

The Role of Distinguishable Biologic Nomenclature in 2021

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When We Last Met in April...

- 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.

72nd INN Consultation, April 2021

Upcoming Poster: "A review of problems with pharmacovigilance programs and biologics"

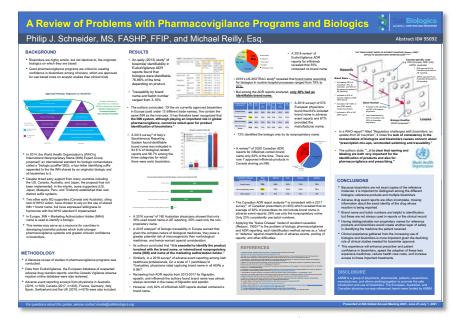
- ASBM will present a poster abstract at the Drug Information Association (DIA) Global Annual Meeting 2021, to be held virtually June 27-July 1, 2021.
- The poster will examine recent literature on the identifiability of biologics, with an emphasis on their identifiability in ADR reporting.



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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.

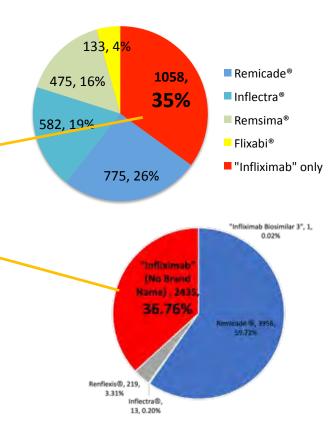


See a video walkthrough of the poster here...



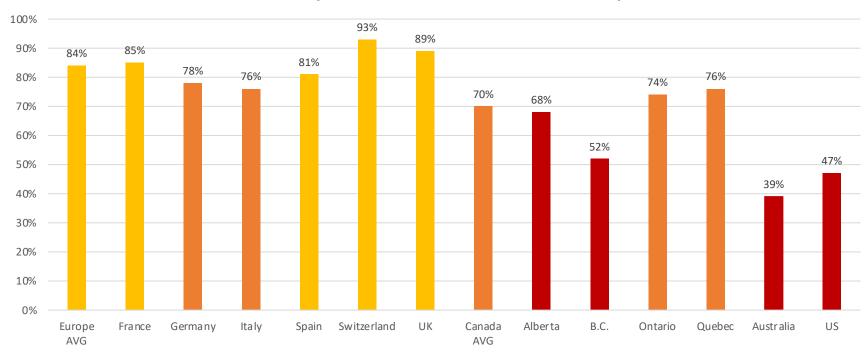
Brand Name Recording in ADR Reports: Wide Variation

- 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

What % of Physicians Include Brand Name in ADR Reports?



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 mixups, 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."

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES Original Article

Regulatory challenges with biosimilars; an update

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Alone, Shared INNs Create Ambiguity: Infliximab

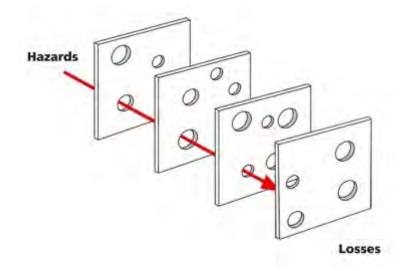
- For example, all 13 products on the right share the INN "infliximab"
- Brand/Trade Names are inconsistently recordedand also <u>differ from country to country.</u>
- This can become confusing and result in:
 - Misattribution of adverse events
 - Inadvertent or inappropriate substitution
 - Inaccurate 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/If ixi
Epirus	Infimab
MabTech/Sorrento	STI-002
MabTech/Sorrento	CMA-B008
Nichi-Iko	NI-071
Nippon Kayaku Ranbaxy	Infliximab BS 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.



Hazards

Brand Name

AE reporting

ADR reports

ADR reports

Included by 39% of Australian, 70% of

Included in 63% of

Irish ADR reports

(varies by product)

physicians.

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

Country-specific code (e.g. DIN (Canada), NDC (US), ARTG, Australia) DIN reported 4% by Canadian physicians in AE reporting ARTG reported 2% by Australian physicians in AE reporting Canadian, and 84% of European physicians in Canada Vigilance ADR **Batch Number** Included in 82-100% of Included in AE reporting by 69% of European physicians Included in 38% of UK Used consistently by 23% of Canadian and Losses **Biologic Qualifier** 29% of Australian

(WHO proposed1)

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

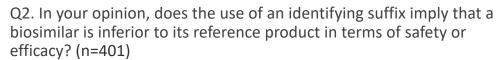
- 403 physicians
- Drawn from specialties in which biologics are routinely prescribed (e.g. dermatology, gastroenterology, nephrology, neurology, oncology, rheumatology, etc.)
- All prescribe biologics.

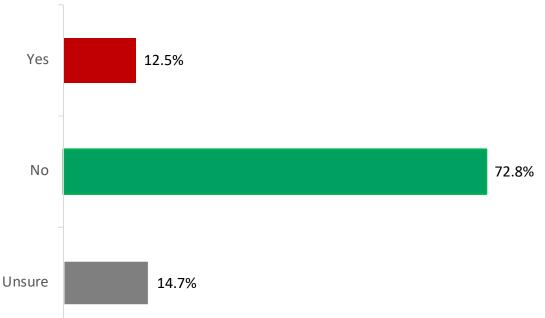
This brand-new survey has not yet been published- you are the first group to see it.



1) Inferiority: Suffixes <u>Do Not Imply Inferiority</u> 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., <u>all new innovator biologics</u> <u>are also issued suffixes</u>, even though older products have not been retroactively renamed.
- Eventually, nearly all originator products will have suffixes, as will their biosimilars.

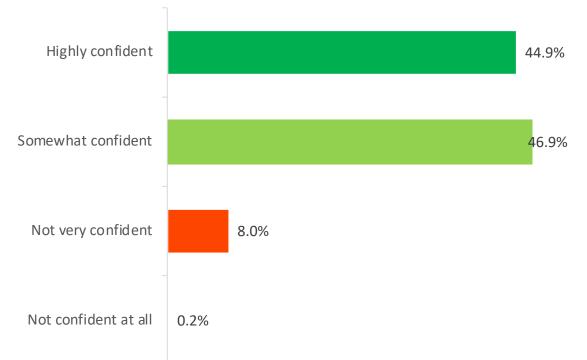




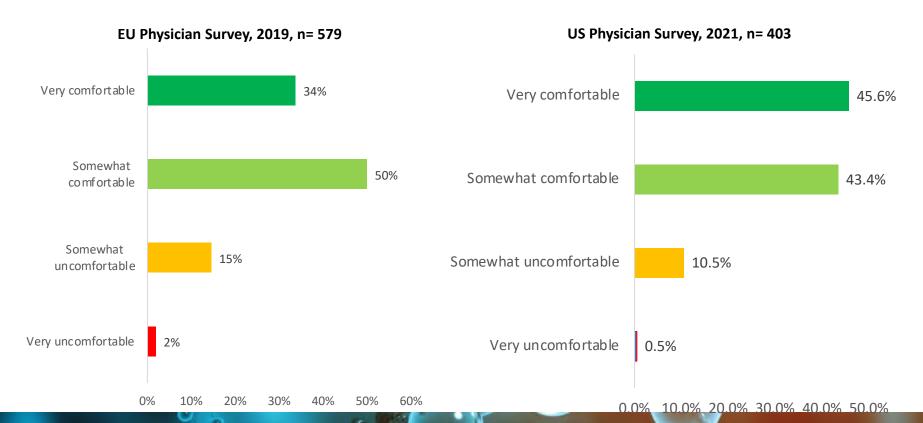
2) Confidence: US Physicians Are <u>Highly Confident</u> in the Safety and **Efficacy of Biosimilars**.

• 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 <u>More Comfortable Prescribing Biosimilars</u> to Naïve Patients than their European Counterparts...

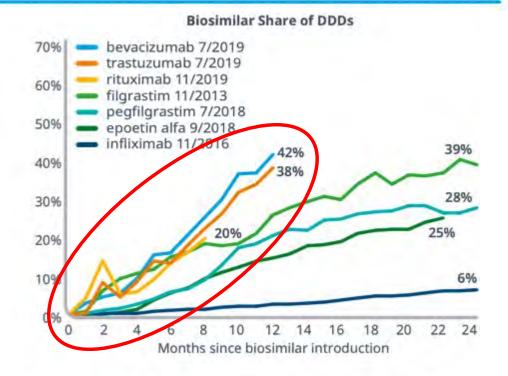


3) Uptake: Distinct Suffixes Have Not Held Back Biosimilars in the U.S.

- 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)

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

<u>Filgrastim/Pegfilgrastim:</u> 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.

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

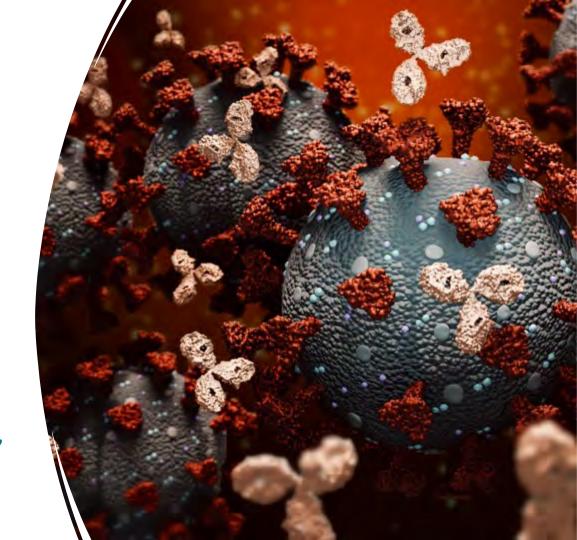
As in Europe, as more and more biosimilars launch in a given product class, competition drives prices downward, discounts increase, and biosimilar market share goes up:



- 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.

While much of our attention remains focused on COVID-19, we are beginning to return to normal and focusing on other policy areasincluding 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)



WORLD DRUGSAFETY

The Largest Drug Safety Congress Globally

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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>U.S. physician survey data shows this is not the case</u>. <u>In fact, confidence in the safety and efficacy of biosimilars, and comfort with switching, is higher among U.S. physicians than European physicians</u>.
- 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).



Thank You For Your Attention