SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES

Physician Perspectives on Biosimilars

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Chair, Alliance for Safe Biologic Medicines

Presented to LIU-Pharmacy

September 30, 2018

Introduction

Madelaine Feldman, MD FACR

- Practicing Rheumatologist
- Chair, Alliance for Safe Biologic Medicines
- President of the Coalition of State Rheumatology Organizations
- Founding Member and Past President of the Rheumatology Alliance of Louisiana
- Clinical Associate Professor of Medicine at Tulane University School of Medicine

About ASBM

- Formed in 2010, currently more than 135 members.
- **<u>Steering Committee composed entirely of patient and physician member organizations.</u>**
- Have presented to FDA, Health Canada, TGA, Spanish and Italian Health Ministries, & European Commission
- Have participated in past 10 of the WHO's INN Consultations
- On July 12th, held the 2nd in a series of stakeholder meetings on International Harmonization of Biologic Nomenclature in Washington, DC with the FDA, Health Canada, and WHO among the participants.

SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES

STEERING COMMITTEE

AfPA Alliance for Patient Access
AAD
American Autoimmune
ACRO
colorectal cancer alliance
Global Colon Cancer Association
GLOBAL HEALTHY LIVING FOUNDATION
HealthHIV
ican
Kidney Cancer Association
LUPUS and ALLIED DISEASES Association, Inc.
NATIONAL PSORIASIS FOUNDATION
NHMA National Hispanic Medical Association
ZERO

Gathering Perspectives from Biologic Prescribers Worldwide

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

Canadian Physician Survey
(December 2014): n=427
(October 2017):n=403

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

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

Australian Physician Survey
(October 2016) N=160

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

All surveys available at www.SafeBiologics.org

Some Key Issues Facing Policymakers…

Distinguishable Naming

Interchangeability & Substitution

Non-Medical Switching

Increasing Uptake

Distinguishable Naming

Biologics are made in living cells and are highly complex so they cannot be exactly copied.

Thus, Biosimilars are NOT Identical to their reference product…….They can only be "SIMILAR"

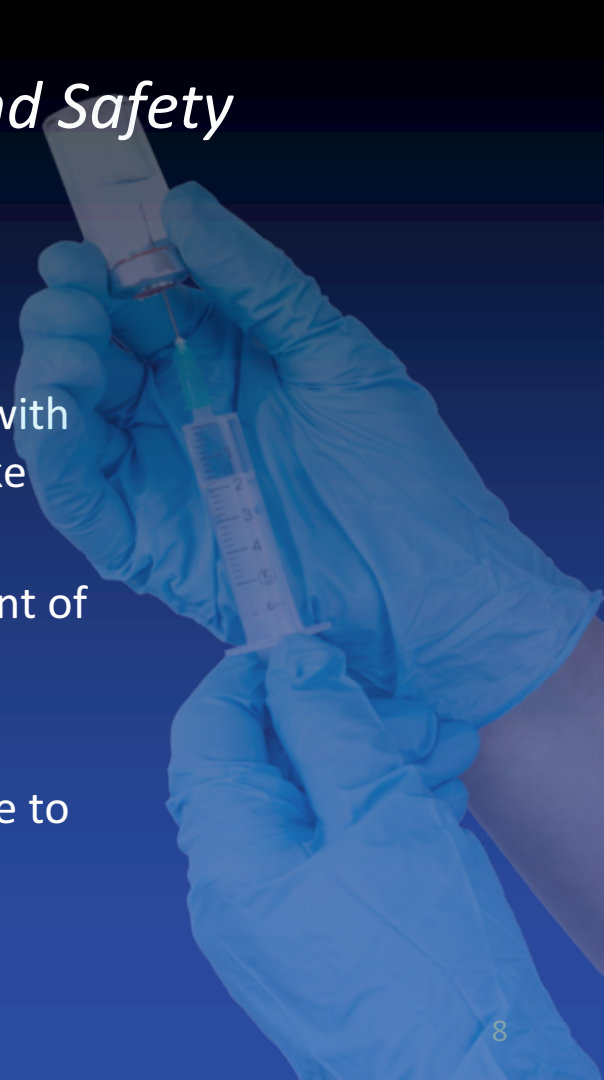
The Role of Names in Pharmacovigilance and Safety

PHARMACOVIGILANCE

- Distinguishable naming helps differentiate products for observing and reporting adverse events.
- Tracking and tracing of biologics is more challenging than with chemical drugs. An adverse impact from a biologic may take months to be recognized.
- Multiple means of product identification avoid a single point of information failure.

MANUFACTURER ACCOUNTABILITY

- Patient response, good or not-so-good, should be traceable to the correct manufacturer's product.
- This helps everyone better understand the effects of each medicine and make improvements as needed.



Broad Support for Distinct Naming Among Physicians Globally

68% *of Canadian physicians support Health Canada issuing distinct names. (2017)*

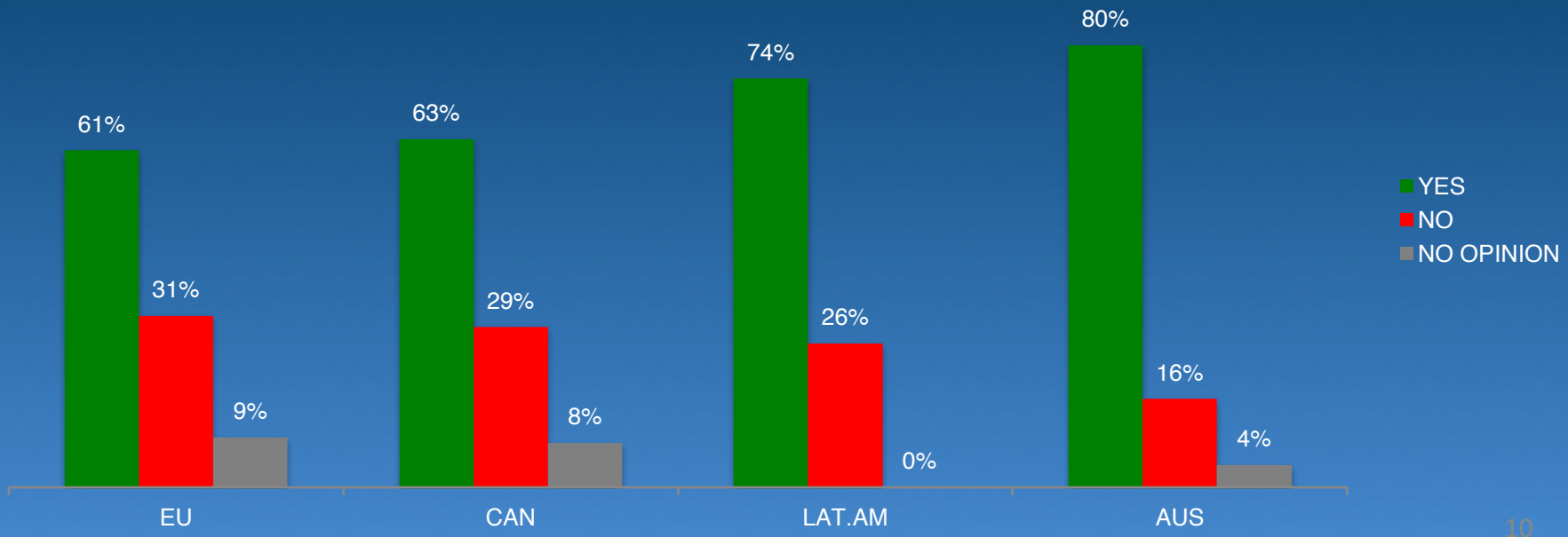
94% *of Latin American Physicians consider WHO's BQ Proposal to be "useful" in helping patients receive the correct medicine. (2015)*

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

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

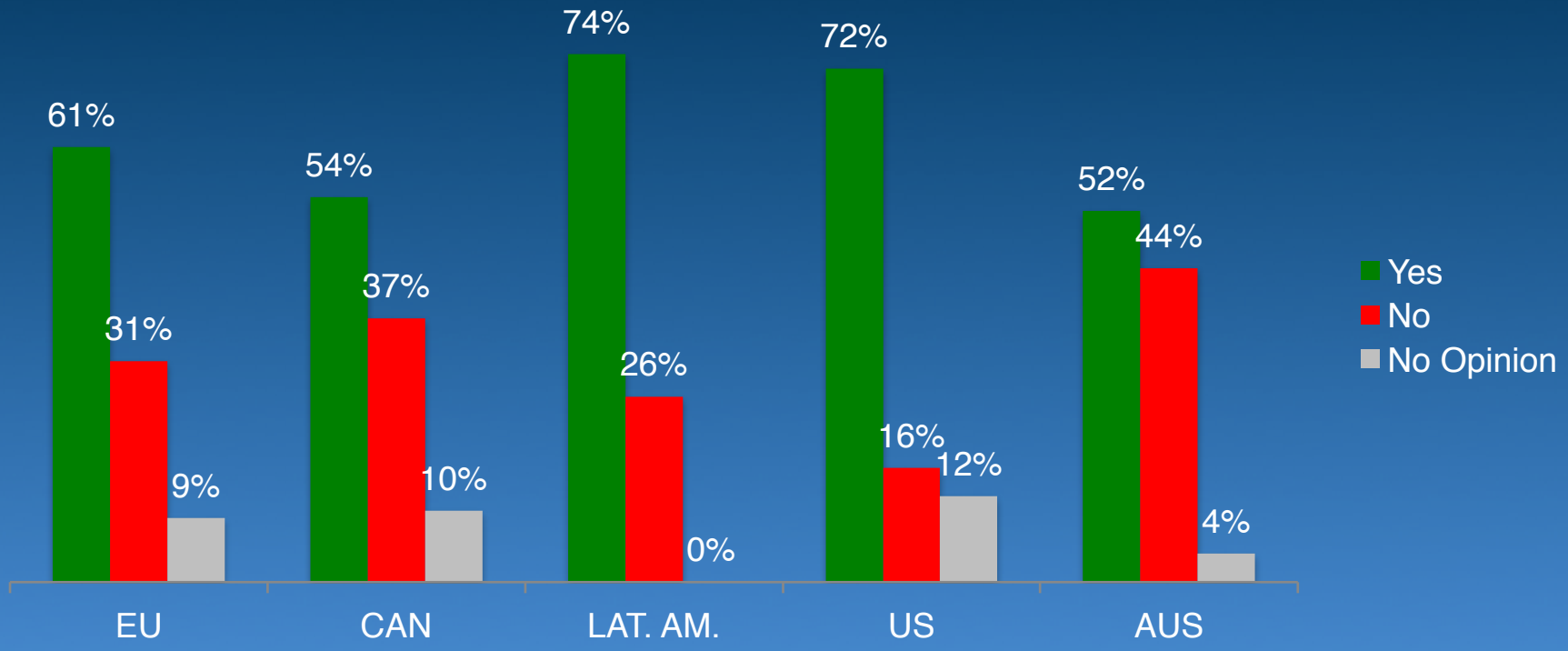
Percentage of Physicians Saying A Biosimilar Sharing an INN with its Reference Product Implies Approval for the Same Indications:

(This may or may not be the case…)



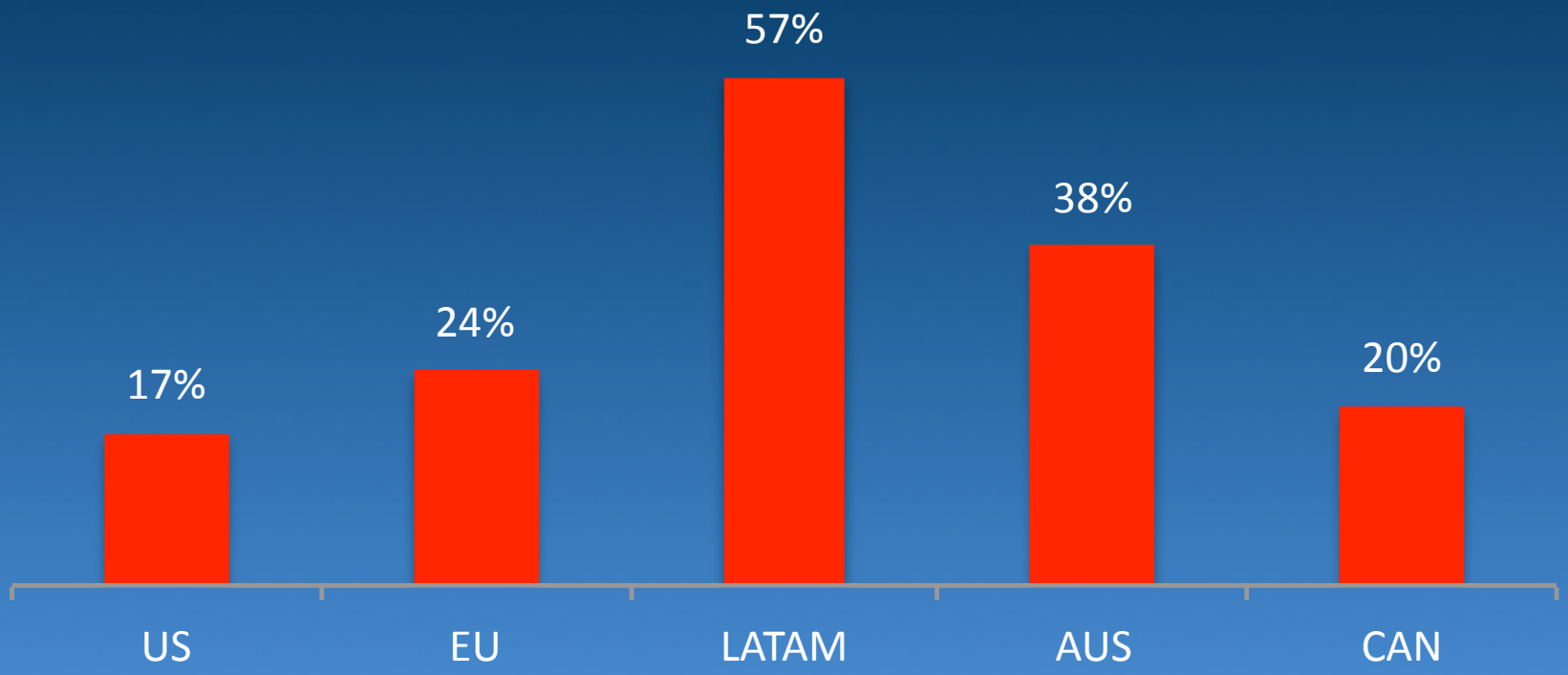
Does Same INN Suggest or Imply Structurally Identical?

(This is not the case, currently impossible)



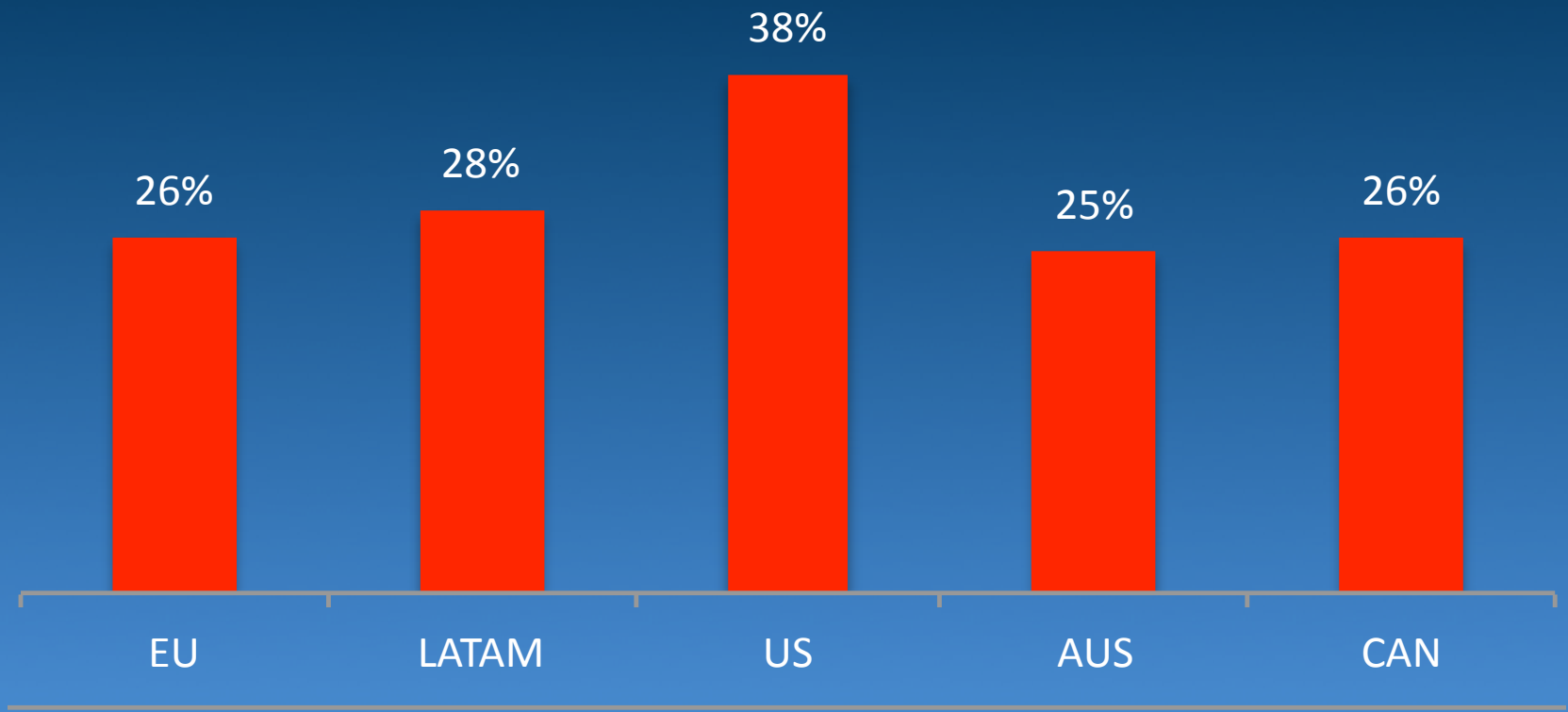
Percent of Physicians Using Only INN when Identifying Medicine in Patient Record

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



Percent of Physicians Using Only INN when Reporting Adverse Events.

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

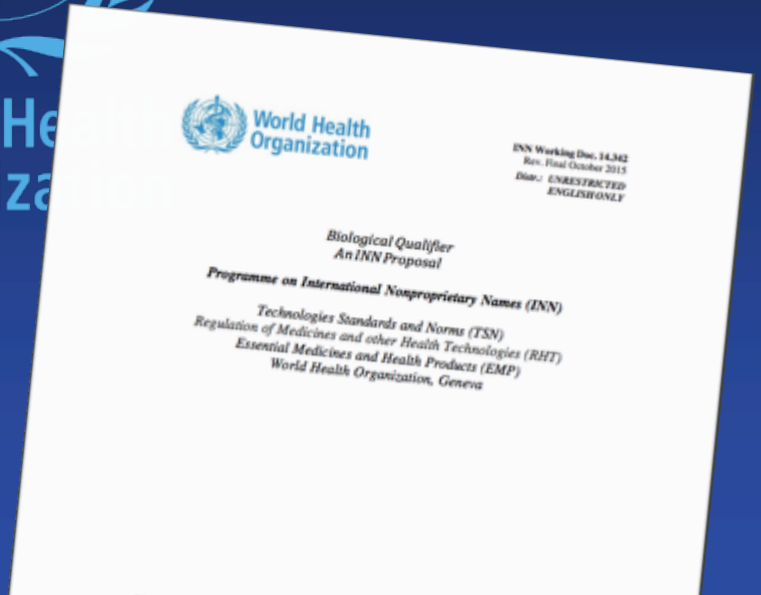


Two Distinct Naming Proposals Using INN + Four-letter Suffix

World He
Organiza

Biologic Qualifier (BQ)

Proposed 2014


World Health Organization

INN Working Doc. 14.342
Rev. Final October 2015
Distr.: UNRESTRICTED
ENGLISH ONLY

Biological Qualifier
An INN Proposal

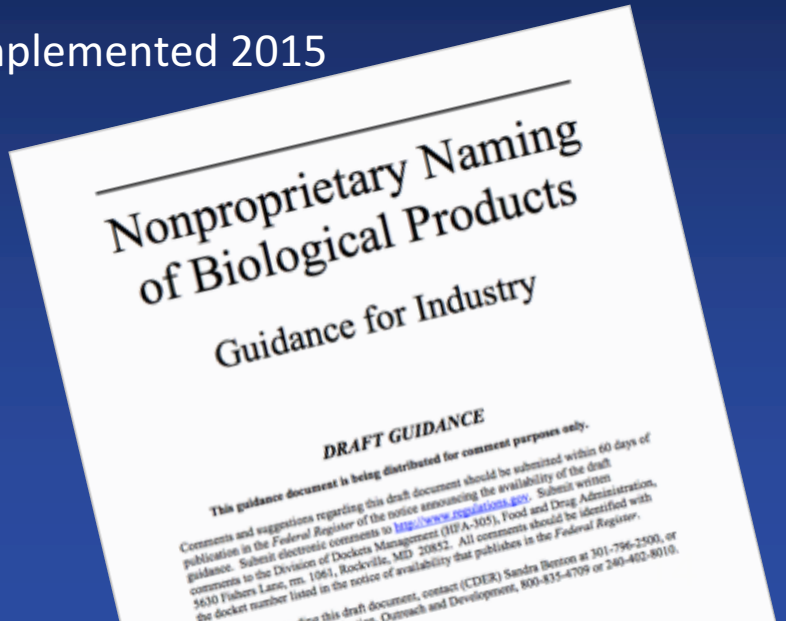
Programme on International Nonproprietary Names (INN)

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

FDA U.S. FOOD & DRUG ADMINISTRATION

Naming Guidance

Implemented 2015


Nonproprietary Naming of Biological Products

Guidance for Industry

DRAFT GUIDANCE

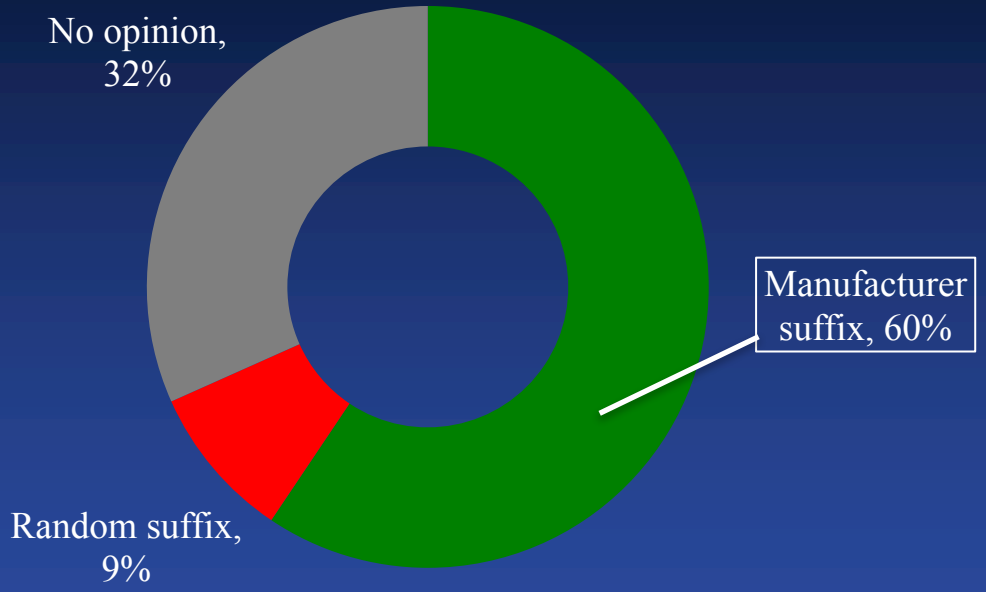
This guidance document is being distributed for comment purposes only.

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 this draft document, contact (CDER) Sandra Benton at 301-796-2500, or
Outreach and Development, 800-835-4709 or 240-402-8010.

Meaningful vs. Random Suffix?

- Our data has shown a strong preference among US physicians not only for distinguishable naming, but for meaningful rather than random suffixes.



400 U.S. BIOLOGIC PRESCRIBERS, 2015

Interchangeability & Biosimilar Substitution

“Interchangeability” (US-Specific Standard)

US-Specific higher regulatory standard. More data is required, including switching studies.

An “INTERCHANGEABLE” Biosimilar :

1) Must be a **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.**

Interchangeability=Transitive?

Automatic Substitution of Interchangeable Biosimilars

- Communication is important - Physicians need to know which medicine the patient is actually receiving to make informed treatment decisions and attribute any adverse events or loss of efficacy to the correct medication.
- If there is more than one biosimilar for a reference product there could be inadvertent automatic substitution with one biosimilar for another

How Important is Communication of a Biosimilar Substitution?

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"*

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)

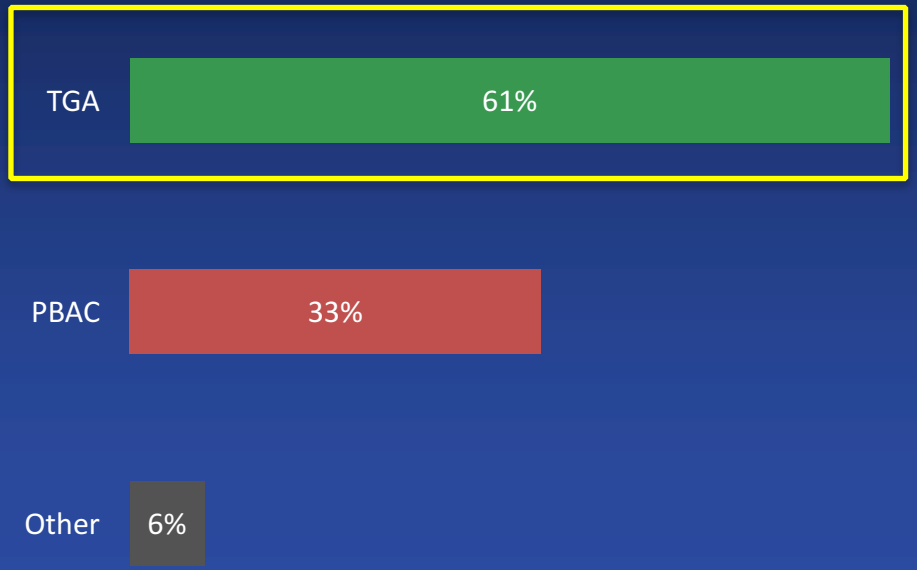
Case Study: Australian Biosimilar Substitution Policy

- 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-medical decision rather than a safety decision.

Australian Survey: Substitution Decision?

Question

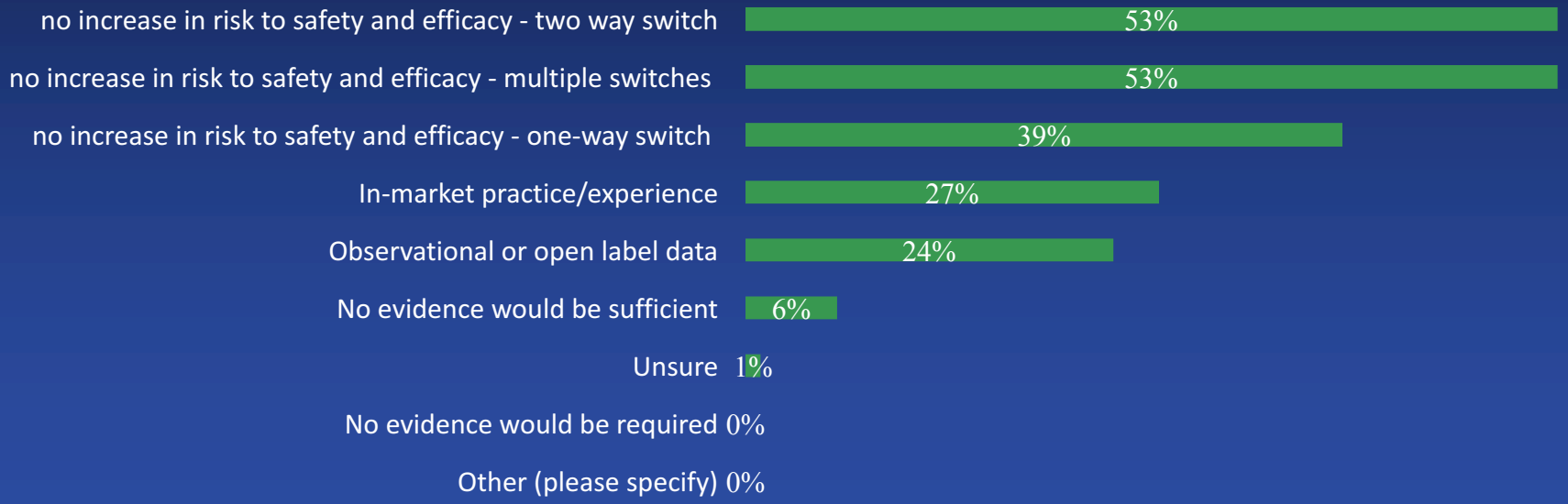
"Which body do you believe should be responsible for providing the primary advice to Government that a product is suitable for pharmacy level substitution?"



Australian Survey: Sufficient Evidence for Substitution?

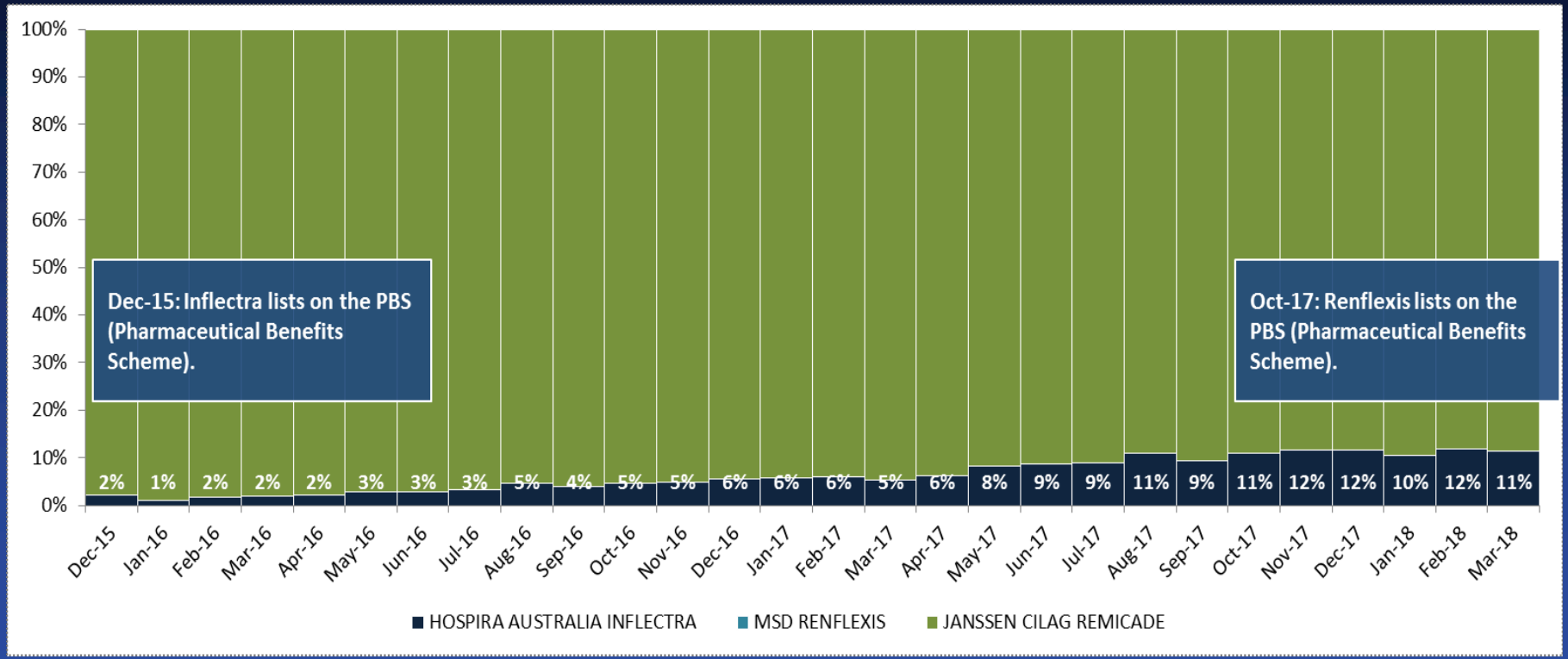
Question

"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."



Three Years later, biosimilar uptake remains LOW in Australia as Physicians write "Dispense As Written"…

Dec 2015 to Mar 2018

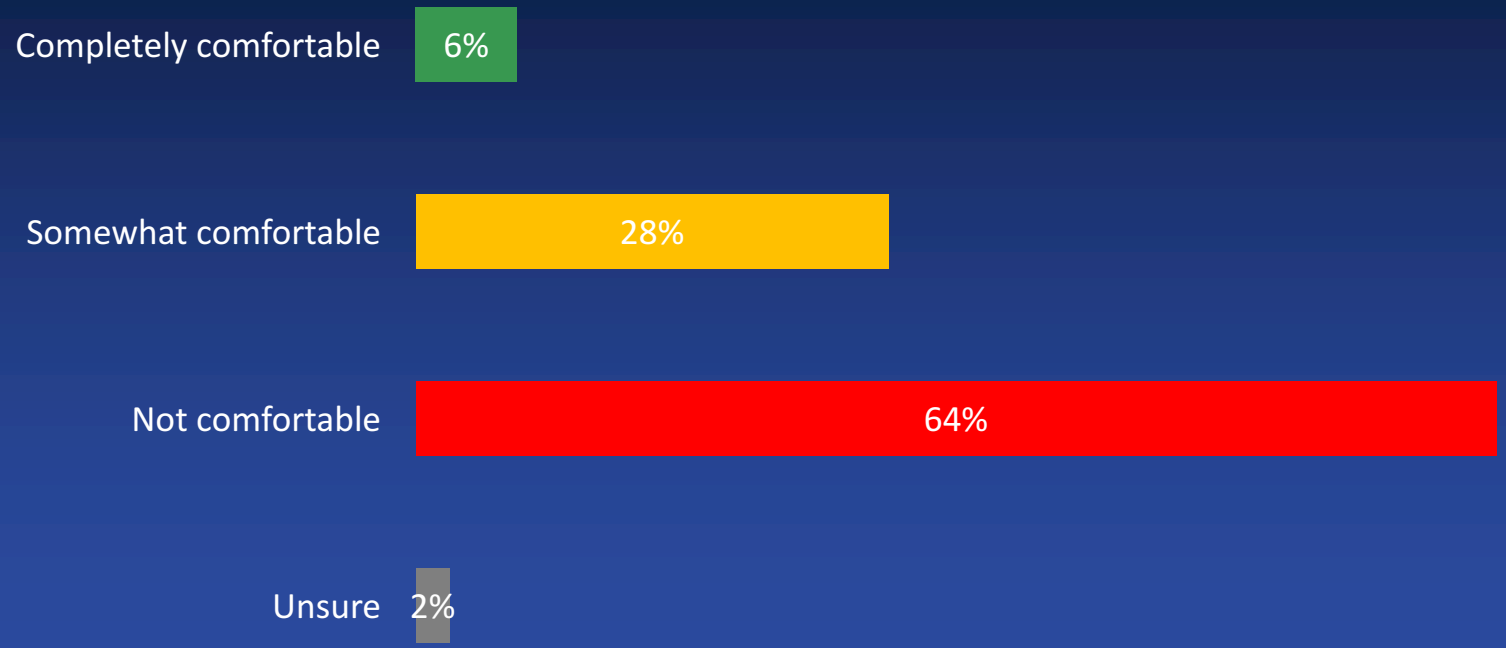


Source: IMS Audits data (Australia only); Market Share is measured as share of dosage unit sales (this is to account for compounding).

Non-Medical Switching

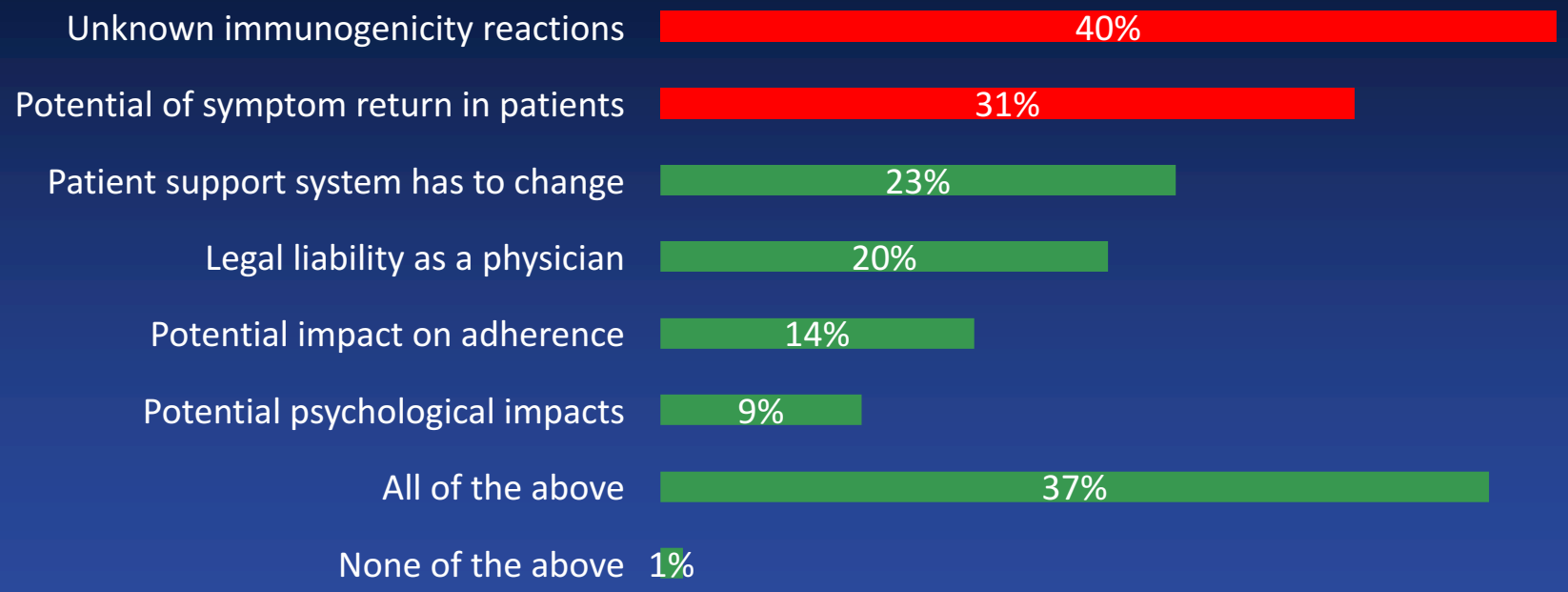
Physician Comfort Level with Third-Party Switching to a Biosimilar

Canadian Survey, Oct. 2017



Physician Concerns with Third-Party Switching to a Biosimilar

Canadian Survey, Oct. 2017

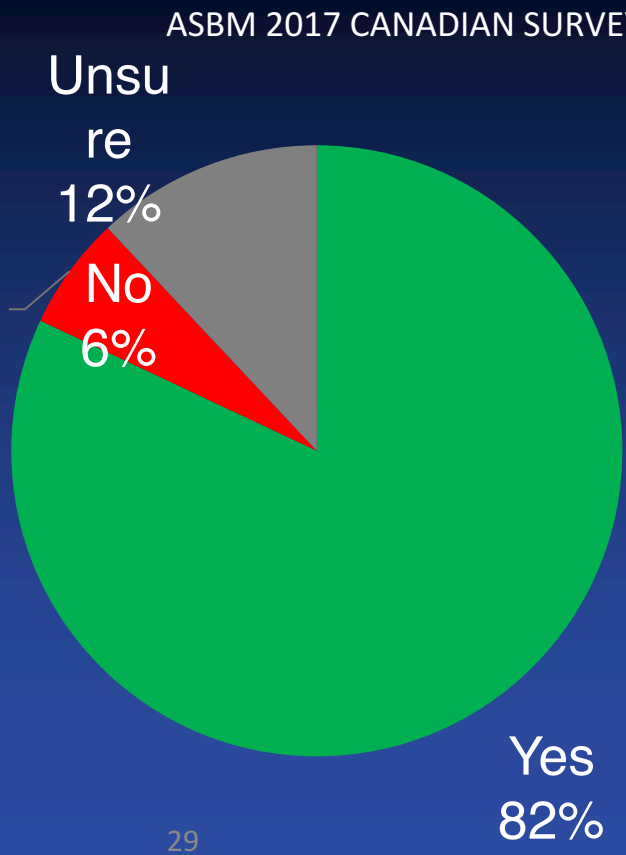


2017 Canadian Survey: Need for Switching Studies?

"While provinces have the authority to determine interchangeability and automatic substitution of medicinal products, Health Canada advises against this practice in the case of biosimilars.

Prior to deciding whether automatic substitution should be allowed by a pharmacist or payer,

Do you believe studies should be conducted that measure the effects of switching on patient safety and product efficacy?" (n=403)



Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcome

- "Thus, the extensive data collected to date suggest that the act of switching from a reference medicine to a biosimilar is not inherently dangerous, and that patients, healthcare professionals, and the public should not assume that it is problematic."

- Drugs. 2018; 78(4): 463–478.
  Published online 2018 Mar 3. doi: 10.1007/s40265-018-0881-y

Comment on: "Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes"

- "We believe that the lack of comprehensive and systematic inclusion of relevant studies, appropriate weighting to reflect strength of evidence, and the combining of results across drugs, diseases, and type of studies, challenge the conclusion reached."

Drugs. 2018; 78(8): 851–852.

Published online 2018 May 21. doi: 10.1007/s40265-018-0918-2

Increasing Biosimilar Uptake

- *Education*
- *Prescriber confidence - Real World Data*
- *Post Approval Obstacles*

FDA – Biosimilar Action Plan- New Educational Materials

- Biosimilar and Interchangeable Products
- Biosimilar Development, Review, and Approval
- Prescribing Biosimilar and Interchangeable Products
- Biosimilar Product Information
- Industry Information and Guidance
- Online Courses, Webinars, and Presentations
- Patient and Prescriber Outreach Materials

- https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/biosimilars/default.htm

According to this headline, 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 director Guido Rasi said. *"Given the role of healthcare professionals on the front line of patient care, it is vital that they have access to reliable information on these medicines: what they are and how they are developed, approved and monitored."*

document contains information covering the definition of biosimilars, the development and approval process, information and EMA assessment reports.

EUROPEAN MEDICINES AGENCY

European Commission

Biosimilars in the EU

Information guide for healthcare professionals

Prepared jointly by the European Medicines Agency and the European Commission

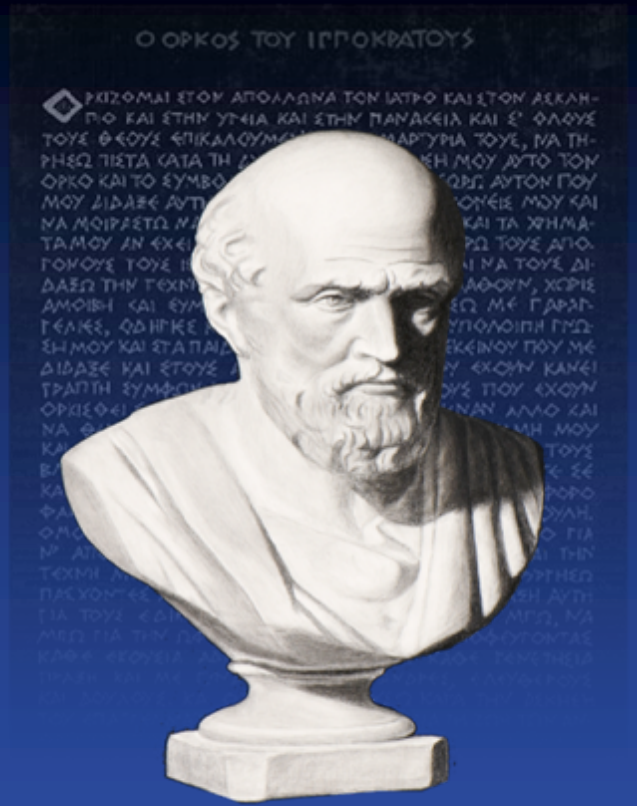
Yet we've not yet seen widespread use when physicians have a choice of using a biosimilar or the originator.

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

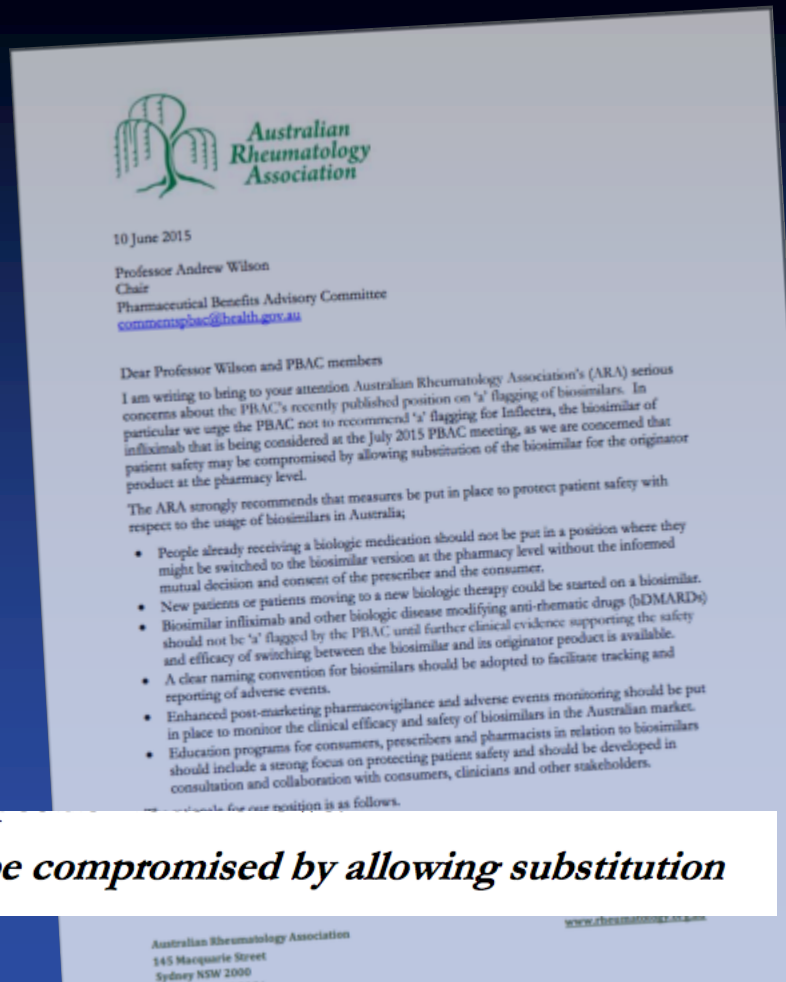
Clinicians are not comfortable with non-medical switching, especially with patients who are doing well on a particular therapy



Hippocratic Oath: "first, do no harm"

Clinicians and Caution

The 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-rheumatic 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.

Patient safety may be compromised by allowing substitution

Australian Rheumatology Association
145 Macquarie Street
Sydney NSW 2000

Physicians Asked for 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

Price Competition Alone - Does Not Ensure Access…

- 12 Biosimilars approved in US, but only 4 on market.
- Despite discounts of 15-33%, biosimilars remain unaffordable without insurance – not on the formulary.
- For 80% of Americans, the top three PBMs determine the formulary & the "preferred list".
- Choosing a medicine becomes to an extent the question: *"What insurance do you have"?*

How does a PBM or insurer determine which medicine gets the "*preferred placement*" on the formulary?

Manufacturers Compete for the Preferred Spot…

COMPETITION DRIVES PRICES DOWN

COMPETITION DRIVES PRICES UP

BUILDING A HOUSE

WINNER= Lowest Bidder

SELLING A HOUSE

WINNER= Highest Bidder

OUR DRUG DISTRIBUTION SYSTEM

- PBMs receive rebates/fees based on a % of the list price of the medicine.
- These price concessions can be over 50% of the list price.
- **This creates a perverse incentive for HIGHER PRICED MEDICINES, not lower, because the HIGHER PRICED MEDICINE can provide the larger rebate fee package.**

Ensuring Real Access Requires Penetrating the "Formulary Wall"

- **Neither lower prices NOR faster approval seem to get a biosimilar medicine on a PBM's preferred formulary list.**
- This poses a critical barrier to access.
- To increase access to biosimilars, FDA must work with other agencies in the government on policies which address this reality.
- Formularies based on efficacy, safety and **lowest list price** – not highest price concession based on a % of the list price.

Summary

DISTINCT NAMING of all biologics, including biosimilars, is important to the physicians worldwide, international harmonization is the next step.

SUBSTITUTION without prescriber input can only be done with “interchangeable” biosimilars

Physicians have concerns regarding THIRD-PARTY SWITCHING of patients, especially for non-medical reasons.

Physicians want DATA SHOWING CONTINUED EFFICACY & SAFETY / pharmacovigilance - including further switching studies, in order to feel comfortable switching patients.

Increasing biosimilar uptake requires INCREASING PHYSICIAN CONFIDENCE through RWE, and addressing POST-APPROVAL BARRIERS.

SafeBiologics

ALLIANCE *for* SAFE BIOLOGIC MEDICINES

Thank You For Your Attention