael@safebiologics.org

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STEERING COMMITTEE

AfPA Alliance for Patient Access
American Autoimmune Related Diseases Association, Inc.
American Academy of Dermatology
ACRO Association of Clinical Research Organizations
Colon Cancer Alliance
Global Colon Cancer Association
Hepatitis Foundation International
ican
Global Healthy Living Foundation
Kidney Cancer Association www.KidneyCancer.org
HealthHIV
ZERO The End of Prostate Cancer

# *Gathering the Perspectives of Providers Around the World*

*Canadian Physician Survey*
*(December 2014): n=427*

*U.S. Physician Surveys*
*(September 2012): n=376*
*Labeling (February 2015): n=400*
*(November 2015): n=400*

*E.U. (France, Italy, Spain, UK) Physician Survey*
*(November 2013): n=470*

*U.S. Pharmacist Survey*
*(September 2015) n=401*

*Latin America (Argentina, Brazil, Colombia, Mexico) Physician Survey*
*(May 2015): n=399*

*Australian Survey*
*(August 2016) n=160*

*All surveys available at www.SafeBiologics.org*

# *Sharing Physician Perspectives With Regulators*

**INTERNATIONAL**

- 2014-2017: 58th-64th WHO INN Consultation and Frontpage meetings
- 2014: Int'l Regulator Conference (Pre-ICDRA), Brazil
- 2014: Presented country-specific survey data to Spain, Italian, and Canadian Health Regulators
- 2015-2016: Presented Latin American survey data at five Biosimilars Conferences, in Panama and Brazil.
- 2017: Shared Australian Survey with Australian Government

**US:**

- 2015: Shared U.S. data and recommendations with U.S. Dept. of Health and Human Services and other Administration officials.
- February and July 2016 FDA Arthritis Advisory Committee Hearings
- Numerous State Legislatures 2010-2017





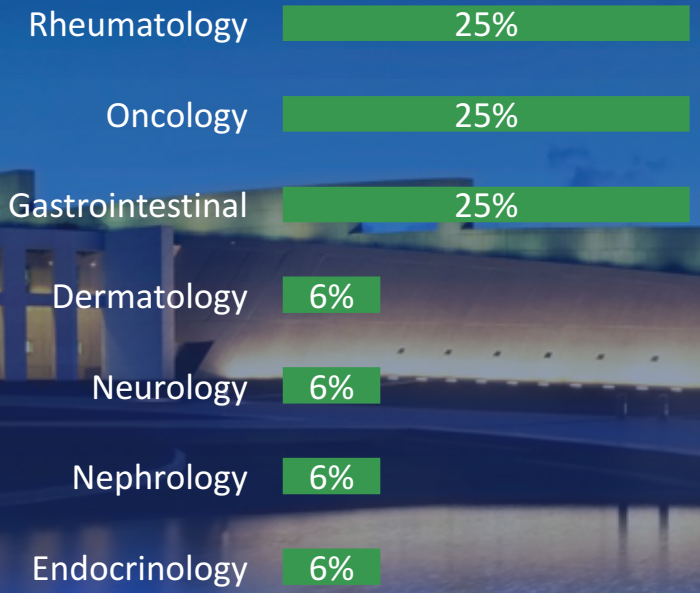


# *Australian Survey*

150 prescribers surveyed in August 2016

In February 2017, ASBM held a series of meetings to share these findings with Australian regulators and policy makers, as well as pharmacy, physician and patient organizations:

- Australian Department of Health
- Therapeutic Goods Administration
- 3 Senior Health Ministers in Parliament
- Arthritis Australia
- Australian Diabetes Society
- Consumer Health Forum
- Crohn's and Colitis Australia
- Australian Rheumatology Association
- Gastroenterology Society of Australia
- Pharmacy Guild of Australia
- Medicines Australia



# *Barriers to Biosimilar Acceptance*

If this headline is to be believed, there should be great confidence among physicians in biosimilars…

BioPharma-Reporter.com

Breaking News on Biopharmaceutical Development & Manufacturing

# Biosimilars in Europe: 11 years, 28 approvals, 0 safety concerns

By Dan Stanton+, 10-May-2017

Related topics: Markets & Regulations, Biosimilars

**The EMA has not experienced any concerns with the safety of the 28 biosimilar products it has recommended, according to an information guide published for healthcare professionals.**

The guide – written in collaboration with the European Commission and published below – aims to provide healthcare professionals with information on the science and regulation underpinning the use of biosimilars and was launched at a stakeholder conference on biosimilar medicines in Brussels last week.

*"Today, biosimilars are an integral part of the effective biological therapies available in the EU,"* the EMA's executive

*"Given the role of healthcare professionals on the front line of patient care, it is vital that they*

*medicines: what they are and how they are developed, approved and*

process.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European Commission

## Biosimilars in the EU

Information guide for healthcare professionals

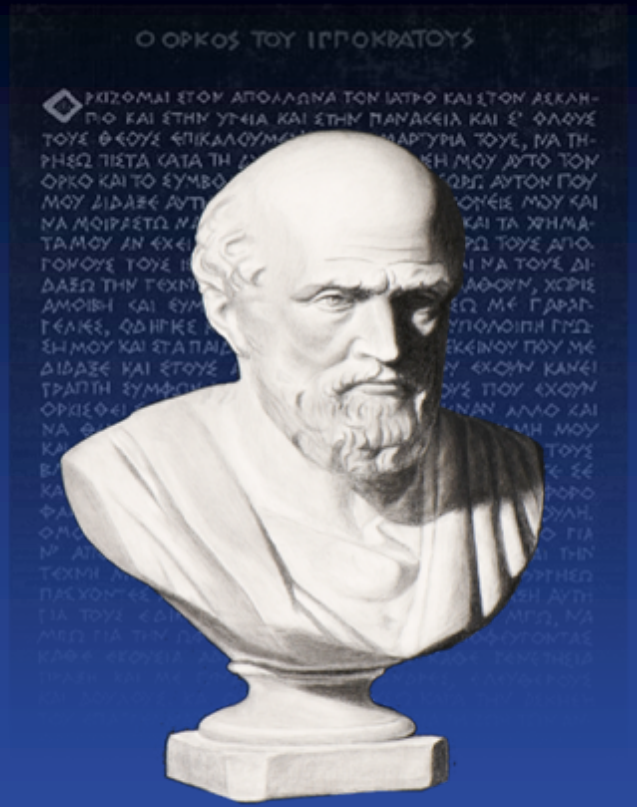
Prepared jointly by the European Medicines Agency and the European Commission

But … we've not yet seen widespread use when physicians have a choice of using a biosimilar or the originator

Why?

# *Clinicians and Caution*

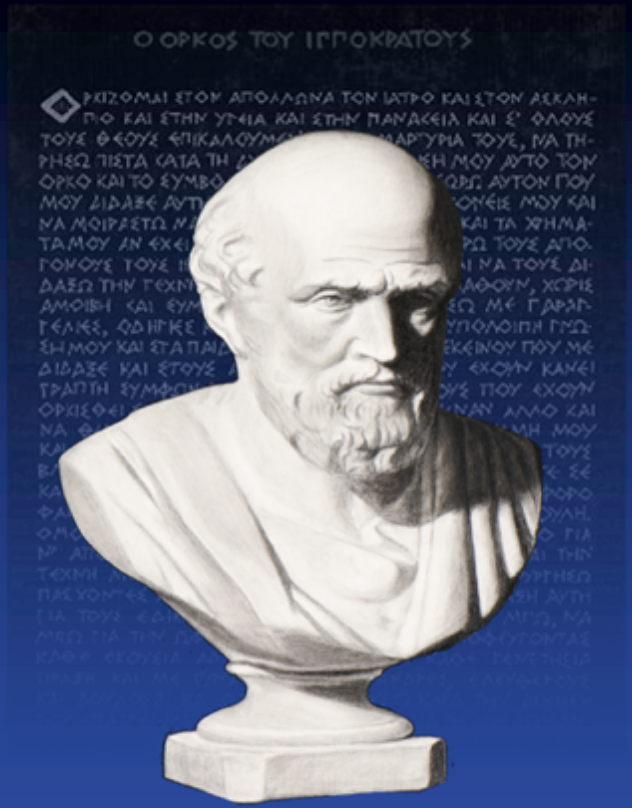
- Clinicians by nature and training are generally conservative regarding treatments and are hesitant to change without sufficient experience, clinical data and independent recommendations
- Clinicians are not comfortable with non-medical switching, especially with patients who are doing well on a particular therapy




*Hippocratic Oath: "first, do no harm"*

# *Clinicians and Caution*

- The conditions treated by biologics are significant chronic diseases that can result in permanent morbidity or other issues if not treated appropriately, leading to *<u>further conservatism of prescribing habits in the absence of convincing clinical data and/or personal experience</u>*
- Physicians think in exceptions - meaning we will look for any/all potential issues or problems when presented with a new issue




*Hippocratic Oath: "first, do no harm"*

# *Cautious Optimism Among Physicians*

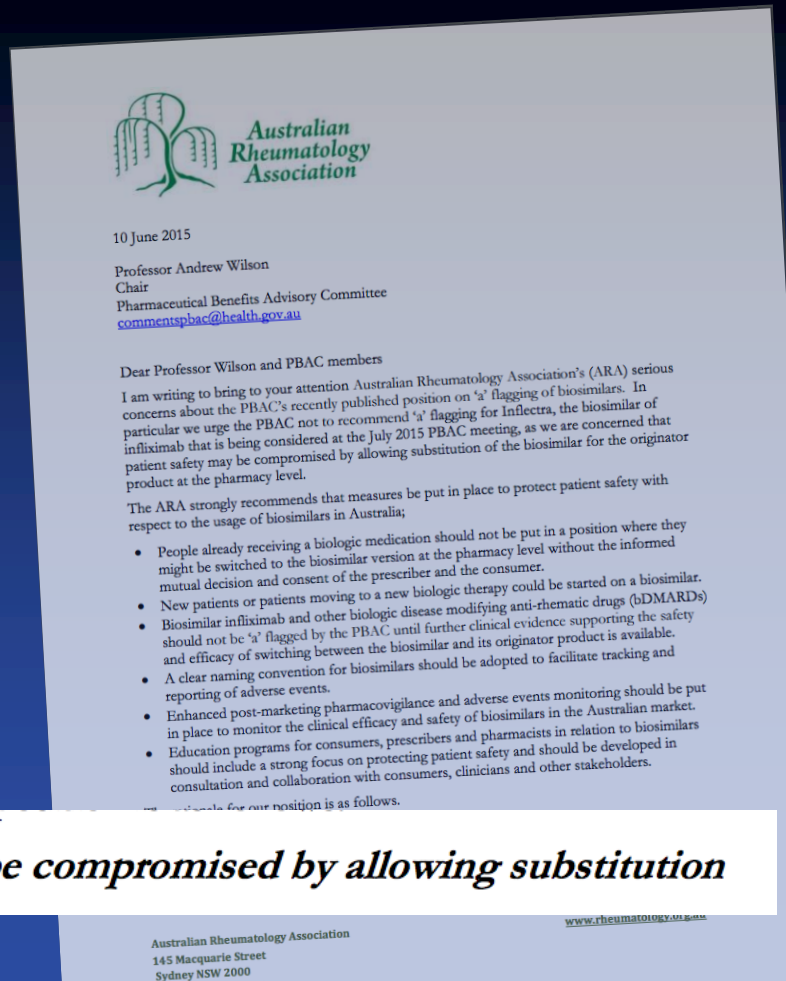
Physicians are cautiously enthusiastic about biosimilars.

We want biosimilars to be made available everywhere - safely

- Appropriate policies and regulations are necessary to achieve this goal
- In a global market- global parameters are ideal
- But there are significant variations between countries, so the ideal is only practical for some aspects- e.g. NAMING

# *Clinicians and Caution*

The recent Australian experience demonstrates potential global issues  if clinician and patient concerns are not adequately and appropriately addressed with more than the assurance that “the analytics are so close, it won’t make a difference”



Australian Rheumatology Association

10 June 2015

Professor Andrew Wilson
Chair
Pharmaceutical Benefits Advisory Committee
commentspbac@health.gov.au

Dear Professor Wilson and PBAC members

I am writing to bring to your attention Australian Rheumatology Association's (ARA) serious concerns about the PBAC's recently published position on 'a' flagging of biosimilars. In particular we urge the PBAC not to recommend 'a' flagging for Inflectra, the biosimilar of infliximab that is being considered at the July 2015 PBAC meeting, as we are concerned that patient safety may be compromised by allowing substitution of the biosimilar for the originator product at the pharmacy level.

The ARA strongly recommends that measures be put in place to protect patient safety with respect to the usage of biosimilars in Australia;

- People already receiving a biologic medication should not be put in a position where they might be switched to the biosimilar version at the pharmacy level without the informed mutual decision and consent of the prescriber and the consumer.
- New patients or patients moving to a new biologic therapy could be started on a biosimilar.
- Biosimilar infliximab and other biologic disease modifying anti-rhematic drugs (bDMARDs) should not be 'a' flagged by the PBAC until further clinical evidence supporting the safety and efficacy of switching between the biosimilar and its originator product is available.
- A clear naming convention for biosimilars should be adopted to facilitate tracking and reporting of adverse events.
- Enhanced post-marketing pharmacovigilance and adverse events monitoring should be put in place to monitor the clinical efficacy and safety of biosimilars in the Australian market.
- Education programs for consumers, prescribers and pharmacists in relation to biosimilars should include a strong focus on protecting patient safety and should be developed in consultation and collaboration with consumers, clinicians and other stakeholders.

...ciple for our position is as follows.

***Patient safety may be compromised by allowing substitution***

www.rheumatology.org.au

Australian Rheumatology Association
145 Macquarie Street
Sydney NSW 2000

# *Australian Biosimilar Substitution Policy*

- On May 26, 2015, Australian Health Minister Sussan Ley announced that Australia would become the first nation in the world to allow so-called “automatic” substitution of biosimilars by pharmacists in place of the biologic prescribed by a physician
- This move came at the recommendation of Australia’s Pharmacy Benefits Advisory Committee (PBAC)- the government payor, not the regulatory agency (Therapeutic Goods Administration)
- This made substitution an economic non-medial decision rather than a safety decision


# *Physicians Want Data*

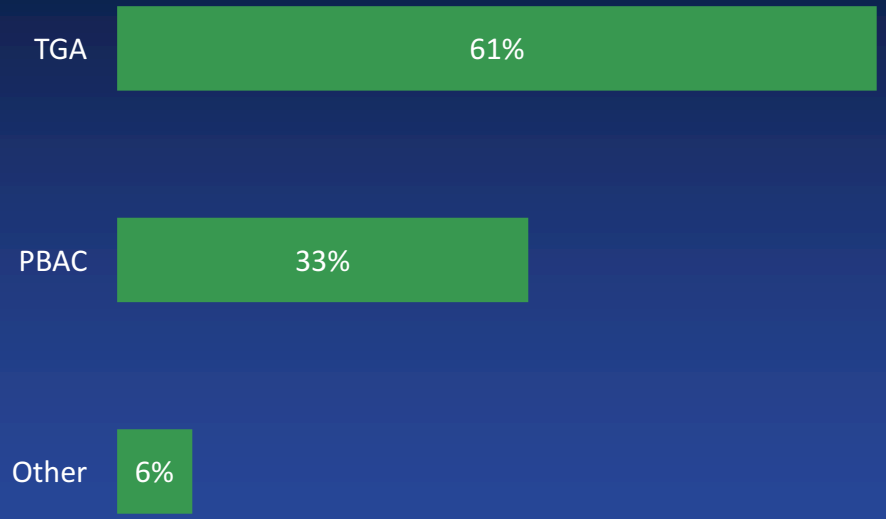
In February 2016, the Australian Rheumatology Association called for a robust pharmacovigilance program to be set up for the REMICADE (infliximab) biosimilar INFLECTRA

Dr. Mona Marabani (ARA):

- "The ARA wants to see biosimilars successfully introduced to the Australian market, but we have expressed concern with respect to substitution and extrapolation of indications because the evidence is just not there … We are hopeful that collection of data, if done comprehensively, may go some way to establishing an evidence base which is so sorely needed

Australian Rheumatology Association

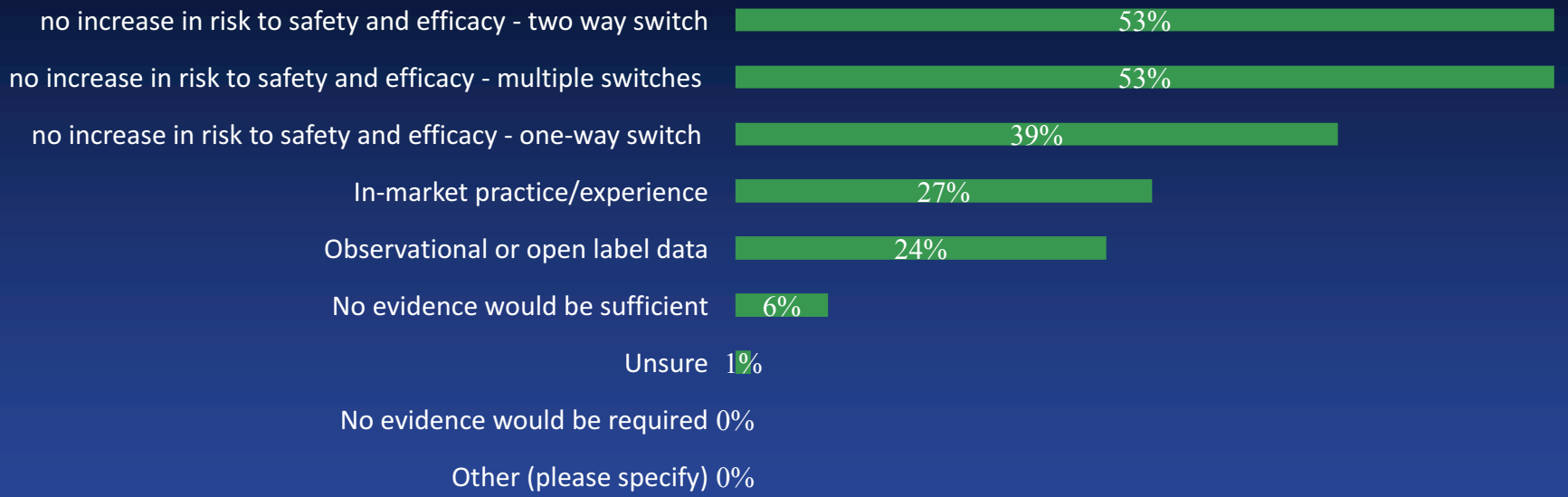
# *Australian Survey: Substitution Decision?*




Question

"Which body do you believe should be responsible for providing the primary advice to Government that a product is suitable for pharmacy level substitution?"

# *Australian Survey: Sufficient Evidence for Substitution?*



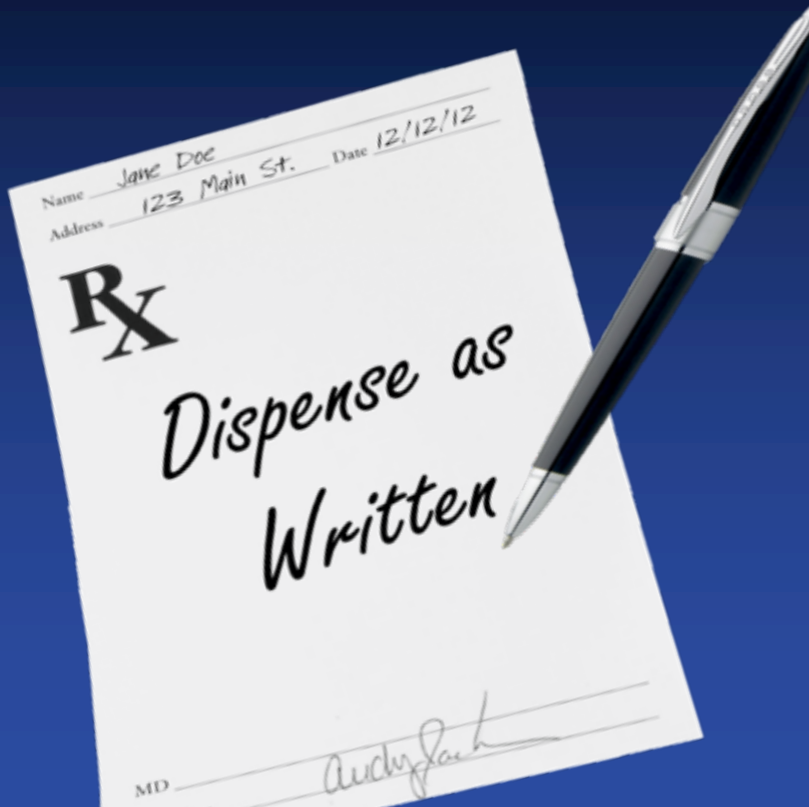

Question

"What evidence would you regard as sufficient to be supportive of the PBAC's conclusion that a biosimilar product is suitable for pharmacy level substitution? Select all that apply."

# *Two Years Later, Biosimilar Uptake Remains Low*

While final numbers are not yet available, uptake is in the single digit percentages … WHY?

Physician groups, like the ARA, suggested that their membership write “DISPENSE AS WRITTEN” on prescriptions, due to a concern for the lack of adequate data now and in the future




# *World Health Assembly- June 2017*

ASBM Co-founder and Steering Committee Member Andrew Spiegel, Executive Director of the Global Colon Cancer Association:

## "The *absence of data* is not data".

While Europe has led on biosimilar approval, they have failed to build confidence in biosimilars through post-market data collection.

# *What Concerns Physicians About Biosimilars*

# *Physician (and Patient) Concerns…*

Many physicians do not yet have great confidence in biosimilars due to a lack, or perceived lack, of convincing data:

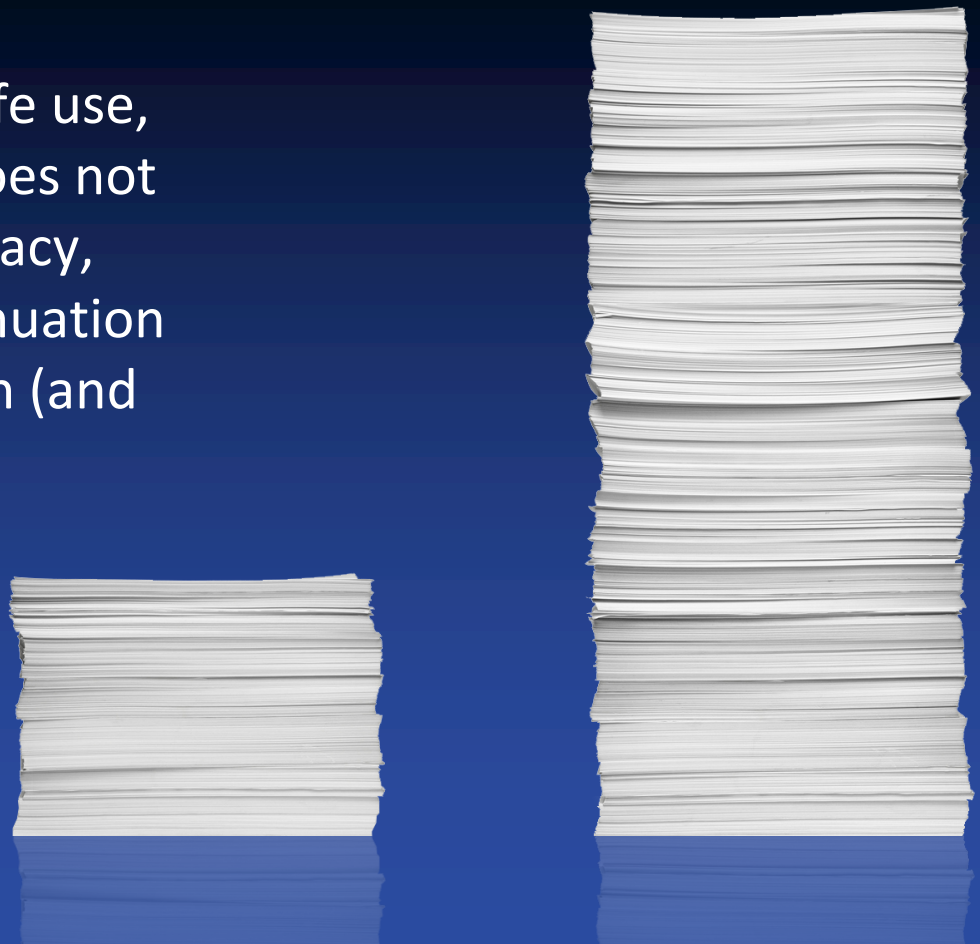
- Clinical studies, especially switching studies
- Over-reliance on analytic data
- Inadequate &/or lack of long-term post-market data or a commitment to its collection

# *Physician (and Patient) Concerns…*

- This does not mean that biosimilars are not viewed as safe or effective - given the limited clinical data and experience, physicians are being cautious
- This is especially true when the imposition of biosimilars is for economic, not necessarily health or safety reasons

# *More Data Builds Confidence*

More data showing that safe use, including safe switching, does not result in differences in efficacy, adverse effects or discontinuation rates will increase physician (and patient) confidence



# *How We Can Use Global Physician Surveys to Increase Confidence in Biosimilars*

# *Universal Concerns and Interests*

- We know that prescribers worldwide have common concerns about the use of biosimilars from our surveys
- They want transparency, identification, pharmacovigilance, collaboration and to maintain the sanctity of the physician-patient relationship and decision-making
- We also know from our patient groups that there is a natural hesitancy to use a new product if the older one has more data and experience
- We understand the need for regulators to focus more on analytics than clinical studies for approval in order to speed up the process and limit expenses, but the cost is increased prescriber and patient concerns and caution

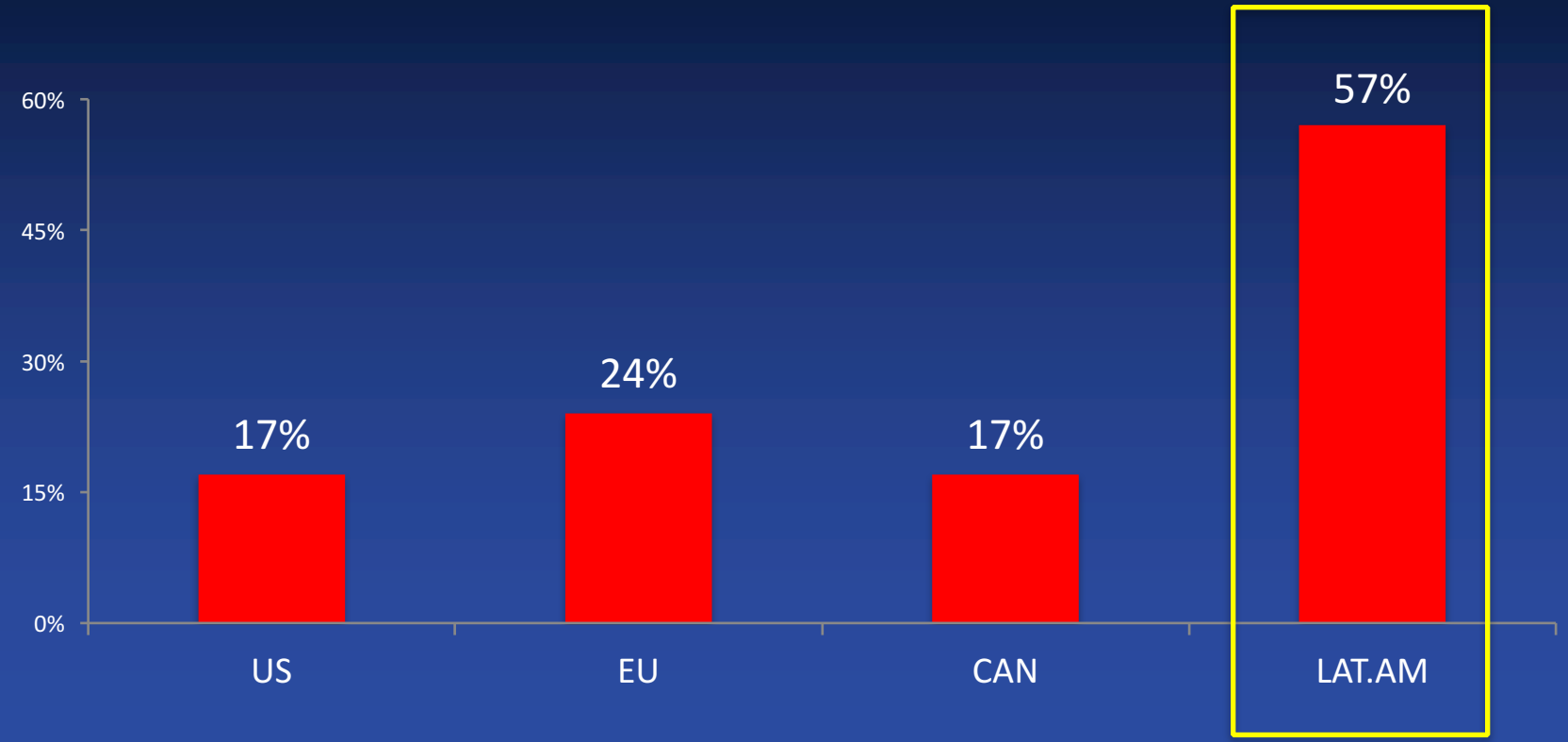
We have a lot of research and teaching to do if physicians, pharmacists and patients are to be sufficiently comfortable accepting and using biosimilars

Just instituting their use without adequate acceptance could further delay their global acceptance and use


*Issue: Naming*

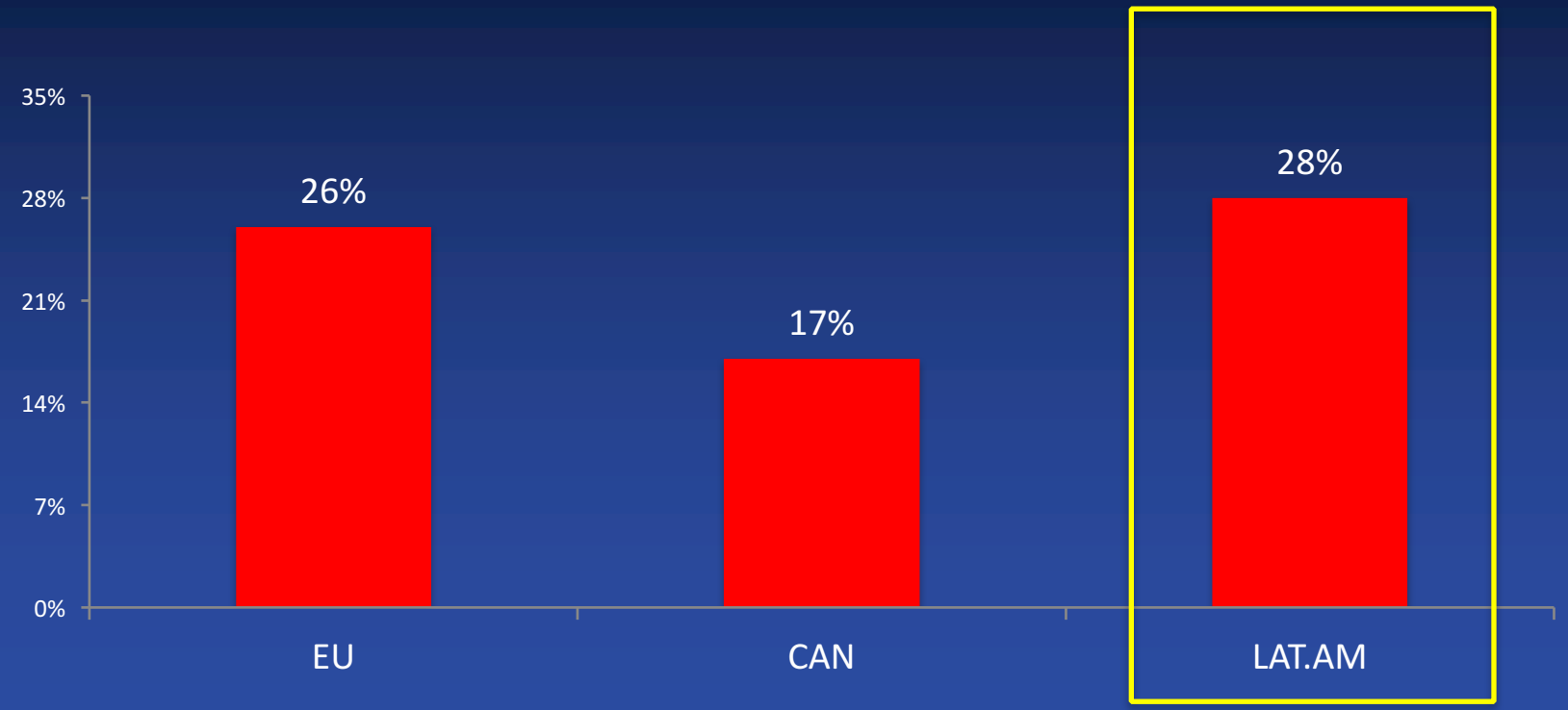
# *Percent of Physicians Using INN Only when Identifying Medicine in Patient Record*

*(This could result in patient receiving the wrong medicine.)*



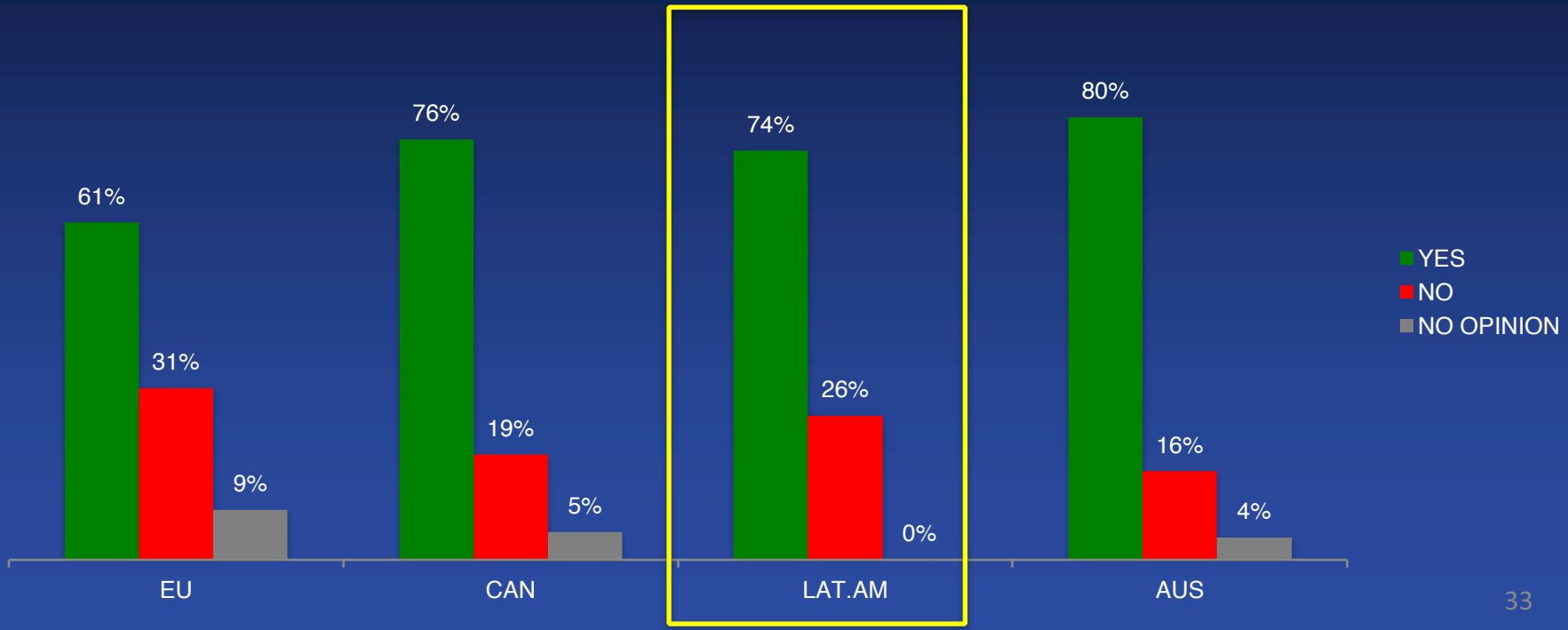
# *Percent of Physicians Using INN Only when Reporting Adverse Events.*

*(This could result in improper attribution or pooling of adverse events.)*



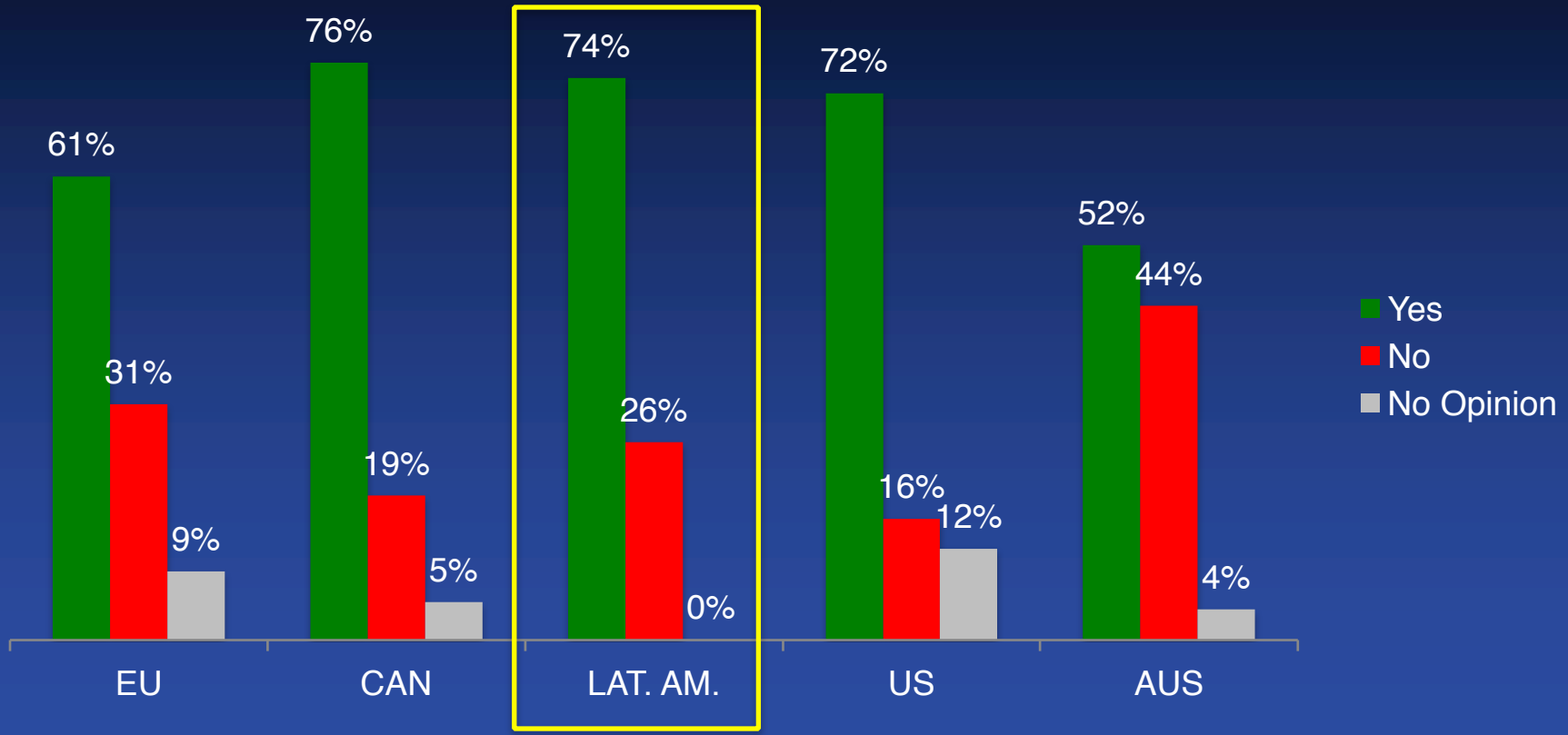
# *Percentage of Physicians Saying A Biosimilar Sharing an INN with its Reference Product Implies Approval for the Same Indications:*

*(This may or may not be the case…)*



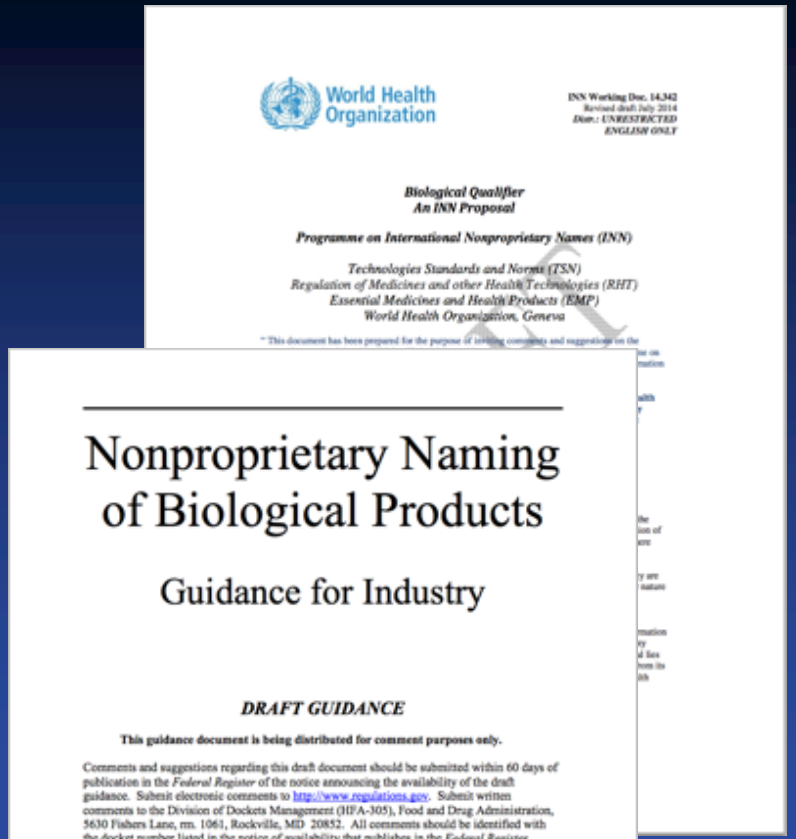
# *Does Same INN Suggest or Imply Structurally Identical?*

*(This is not the case, currently impossible)*



# *WHO and FDA: Distinguishable Naming Proposals*

- Both regulators are updating their naming systems for biosimilars.
- Distinguishability aids in clear communication throughout treatment, improves tracking of safety and efficacy, and promotes manufacturer accountability.
- Both call for similar biologics (including biosimilars) to have a shared root name (International Nonproprietary Name/ INN) followed by a four-letter suffix.
- The WHO calls this a “Biological Qualifier”


World Health Organization

INN Working Doc. 14.342
Revised draft July 2014
Distr.: UNRESTRICTED
ENGLISH ONLY

***Biological Qualifier***
***An INN Proposal***

***Programme on International Nonproprietary Names (INN)***

*Technologies Standards and Norms (TSN)*
*Regulation of Medicines and other Health Technologies (RHT)*
*Essential Medicines and Health Products (EMP)*
*World Health Organization, Geneva*


Nonproprietary Naming of Biological Products

Guidance for Industry

***DRAFT GUIDANCE***

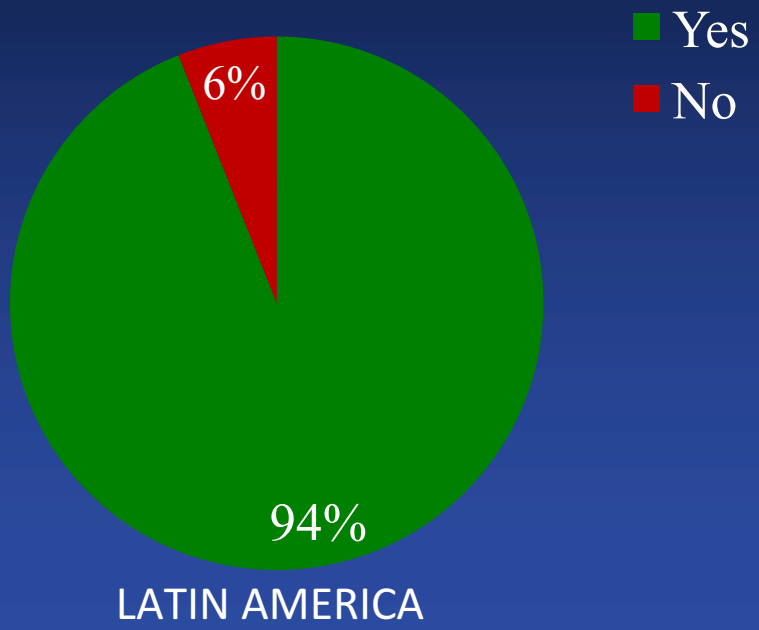
**This guidance document is being distributed for comment purposes only.**

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Sandra Benton at 301-796-2500, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

# *Latin American Physicians Overwhelmingly Consider WHO's Biological Qualifier Proposal Useful…*

*"Do you think [The WHO's proposed] "biologic qualifier" would be useful to you to help you ensure that your patients receive the right medicine that you have prescribed for them?" (N=399)*



# *Australian Results are Consistent With Those of Physicians Worldwide*

**79%** *of Canadian physicians support Health Canada issuing distinct names. (2014)*

**94%** *of Latin American Physicians consider WHO's BQ Proposal to be "useful" in helping patients receive the correct medicine. (2015)*

**66%** *of US physicians support FDA issuing distinct names. (2015)*

**76%** *of Australian physicians support TGA issuing distinct names (2016)*

# *April 4, 2017: WHO 64th INN Consultation*

- On April 4rd, in Geneva, Switzerland, ASBM participated in the World Health Organization's 64rd Stakeholder Consultation on International Nonproprietary Names.
- ASBM has been a regular participant at the INN Consultations since 2013.
- ASBM's Chairman Harry L. Gewanter, Advisory Board Chair Philip Schneider, MS, FASHP and Advisory Board Member Jeff Jones, PhD represented ASBM at this meeting.

# *Benefits of the BQ:*

CLEAR PRODUCT IDENTIFICATION - Distinguishable from reference product, and other approved biosimilars.

CLEAR COMMUNICATION - between physician, patient and pharmacist

CLEAR PRESCRIBING & DISPENSING - Helps prevent inadvertent and inappropriate substitution.

BETTER PHARMACOVIGILANCE - proper attribution of adverse events.

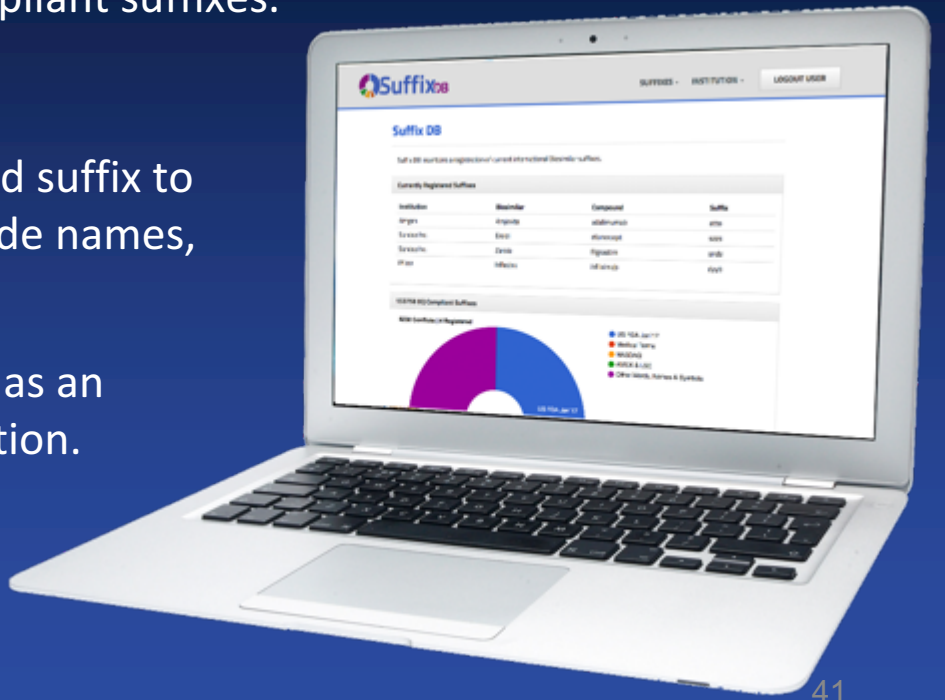
INCREASED MANUFACTURER ACCOUNTABILITY - suffixes tied to manufacturer/facility

# *BQ Feasibility*

One argument against the BQ is the difficulty of generating and assigning them – avoiding suffixes that are similar to words, company names, etc.

# *BQ Generating Algorithm Demo: SuffixDB*

- ASBM helped development
- Applies naming rules to generate BQ-compliant suffixes.
- Detects conflicts in proposed suffixes.
- Rates high and low similarity of a proposed suffix to currently used suffixes, English words, trade names, stock symbols, medical terms, etc.
- We have offered to regulators worldwide as an example of one potential BQ implementation.



# *Example: Biosimilar Substitution*

# How Important is "Dispense as Written" (DAW) Authority?

**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)

# *Physician Opinions of a Pharmacist Determining Which Biologic is Dispensed at Initiation of Treatment:*

**71%** *of Canadian physicians consider it "not acceptable" (2014)*

**62%** *of EU physicians consider it "not acceptable'" (2013)*

**85%** *of Latin American physicians consider it "not acceptable" (2015)*

# How Important is Notification of Which Medication Is Dispensed?

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"

89% of Australian physicians consider it "very important" or "critical"

# *Importance of Sole Prescription Authority*

*90% of Australian physicians consider it "very important" or "critical" (2016)*

*90% of Latin American physicians consider it " very important" or "critical" (2015)*

# *Suggestions for Building Physician Confidence in Biosimilars*

We believe that physician, patient and pharmacist concerns must be adequately addressed by regulators, policymakers and payers since we have shown these concerns and potential barriers are universal if we want to encourage the acceptance and uptake of biosimilars

# *Suggestions*

- Global acceptance of the WHO BQ proposal - to address the concerns re: product identification and allow for adequate & appropriate tracking
- Transparent labeling - to increase knowledge of the medication dispensed as well as ensuring the desired medication is being used
- Communication and collaboration among all involved parties (patients, prescribers, pharmacists, regulators, policymakers, manufacturers, researchers) - to agree on policies and regulations that will best meet the patients' needs with the least interference of the prescriber-patient relationship and provide the safest use for everyone

# *Suggestions*

- Policies to ensure that switching only occurs with the approval of the physician and patient, not just for economic or other nonmedical reasons
- Adequate and long-term passive pharmacovigilance policies to address potential post-marketing issues that may arise with the more expansive use of these medications, both positive and negative, as this will help allay many of the prescriber and patient concerns

We believe that incorporating at least these common-sense proposals will enhance the acceptance and uptake of biosimilars while addressing the concerns that have led to the relatively slow uptake in Europe, Australia and elsewhere

SafeBiologics

ALLIANCE *for* SAFE BIOLOGIC MEDICINES

*Thank You For Your Attention*