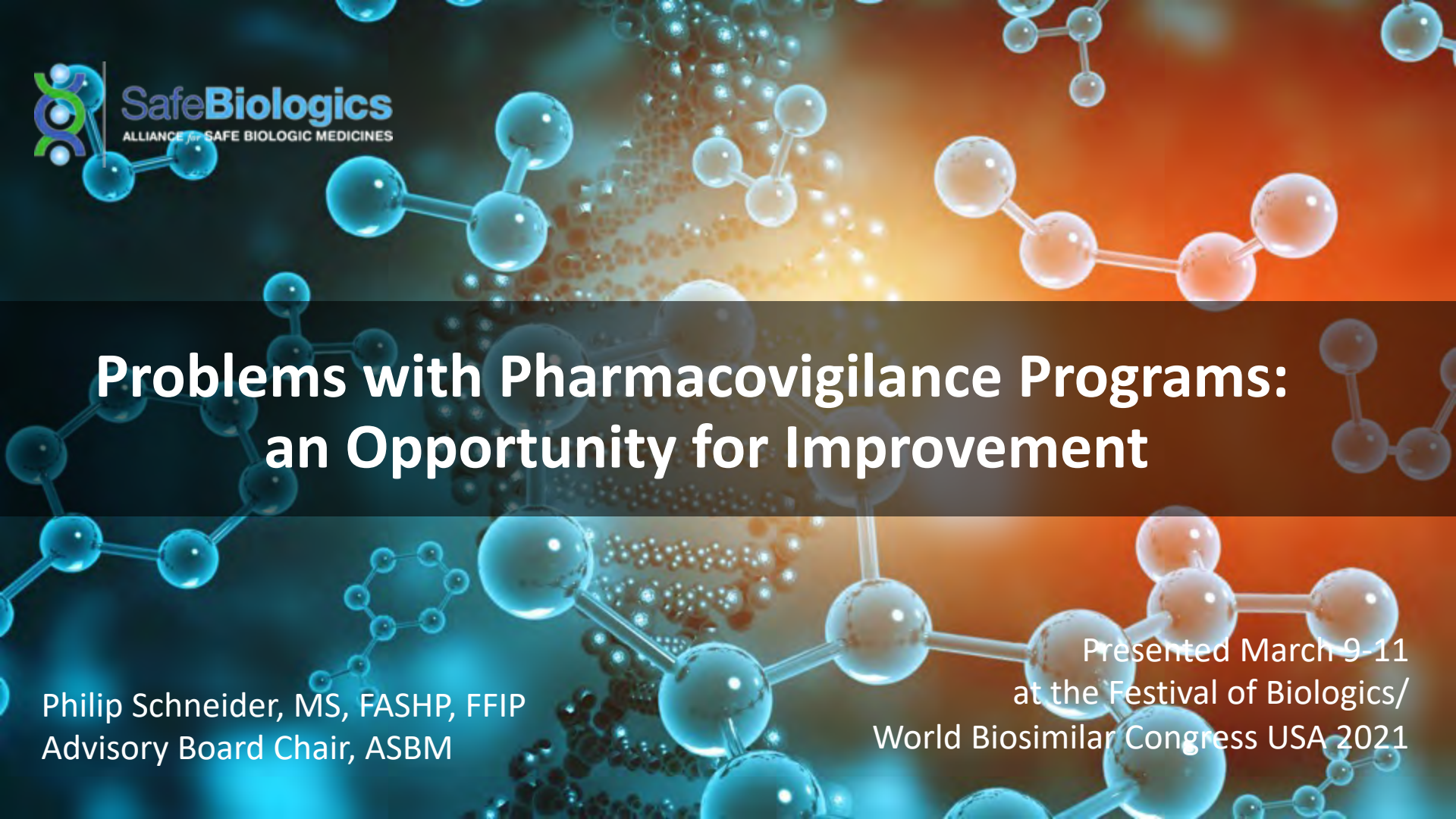


Problems with Pharmacovigilance Programs: an Opportunity for Improvement

Philip Schneider, MS, FASHP, FFIP
Advisory Board Chair, ASBM

Presented March 9-11
at the Festival of Biologics/
World Biosimilar Congress USA 2021

Introduction

- **Philip Schneider, MS, FASHP, FFIP**
- Advisory Board Chair, Alliance for Safe Biologic Medicines
- Past Vice President, International Pharmaceutical Federation (FIP)
- Past-President, American Society of Health-system Pharmacists
- Professor of Pharmacy, Ohio State University

About ASBM

SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES

Formed in 2010 with the passage of the Affordable Care Act (ACA) and Biosimilar Price Competition and Innovation Act (BPCIA); with the goal of keeping patient safety at the forefront of biosimilar policy discussions.

ASBM's Steering Committee is composed entirely of patient and physician member organizations.

- PATIENT ADVOCATES
- PHYSICIANS
- PHARMACISTS
- RESEARCHERS
- MANUFACTURERS (INNOVATOR & BIOSIMILAR)

LYMPHOMA COALITION
Worldwide Network of Lymphoma Patient Groups

American Gastroenterological Association

CSRO
Coalition of State Rheumatology Organizations

More than 130 organizations spread across six continents; the More than 130 organizations spread across six continents; the majority of these are patient groups, including several patient coalitions.

ASBM Physician and Pharmacist Surveys

U.S. Physicians
2012: n=376
2015 n=400
2015: n=400
2019: n=202
2021 n= 400

U.S. Pharmacists
2015 n=401

Latin American Physicians
(Argentina, Brazil, Colombia, Mexico)
2015: n=399

Canadian Physicians
2014: n=427
2017: n=427
2021 (planned)

European Physicians
(France, Italy, Germany, Spain, Switzerland, UK)
2013: n=470
2019: n=579

Australian Physicians
2016: n=160

All surveys available at www.SafeBiologics.org/surveys

Sharing Perspectives With Regulators

WORLD HEALTH ORGANIZATION INN CONSULTATIONS
(2013-2022)

AUSTRALIAN DEPARTMENT OF HEALTH,
THERAPEUTIC GOODS ADMINISTRATION (2017)

HEALTH CANADA, CANADIAN HEALTH MINISTRY (2017)

INTERNATIONAL CONFERENCE OF DRUG REGULATORY
AUTHORITIES (ICDRA) (2016, 2018)

ASBM INTERNATIONAL REGULATOR FORUMS
ON NOMENCLATURE HARMONIZATION
(FDA, HEALTH CANADA, WHO) 2018-2019

EU COMMISSION/EMA BIOSIMILARS MEETING (2019)

U.S. FDA/FEDERAL TRADE COMMISSION WORKSHOP ON BIOSIMILAR COMPETITION
(MARCH 2020)

SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES

World Health Organization

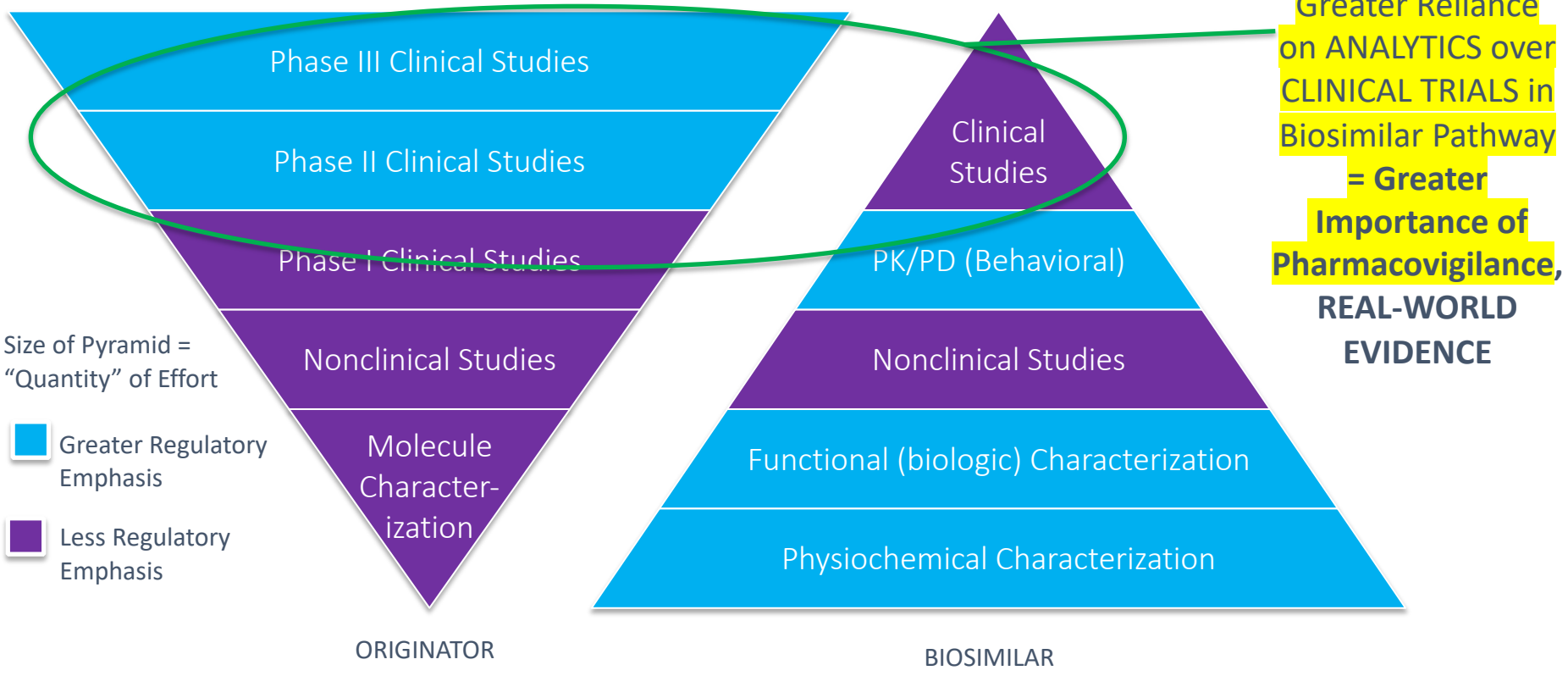
Health Canada Santé Canada

FDA

Australian Government
Department of Health
Therapeutic Goods Administration

ANVISA

Approval Pathway: Originator vs. Biosimilar



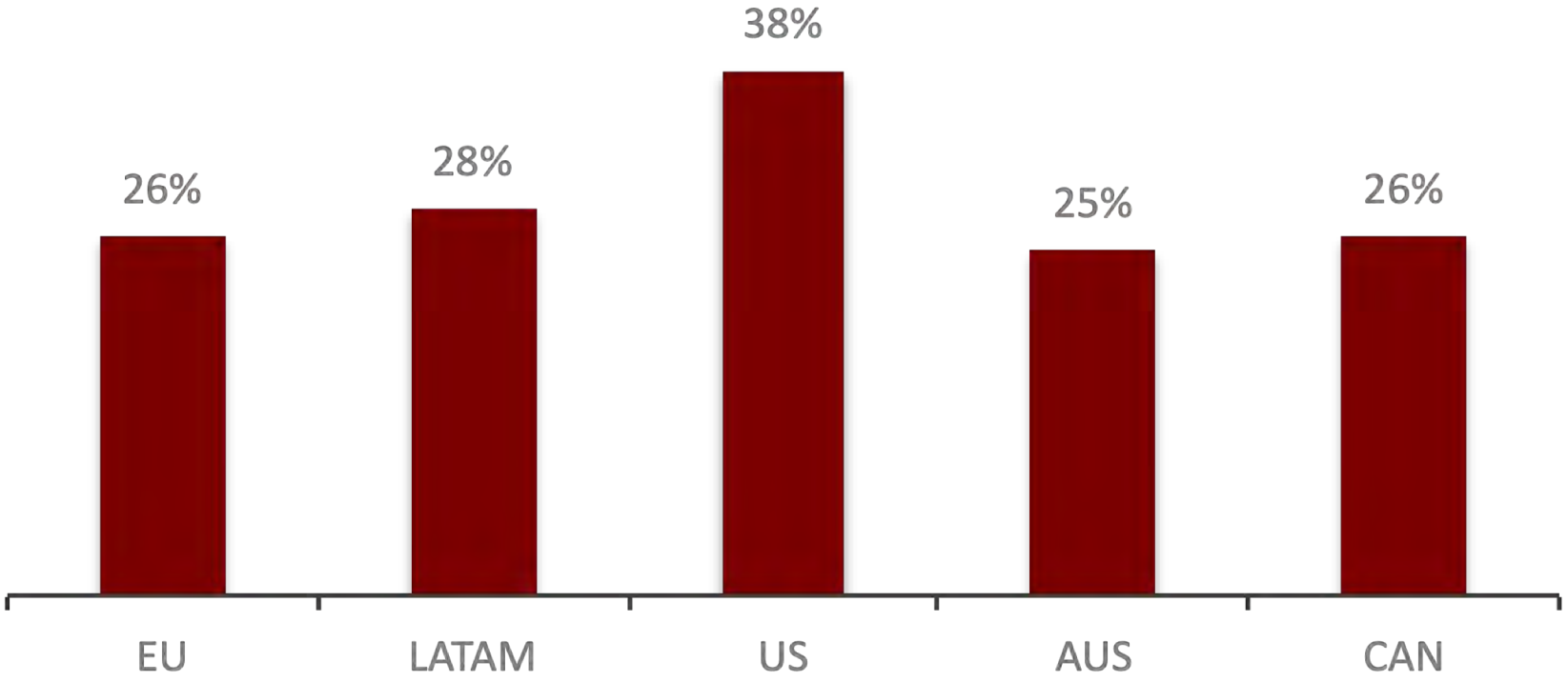
Challenge: Originator Product and Biosimilars share an WHO-assigned International Proprietary Name (INN)

- **For example, all the products on the right use the INN "infliximab"**
- Trade names differ from country to country.
- **This can become confusing and result in:**
  - **Misattribution of adverse events**
  - **Inadvertent or inappropriate substitution**
  - **Inaccurate patient records**
  - **Inability to do targeted recalls**

Manufacturer	Trade Name(s)
Janssen	Remicade
Amgen	Avsola
BCD-055	Biocad
Celltrion/Hospira (Pfizer)	Remsima/Inflectra/Flammegis/Ifixi
Epirus	Infimab
MabTech/Sorrento	STI-002
MabTech/Sorrento	CMA-B008
Nichi-Iko	NI-071
Nippon Kayaku	Infliximab BS
Ranbaxy	BOW015
Samsung Bioepis	Flixabi
Sandoz	Zessly
Shanghai Biomabs	Baimaibo

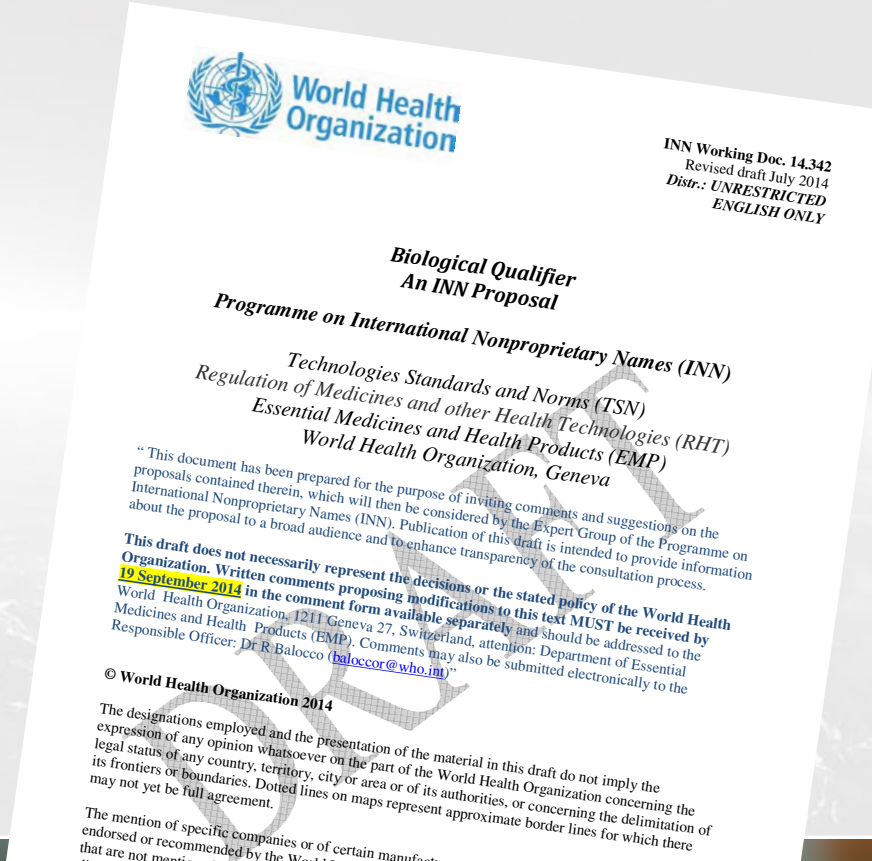
ASBM Surveys (2013-2017): Percent of Physicians Using Only INN when Reporting Adverse Events.

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



In 2014, the WHO's International Nonproprietary Names (INN) Expert Group recommended a four-letter distinguishing suffix be appended to each biologic that shares an INN, traceable to its marketing authorization holder.

The "Biologic Qualifier" or (BQ).



World Health Organization

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

Biological Qualifier
An INN Proposal

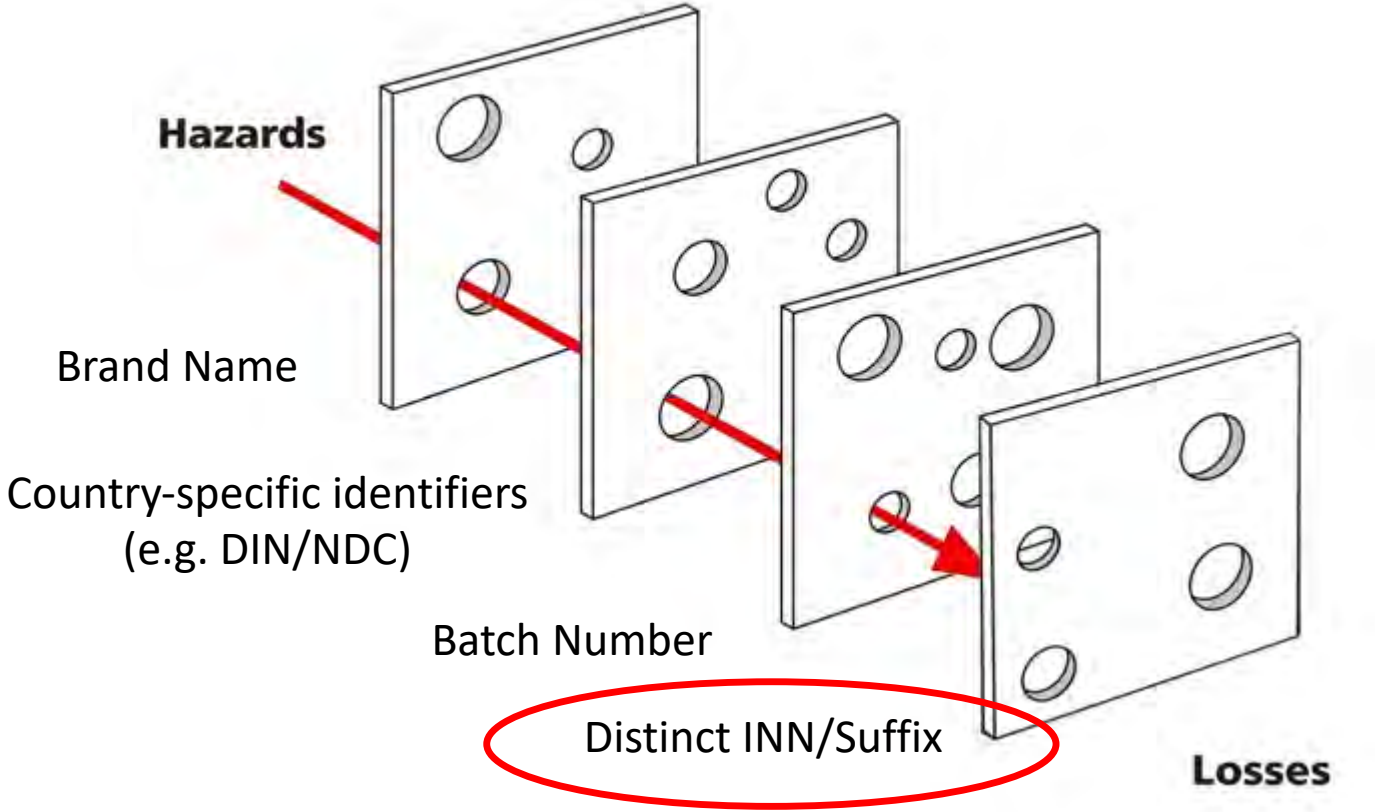
Programme on International Nonproprietary Names (INN)

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

" This document has been prepared for the purpose of inviting comments and suggestions on the proposals contained therein, which will then be considered by the Expert Group of the Programme on International Nonproprietary Names (INN). Publication of this draft is intended to provide information about the proposal to a broad audience and to enhance transparency of the consultation process.

This draft does not necessarily represent the decisions or the stated policy of the World Health Organization. Written comments proposing modifications to this text MUST be received by 19 September 2014 in the comment form available separately and should be addressed to the World Health Organization, 1211 Geneva 27, Switzerland, attention: Department of Essential Medicines and Health Products (EMP). Comments may also be submitted electronically to the Responsible Officer: Dr R Balocco (baloccor@who.int)"

Distinguishable INN/Suffix as a “Defense” in Identification of Biologic Medicines



Objections to the use of distinguishing suffixes included concerns that these would:

1) **Imply inferiority**
2) Undermine physician confidence
3) Hurt biosimilar uptake

The U.S. experience, however, has now definitively shown that this is not the case.

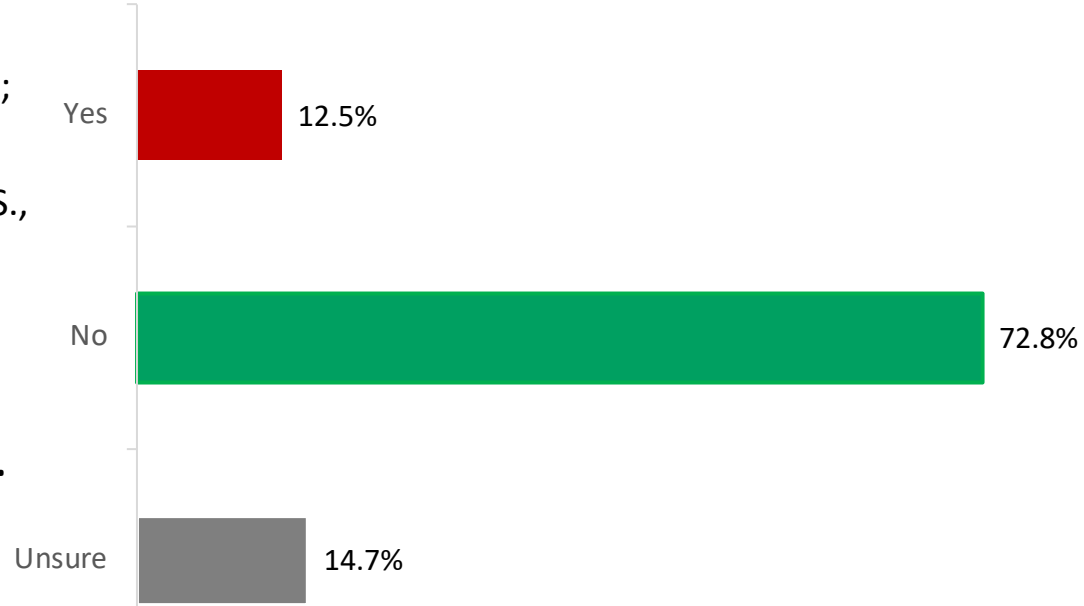
ASBM
2021 US Physician Survey

- 401 physicians
- Drawn from specialties in which biologics are routinely prescribed (e.g. dermatology, gastroenterology, nephrology, neurology, oncology, rheumatology, etc.)
- All prescribe biologics.

1) Inferiority: Suffixes Do Not Imply Inferiority to the Vast Majority of US Physicians.

- **73% do NOT think a suffix implies inferiority to its reference product.**
- 12.5% think YES it implies they are inferior; and 14.7 are unsure.
- It is important to remember that in the U.S., all new innovator biologics are also issued suffixes, even though older products have not been retroactively renamed.
- **Eventually, nearly all originator products will have suffixes, as will their biosimilars.**

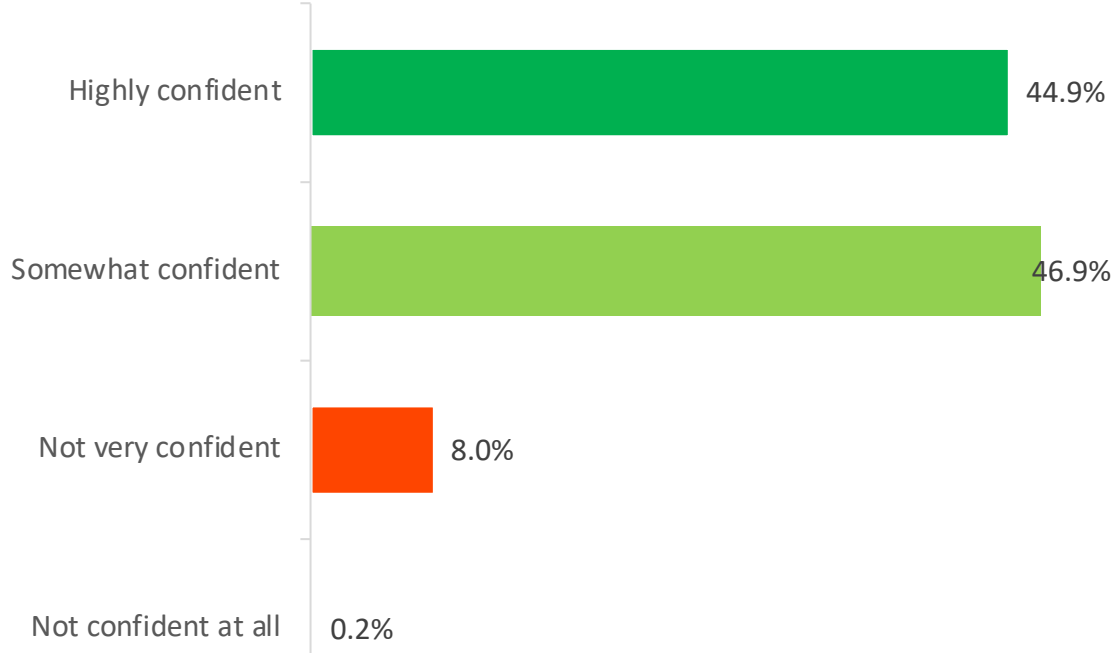
Q2. In your opinion, does the use of an identifying suffix imply that a biosimilar is inferior to its reference product in terms of safety or efficacy? (n=401)



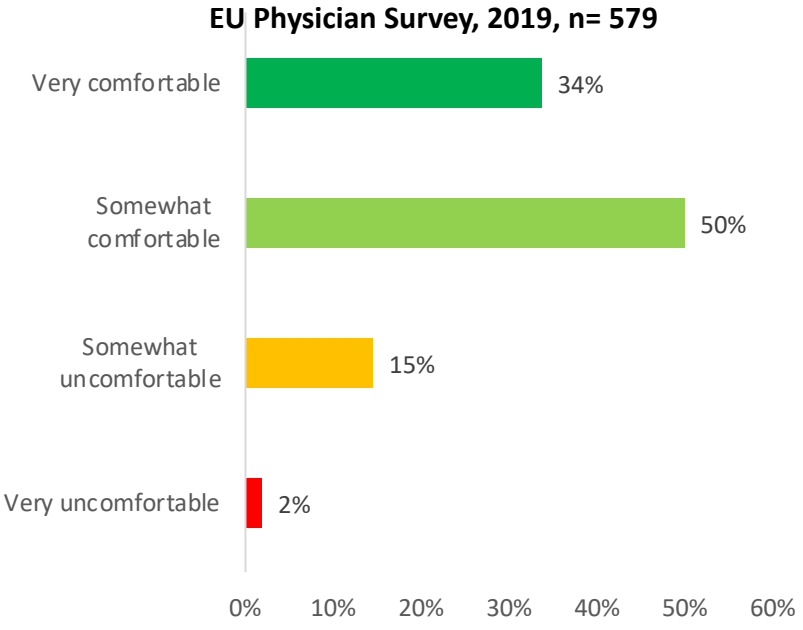
2) Confidence: US Physicians Are Highly Confident in the Safety and Efficacy of Biosimilars.

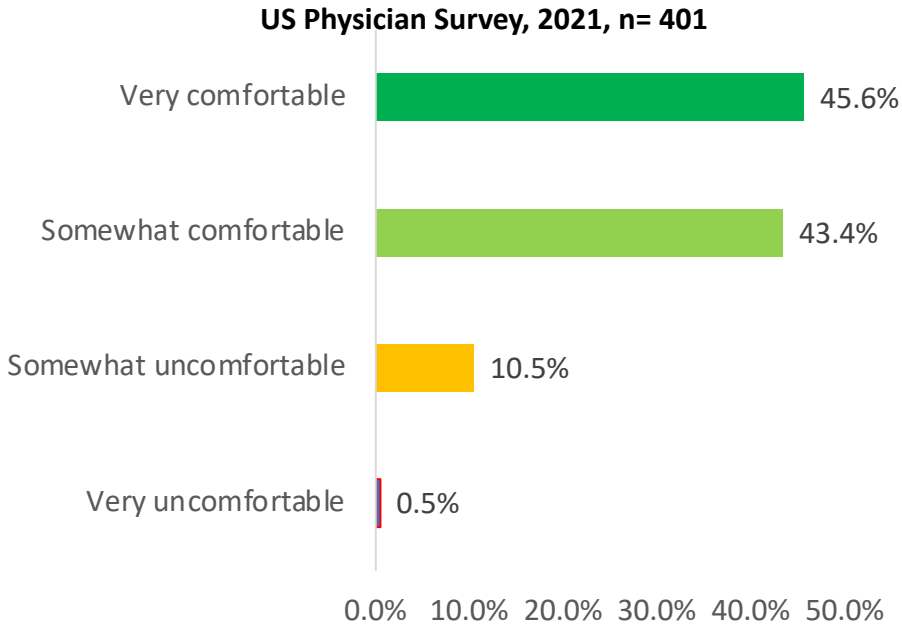
- **91.8% somewhat or highly confident in safety and efficacy of biosimilars,** with 45% (44.9) highly confident.

- Q1. How would you describe your personal confidence level in the safety and efficacy of biosimilars? (n=401)



2) Confidence: US Physicians as (or more) Comfortable Prescribing Biosimilars to Naïve Patients than their European Counterparts…





3) Uptake: Distinct Suffixes Have Not Held Back Biosimilars in the U.S.

- 33 Approved, 21 are on the market.
- Biosimilars launch at wholesale acquisition cost (WAC) 15% to 37% lower than their reference products and up to 40% below the reference product's average sales price (ASP).
- **In the US, biosimilars have gained significant share in the majority of therapeutic areas in which they have been introduced:**
- 80% for filgrastim biosimilars, 70% for trastuzumab and bevacizumab biosimilars, and 55% for rituximab biosimilars.
- Rituximab and infliximab have had the most limited adoption, with approximately 20% market share.
- As more become available, the increased competition has **driven down prices of both biosimilars and innovator biologics.**

FDA U.S. FOOD & DRUG ADMINISTRATION

According to the FDA's Janet Woodcock, the savings from biosimilars was $2.5 billion in 2019, and **more than three times that much in 2020**.

3) Uptake: US Biosimilar Uptake Rates Are Now Comparable to Those of Many European Countries. (20-80% range)

Total Biosimilar Volume: Denmark: 63%; UK: 45%; Germany 40%; France 34%, Belgium and Switzerland tied at 14%.

Filgrastim/Pegfilgrastim: 16 European countries had > 90% biosimilar utilization in 2018, Ireland was just 27%.

Anti-TNF biosimilars (adalimumab, etanercept and infliximab), Norway and Denmark had 81% and 96% biosimilar uptake, respectively, while every other country's utilization was less than 50% .

Variations are influenced by government involvement, reimbursement structures and tender procurement policies.

Source: KPMG/Medicines for Europe Analysis (March 2019)

Price- Not Nomenclature-Seems to Be the Predominant Factor in Increasing Biosimilar Uptake

As in Europe, as more and more biosimilars launch in a given product class, competition drives prices downward, discounts increase, and biosimilar market share goes up:

- First U.S. filgrastim biosimilar launched with 15% discount over its reference product. Today, with increased competition, its discount has increased to 35% and it has now attained a majority market share (55%), with an 80% total market share for all filgrastim biosimilars.
- First U.S. rituximab biosimilar launched at a 10% discount over its reference product. A few months later the second launched at a larger, 24% discount to compete.
- As it becomes routine to have 3, 4, or 5 biosimilars approved for a reference product we expect this trend- and savings- to continue.

https://www.pacificresearch.org/wp-content/uploads/2019/07/BiosimilarsCompetition_F.pdf
https://pharmaintelligence.informa.com/resources/product-content/teva-debuts-us-rituximab-at-a-10-discount
https://generics.pharmaintelligence.informa.com/GB149550/Pfizers-US-Rituximab-Launched-At-A-24-Discount

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)*

85% *of US physicians support FDA issuing distinct names. (2019)*

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

In the absence of WHO action, regulators have been forging their own paths…

- TGA, initially supportive of WHO, has reversed itself.
- FDA implemented its own BQ-like distinct suffix system.
- Health Canada attempted to harmonize with US, but eventually went with a system based on Shared INN + Drug Identification Number (DIN).

Biosimilar Naming: As It Stands Today

World Health Organization

INN + 4-letter random suffix
(unimplemented)

FDA U.S. FOOD & DRUG ADMINISTRATION

INN + 4-letter random suffix
(WHO-compatible)

EUROPEAN MEDICINES AGENCY

Australian Government
Department of Health
Therapeutic Goods Administration

pmda

กระทรวงสาธารณสุข MINISTRY OF PUBLIC HEALTH

PERÚ Ministerio de Salud

Ministry of Health Malaysia

Health Canada

Japan, Thailand, Malaysia, Peru
Shared INN plus suffix systems
Willing to harmonize with WHO

<u>Shared INN + trade name</u>
Past WHO supporters Health Canada and TGA remain willing to harmonize with WHO

2020 WHO Report: Inconsistent Nomenclature Remains a Challenge

The report, titled *"Regulatory challenges with biosimilars: an update from 20 countries"* notes:

"the **lack of consistency in the nomenclature of biologics and biosimilars causes concern about "prescription mix-ups, unintended switching and traceability."**

In recent meetings with the WHO's International Nonproprietary Names (INN) Programme, ASBM has offered to work with the WHO to **circulate a survey or petition to document support among national regulatory authorities for distinct naming and global harmonization.**


ANNALS OF THE NEW YORK ACADEMY OF SCIENCES

Original Article

Regulatory challenges with biosimilars: an update from 20 countries

Source: 13. Kang et al. Regulatory challenges with biosimilars: an update from 20 countries. Ann N Y Acad. Sci. ISSN 0077-8923

Summary

- **Reliance on brand name + shared INN is inadequate to consistently identify the biologic in ADR reports-** the degree of ambiguity varies by country and by setting, including within a country, but we routinely see 30-40% of AE reports without brand name, and higher in some settings.
- Widespread recognition of the importance of including brand names, and requirements to include it, have not resulted in an increase of its use in reporting.
- **WHO has identified lack of a naming standard as a remaining regulatory challenge** that undermines the strong pharmacovigilance needed for biologics and biosimilars.
- **Early concerns with distinct naming have proven to be unfounded**. The use in the U.S. of a distinct naming system similar to that proposed by the WHO (INN +suffix) has NOT created negative perceptions of biosimilars among physicians. **Confidence in biosimilars is high among U.S. physicians, and uptake is reaching levels comparable to those in Europe.**
- A distinct international naming system (such as WHO-proposed INN + BQ suffix) would provide an additional layer of “defense” in biologic PV globally, ensuring more accurate attribution of AEs. This would be especially useful in developing countries without advanced pharmacovigilance programs.

SafeBiologics

ALLIANCE *for* SAFE BIOLOGIC MEDICINES

Thank You For Your Attention