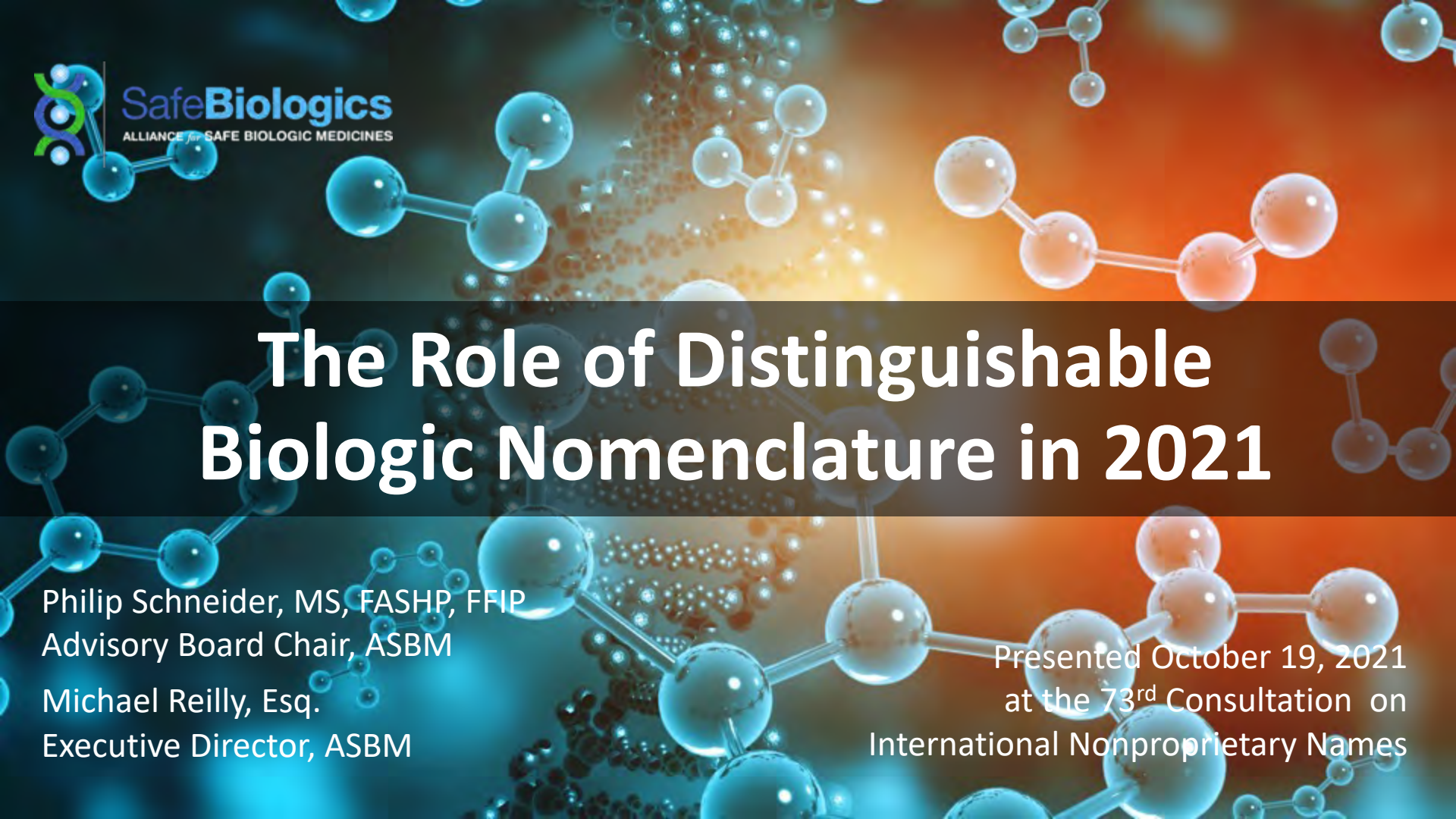

The Role of Distinguishable Biologic Nomenclature in 2021

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Executive Director, ASBM

Presented October 19, 2021
at the 73rd Consultation on
International Nonproprietary Names

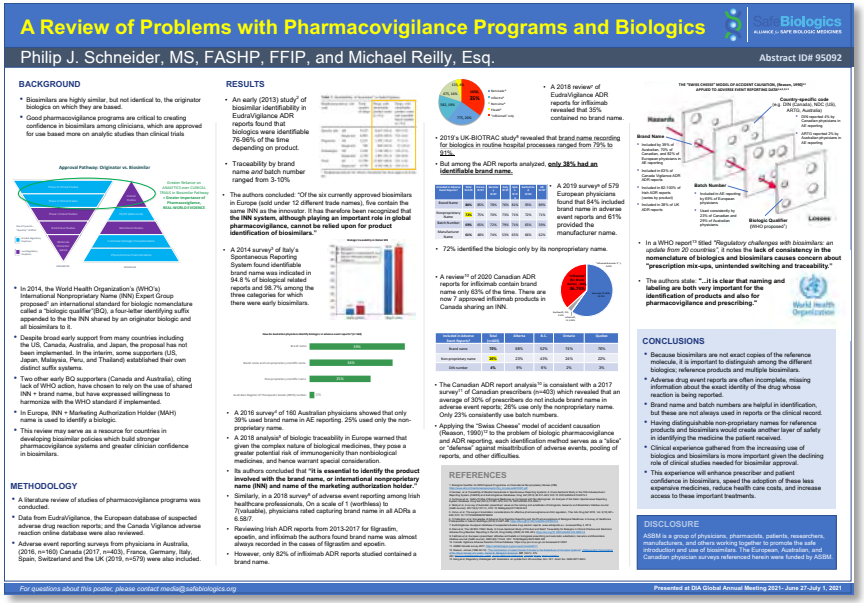
When We Last Met in April…

72nd INN Consultation, April 2021

- ASBM was preparing a poster for DIA 2021
- Today we'd like to follow up and look at the poster, its findings, and how these are being used in discussions with regulators and others internationally.
- We will also preview some new data from a brand-new 2021 U.S. physician survey.

DIA 2021 Poster: “A Review of Problems with Global Pharmacovigilance” (June 27-July 1)

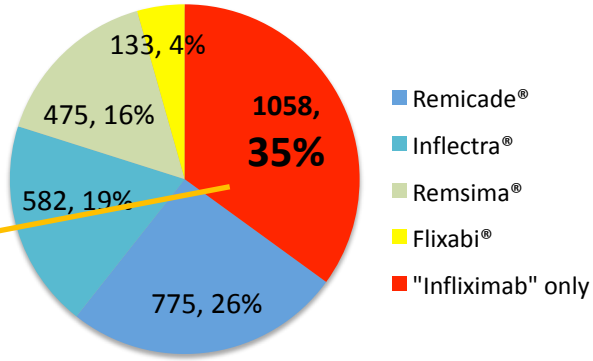
- Examined published literature on identifiability of biologic products.
- Focused on problems in adverse event reporting
- Found that identifiability to the product level is important to physicians.
- **Yet recording of brand names in adverse event reporting varies wildly from country to country, and between practice settings.**
- **More than a third of AE reports in Canada and Europe do not contain brand name.**

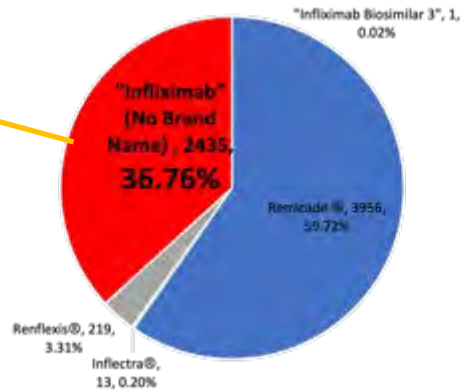


See a video walkthrough of the poster here…

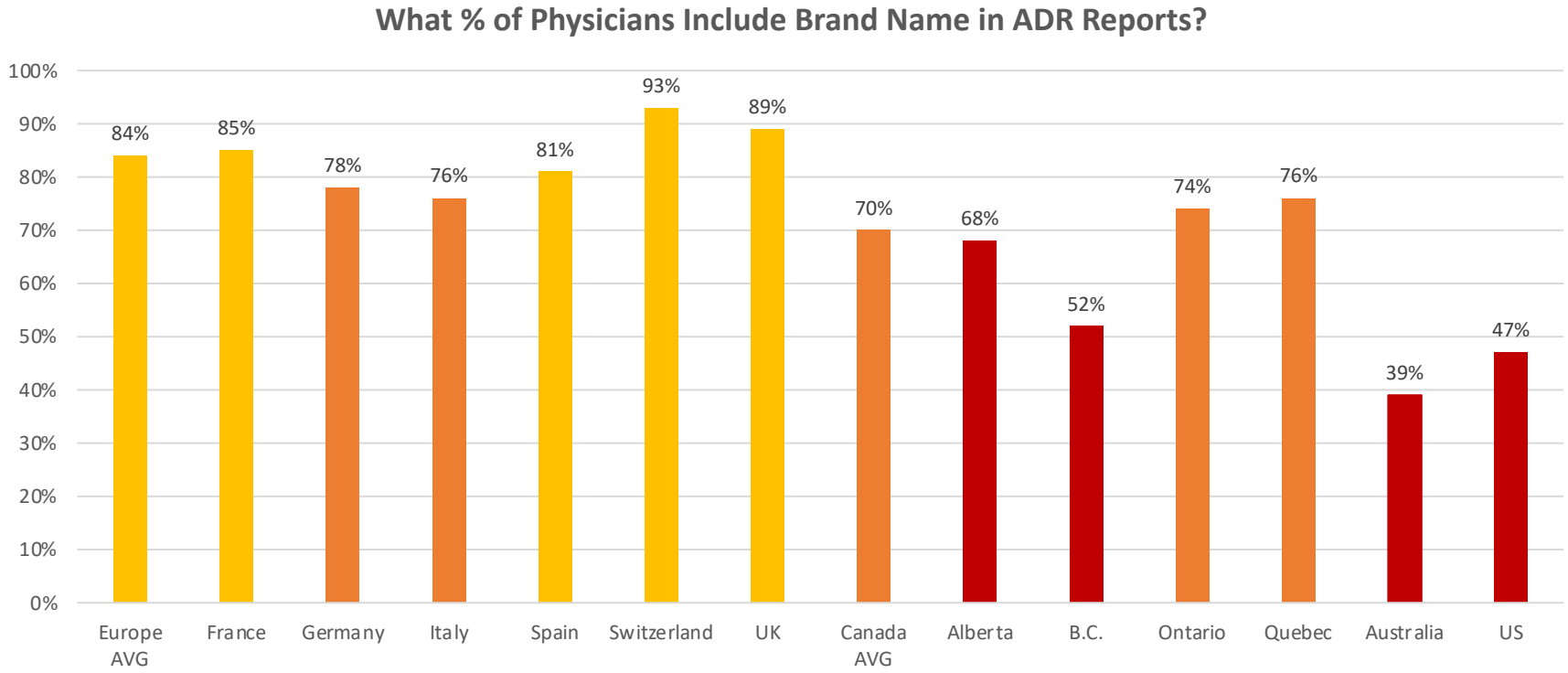
Brand Name Recording in ADR Reports: Wide Variation

- 2018 Irish ADR reports for infliximab: **18% missing brand name**
- A 2018 review of EudraVigilance ADR reports for infliximab revealed that **35% contained no brand name.**
- A review of 2020 Canadian ADR reports for infliximab **are missing brand name 37% of the time.**
- 2019 UK BIOTRAC study: **only 38% of ADR Reports had an identifiable brand name.**





Brand Name Recording by Physicians: ASBM Survey Data



Source: Australia, Europe, and US physician surveys (2016-2019) www.safebiologics.org/surveys

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.”

"...it is clear that naming and labeling are both very important for the identification of products and also for pharmacovigilance and prescribing."

Source: 1S. Kang et al, Regulatory challenges with biosimilars: an update from 20 countries, Ann. N.Y. Acad. Sci. ISSN 0077-8923

Alone, Shared INNs Create Ambiguity: Infliximab

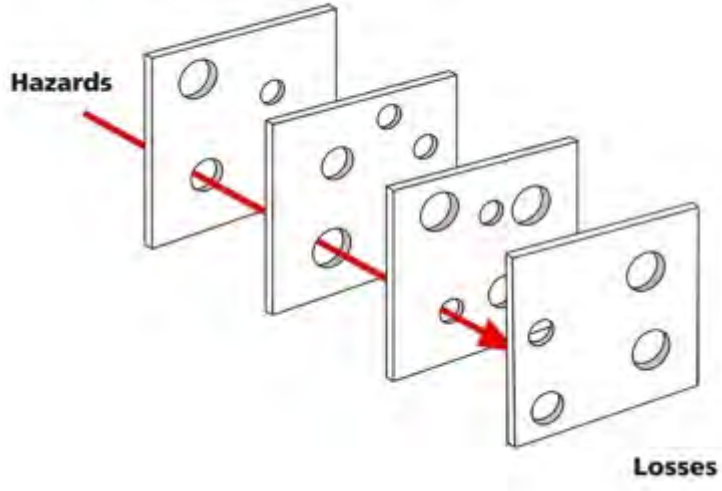
- **For example, all 13 products on the right share the INN "infliximab"**
- Brand/Trade Names are inconsistently recorded- ***and also differ from country to country.***
- **This can become confusing and result in:**
  - **Misattribution of adverse events**
  - **Inadvertent or inappropriate substitution**
  - **Inaccurate patient records**
  - **Inability to do targeted recalls**
- **Continued proliferation of biosimilars makes this a more pressing challenge- *one that the WHO is uniquely positioned to solve.***

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

Among the Poster's Conclusions: An Additional "Layer of Defense" Needed.

- **Adverse drug event reports are often incomplete**, missing information about the exact identity of the drug whose reaction is being reported.
- Brand name and batch numbers are helpful in identification, but these are **not always used in reports or the clinical record.**

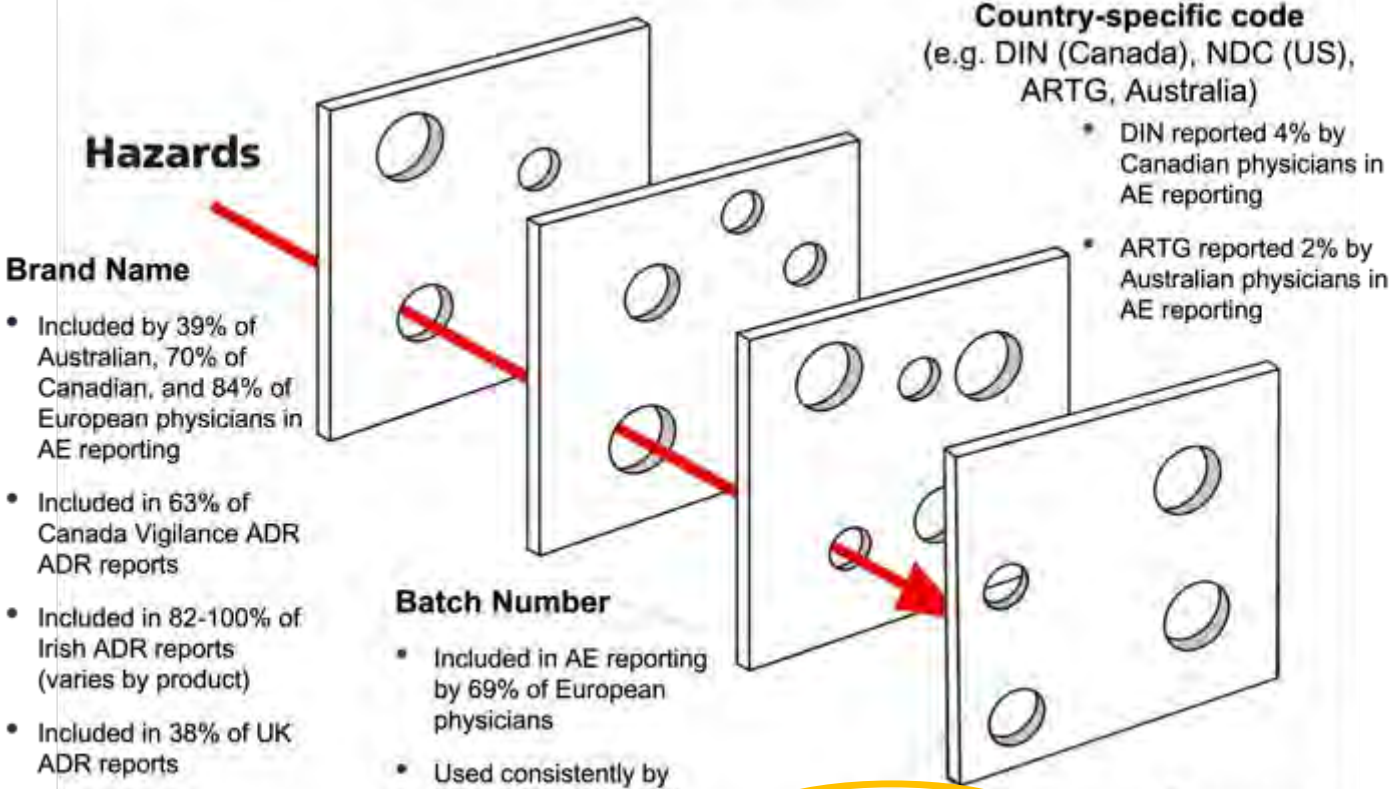
THE "SWISS CHEESE" MODEL OF ACCIDENT CAUSATION, (Reason, 1990)[12]



- **Having distinguishable non-proprietary names for reference products and biosimilars would create another layer of safety in identifying the medicine the patient received.**

The INN Expert Group of course, recognized these problems long ago…and proposed a solution.

THE "SWISS CHEESE" MODEL OF ACCIDENT CAUSATION, (Reason, 1990)[12] APPLIED TO ADVERSE EVENT REPORTING DATA[4,6,8,9,11]



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.

Preview: 2021 US Physician Survey

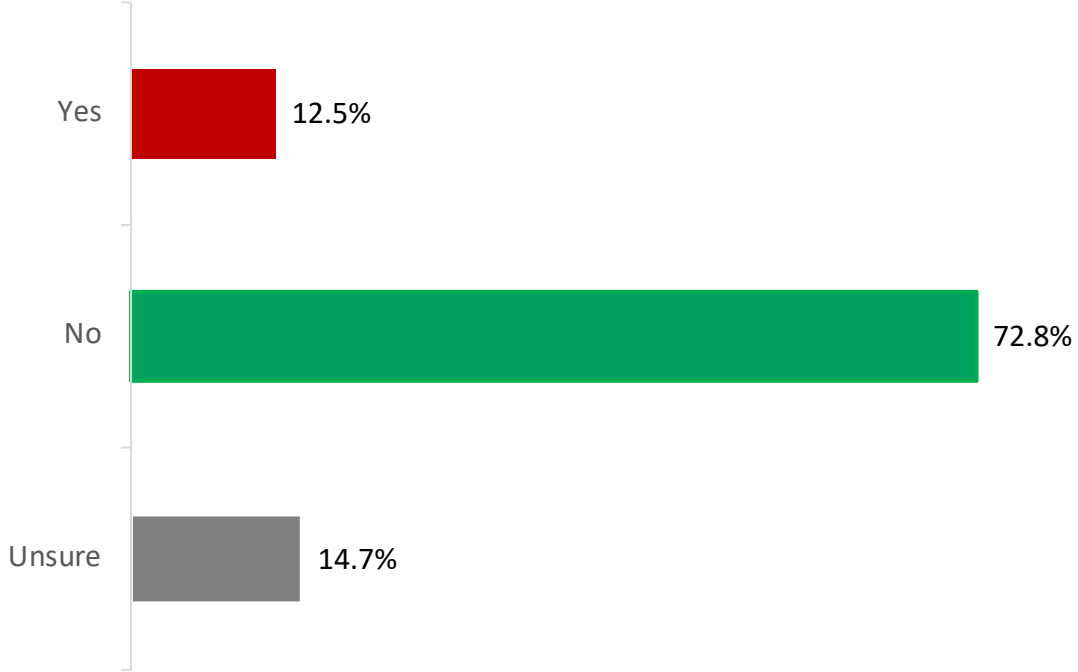
- 403 physicians
- Drawn from specialties in which biologics are routinely prescribed (e.g. dermatology, gastroenterology, nephrology, neurology, oncology, rheumatology, etc.)
- All prescribe biologics.

This brand-new survey has not yet been published- you are the first group to see it.

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.**

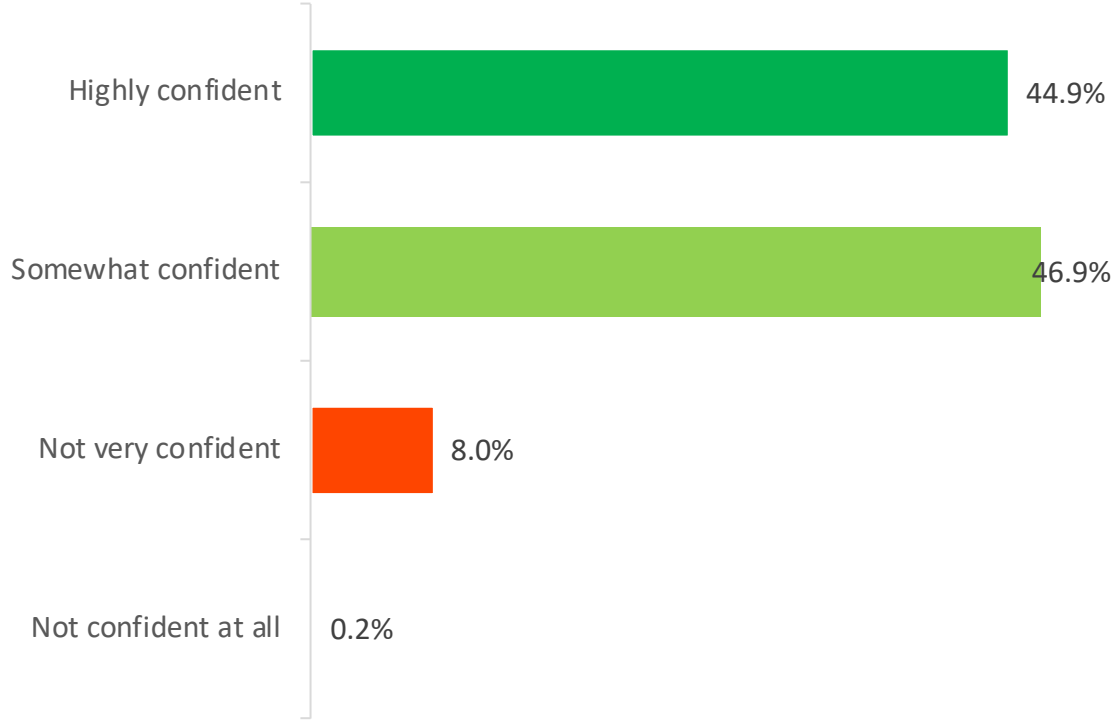
Q2. In your opinion, does the use of an identifying suffix imply that a biosimilar is inferior to its reference product in terms of safety or efficacy? (n=401)



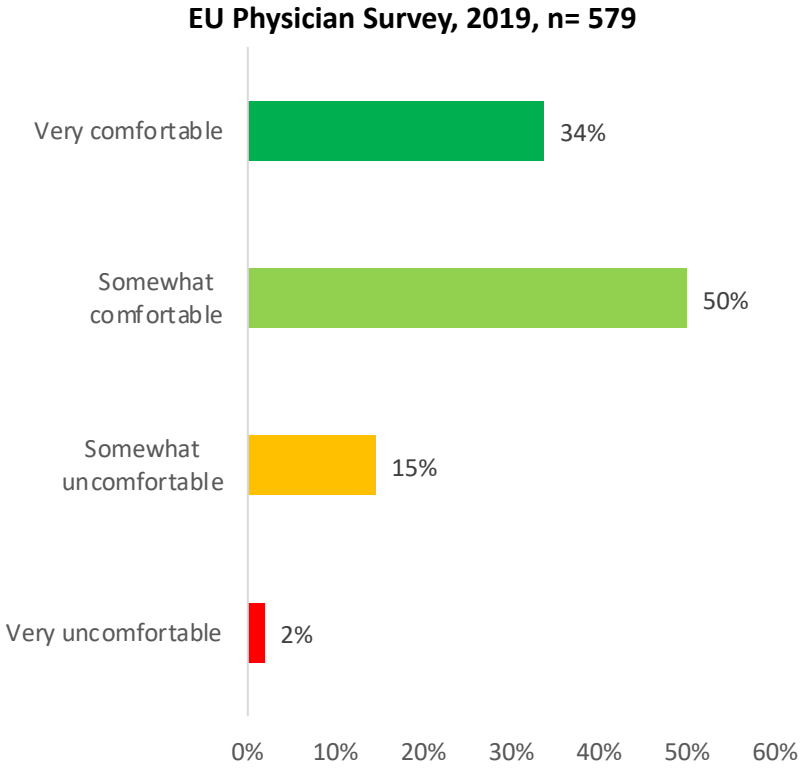
2) Confidence: US Physicians Are Highly Confident in the Safety and Efficacy of Biosimilars.

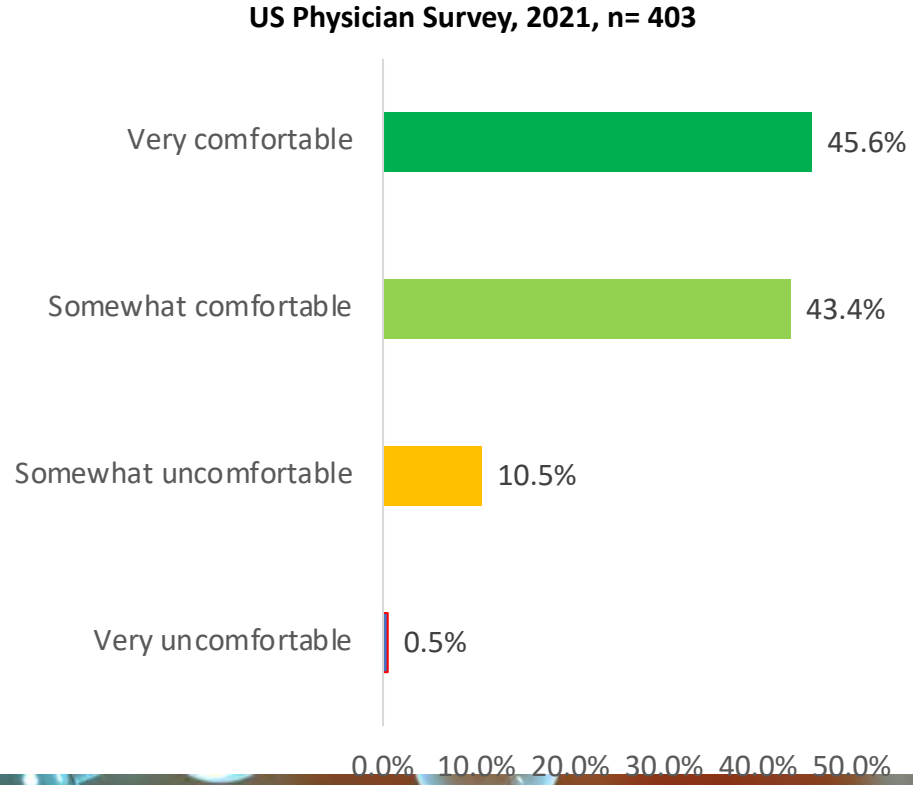
- **91.8% somewhat or highly confident in safety and efficacy of biosimilars,** with 45% (44.9) highly confident.

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



2) Confidence: US Physicians More Comfortable Prescribing Biosimilars to Naïve Patients than their European Counterparts…



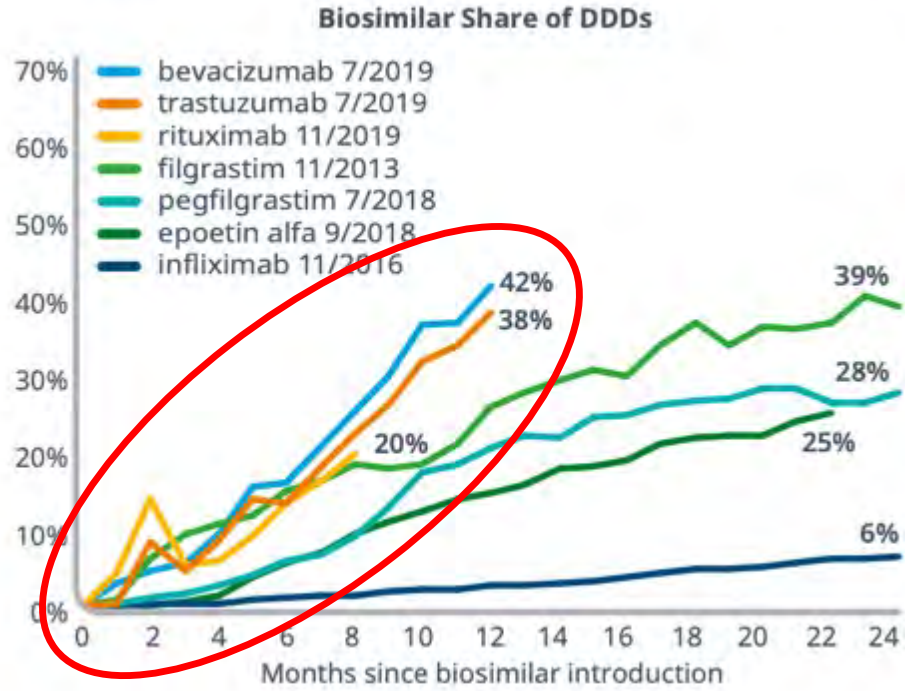


3) Uptake: Distinct Suffixes Have Not Held Back Biosimilars in the U.S.

- 30 Approved, 20 on the market.
- In the US, biosimilars have gained significant share in the majority of therapeutic areas in which they have been introduced:
- Filgrastim biosimilars have been on the market the longest at five years and have achieved an **80% share.**
- **Average 20% to 25% within the first year of launch**, with some projected to reach <50% within the first two years:
- Bevacizumab and trastuzumab biosimilars have approximately **40% share**- **these are expected to reach "European" levels of uptake 50-60% within 2 years.**
- Rituximab and infliximab have had the most limited adoption, with approximately **20% market share- although Rituximab is also on track to reach ~50% within 2 years.**

Recent biosimilars have achieved high volume shares, projected to reach more than 50% within the first two years, varying by channel

Newer U.S. biosimilars are achieving significant market share faster than earlier launches.



Source: IQVIA MIDAS®, Jun 2020; IQVIA National Sales Weekly, Aug 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

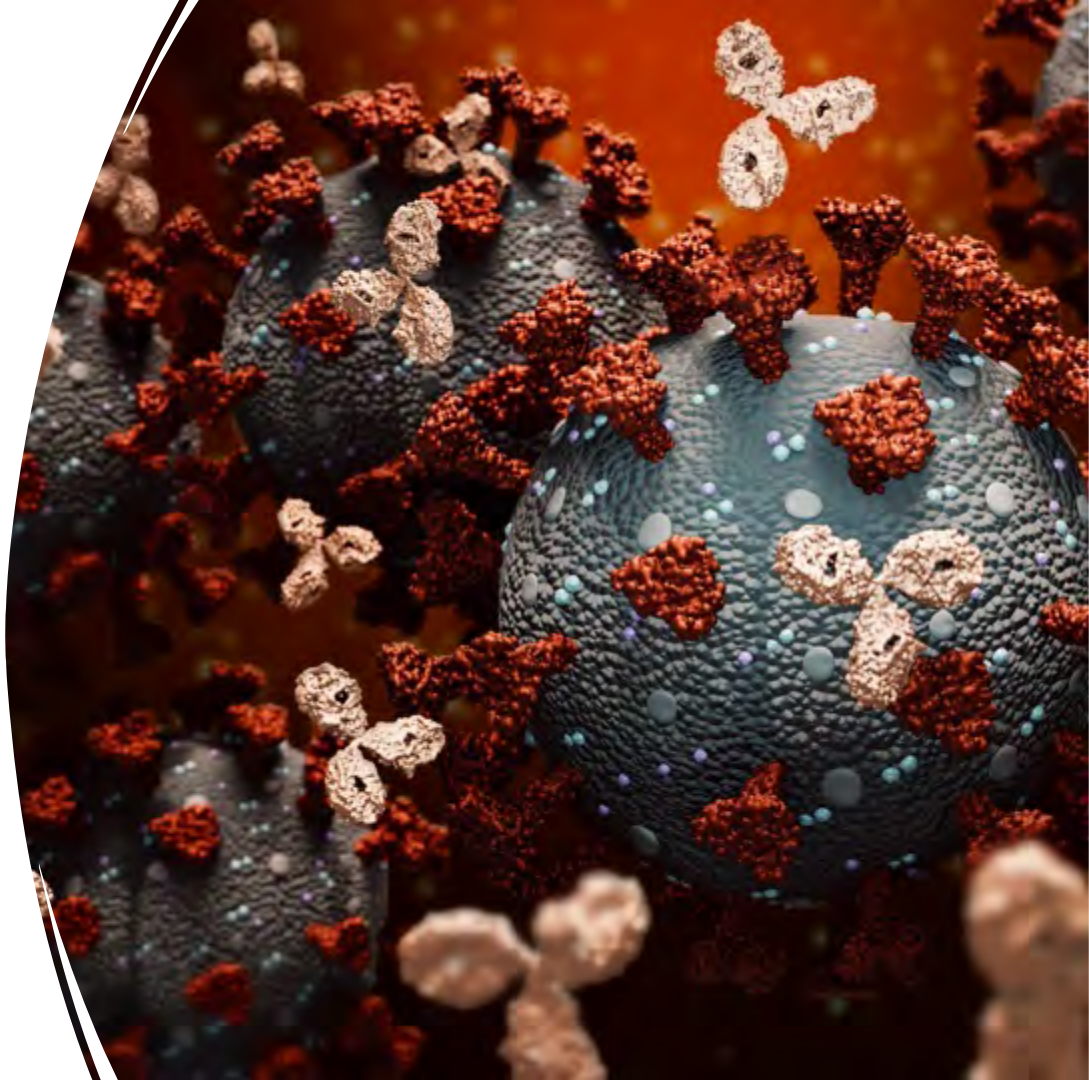
As in Europe, as more and more biosimilars launch in a given product class, competition drives prices downward, discounts increase, and biosimilar market share goes up:

- 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

While much of our attention remains focused on COVID-19, we are beginning to return to normal and focusing on other policy areas- **including pharmacovigilance and the role of biologic nomenclature**-

Increasingly, we have found renewed interest in this issue, and a desire for leadership…



Malta Medicines Authority Biosimilars Seminar (Aug. 26)

- Daylong seminar
- **Invited by Malta Medicines Authority** to present on several important topics on biosimilars
- **Among these were the pharmacovigilance challenges posed by the advent and proliferation of biosimilars; physician reporting practices, the role of the WHO, and potential solutions.**

World Drug Safety Congress Americas

Boston, MA, USA (Oct. 20-21)

PANEL: Improving pharmacovigilance programs around the world

- How can reporting rates be improved?·
- How can event reporting be harmonized globally to strengthen pharmacovigilance worldwide?·
- How can the accuracy and completeness of information in event reports be improved?

World Biosimilar Congress Europe 2021

Basel, Switzerland (Nov. 11)

- **Will be presenting these data and our policy recommendations as a part of a Session on “Real World Evidence and Pharmacovigilance”**

Summary

- Even in advanced countries, reliance on Brand Name + INN does not ensure accurate product identification. **Distinct naming will act as an additional defense.**
- **The benefits of distinguishable naming** are clear: more accurate attribution of adverse events; improved pharmacovigilance overall, and greater manufacturer accountability for their products. *This is especially true for patients in countries without the resources for a robust PV system of their own.*
- Opponents of distinguishable naming were concerned that use of a suffix would imply inferiority to the originator product and result in low physician confidence. U.S. physician survey data shows this is not the case. **In fact, confidence in the safety and efficacy of biosimilars, and comfort with switching, is higher among U.S. physicians than European physicians.**
- Opponents also said distinct suffixes would hurt uptake. Yet U.S. uptake levels are approaching those seen in Europe, showing these fears to be unfounded.
- The WHO itself recognizes the lack of a global nomenclature standard remains an obstacle to increasing biosimilar uptake. Past and present supporters of the BQ remain willing to harmonize should the WHO make a voluntary standard available.
- **ASBM will continue to work with regulators globally to move a nomenclature policy forward (BQ or otherwise).**

SafeBiologics

ALLIANCE *for* SAFE BIOLOGIC MEDICINES

Thank You For Your Attention