Biologic and Biosimilar Naming

Clinical Perspectives and International Harmonization

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Biologic Naming: Why It's a Key Policy Issue

How should biologics, including biosimilars, be named…

- …to show that they are highly similar, but not identical?
- …to differentiate biosimilar from its reference product?
- …to differentiate biosimilar A from biosimilar B, C, D, etc.?

Currently this is handled on a country-by-country basis.

Some Benefits of Distinguishable Naming

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.

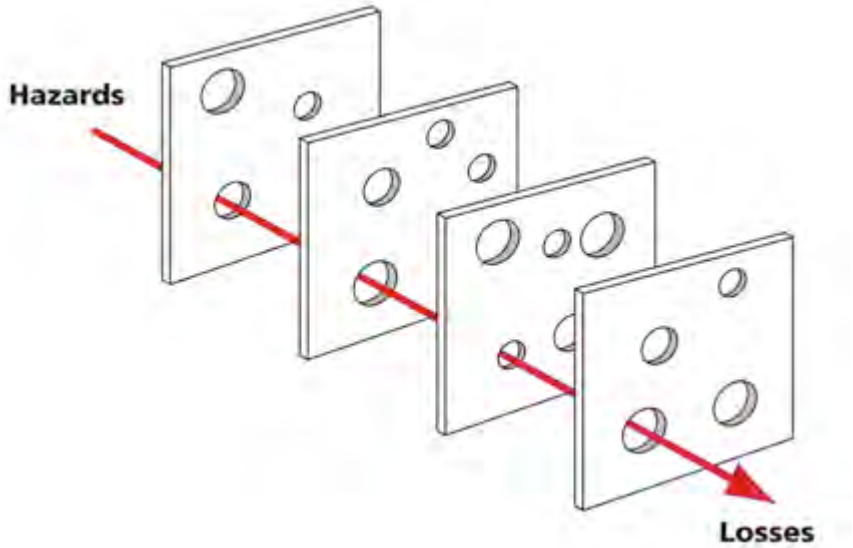
BETTER PHARMACOVIGILANCE - proper attribution of adverse events.

INCREASED MANUFACTURER ACCOUNTABILITY – different nonproprietary names, or shared nonproprietary names with differentiating suffixes tied to manufacturer, would accomplish this.

Safety Science: High Reliability Systems

- High-reliability systems need multiple checks: airlines, healthcare, medication systems.

- The "Swiss cheese model" from industrial psychologist James Reasons is used worldwide to design high reliability safety systems.



- Each "slice" ("defense") is a protection against hazardous conditions becoming an accident.

Pharmacists and Distinct Naming

- Pharmacists have a long history of avoiding look-alike, or sound-alike names for medicines.
- Yet a disconnect remains between practicing pharmacists and their professional associations.
- U.S. Pharmacist Associations (APhA and ASHP) have opposed distinct nonproprietary names, including WHO and FDA proposals.
- **<u>Yet we found through our continuing education courses, that pharmacists were very supportive.</u>**

May 25, 2015

Chapman University College of Pharmacy; Irvine, CA

40 pharmacists, 93% support for distinct naming

Pharmacists and Distinguishable Naming

SOME SUGGESTED WAYS OF DISTINGUISHING BIOSIMILARS:

Unique USAN/INN?

Shared USAN/INN + Suffix?

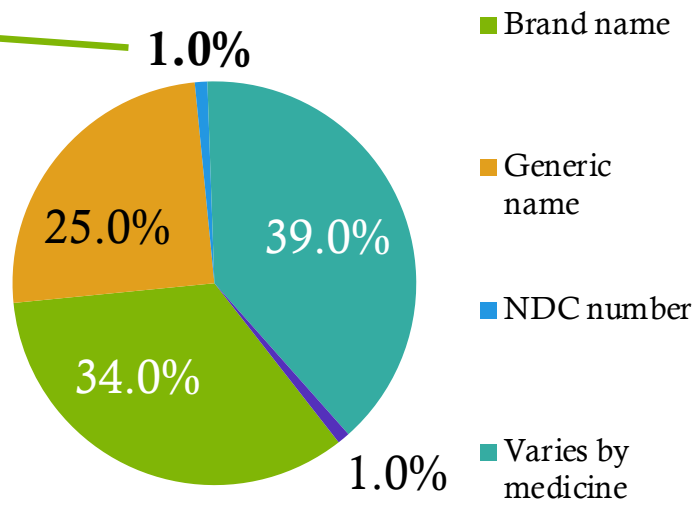
Shared USAN/INN + NDC Code

Prefix + Shared USAN/INN?

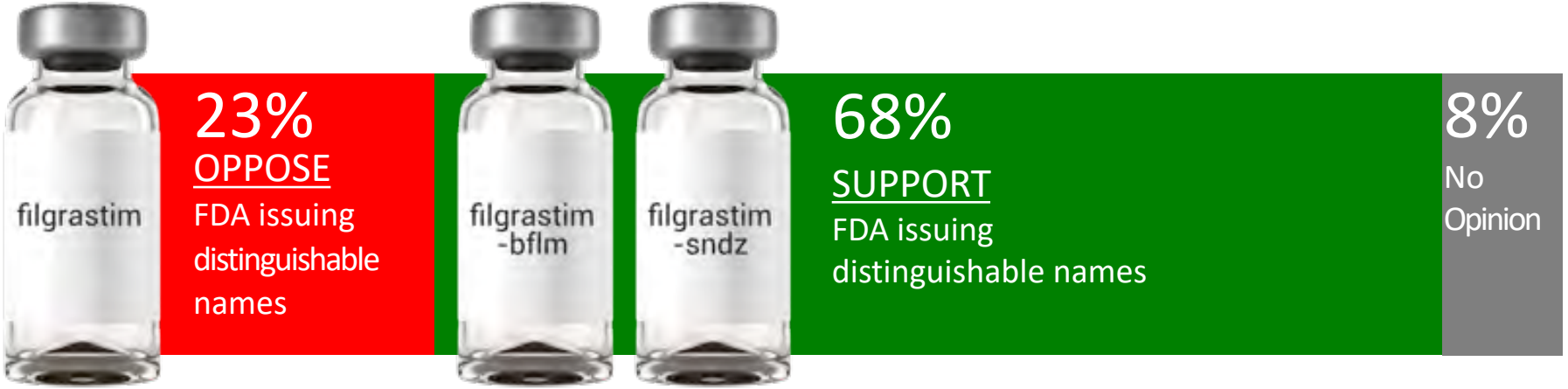
Is the NDC Code an Adequate Solution?

- ASBM 2015 Survey of 400 U.S. physicians who prescribe biologics showed that NDC codes were **not used by physicians to identify in patient record (1%).**
- NDC codes are not routinely used in billing systems. Thus the identifier is missing in many circumstances where product-specific identification is important.
- Additionally, NDC code is fundamentally an attempt at **a LOCAL solution to what is essentially a GLOBAL problem.**

When you identify a medicine for prescription or recording in a patient record, are you more likely to identify the medicine by brand name, non-proprietary / generic name, or NDC number?



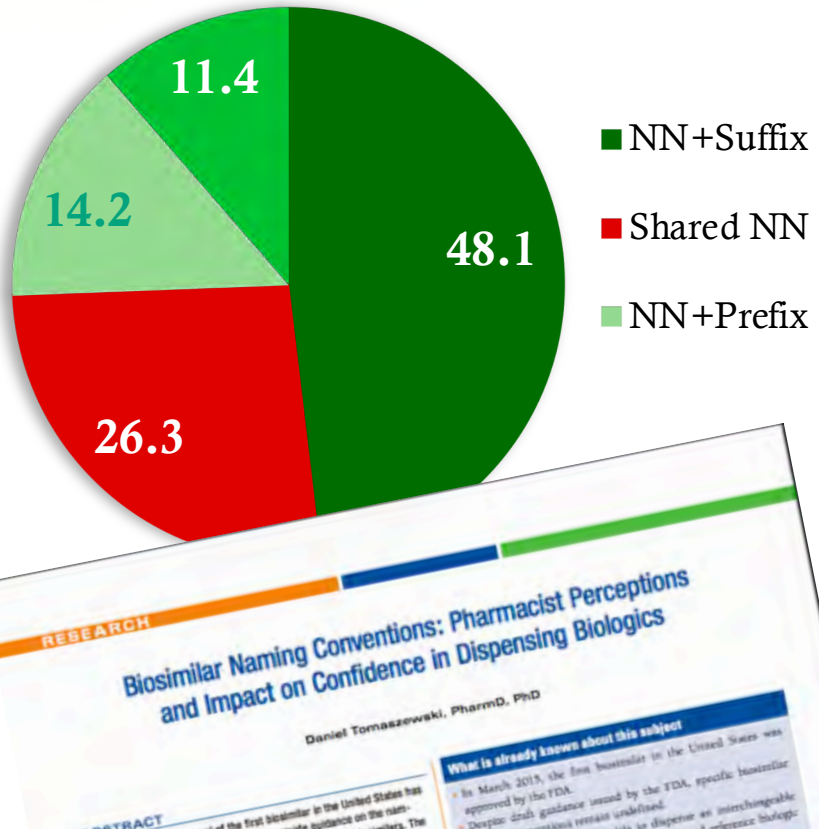
ASBM 2015 U.S. Pharmacist Survey Showed Strong Support For Distinguishable Naming



ASBM Survey of 401 U.S. Pharmacists, September 2015

2016 AMCP Study Confirmed ASBM's Results

- Published August 2016 in *Journal of Managed Care and Specialty Pharmacy, Vol. 22 (8). Author, Dr. Daniel Tomaszewski, will present later today.*
- Funded by Academy of Managed Care Pharmacy (AMCP); Surveyed 781 members of AMCP the and the Hematology/Oncology Pharmacy Association (HOPA)
- Again we see a disconnect between the professional organizations and the rank-and-file pharmacists… *While AMCP does not support distinct naming, their constituents do*.
- ***74% support distinct naming, 48% support distinguishing suffixes.***



FIP Draft Statement of Policy: Therapeutic Interchange and Substitution

fip

FIP STATEMENT OF POLICY

Pharmacist's authority in product selection: therapeutic interchange and substitution of pharmaceutical products

Introduction

In 1992, FIP issued a statement calling on all countries to ensure the adequate quality of pharmaceutical products. Since then, countries have developed systems that guarantee that all pharmaceutical products, both manufactured locally and imported, meet satisfactory standards of quality, safety, bioavailability, bioequivalence and efficacy. As recommended by FIP at the time, governments apply the same principles for quality, safety and efficacy standards to branded and generic products.

Until recently, the marketing of some pharmaceutical products was based on the premise that the brand-name product is different from its competitors in scientifically and clinically important ways. However, it is now clear, that with appropriate exercise of medical and pharmaceutical judgement, pharmaceutical products may be interchanged according to defined criteria and the needs of the patient without compromising patient outcomes.

The WHO-FIP Joint Guidelines on Good Pharmacy Practice (2011) outline the key roles of the pharmacist. Amongst other points, it urges action by all governments, in collaboration with national pharmaceutical associations, to make full use of the expertise of the pharmacist at all levels of the health care system. It also recommends generic substitution where possible as part of the pharmacist's dispensing role.

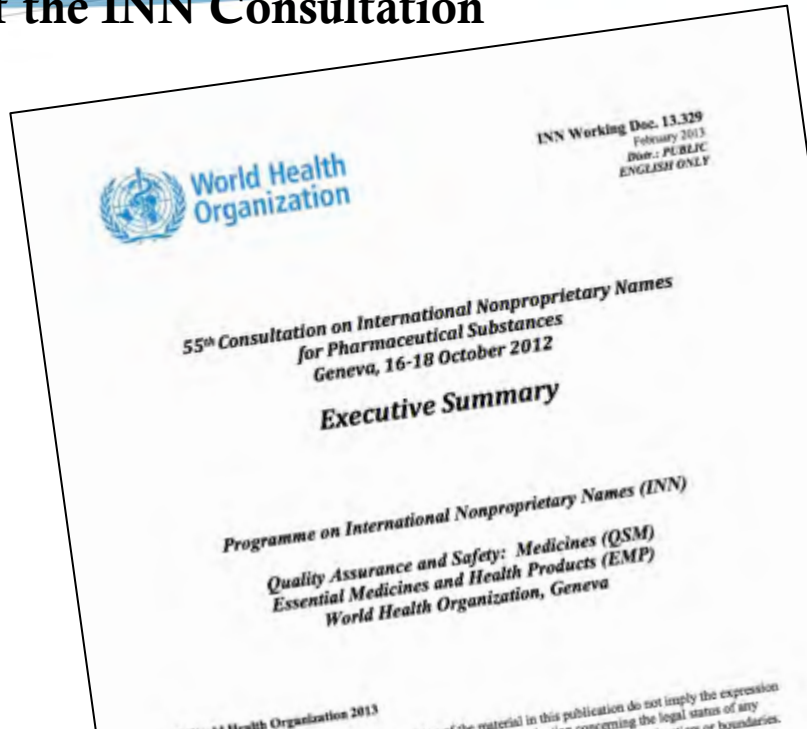
"If appropriate, the use of international non-proprietary names (INN) for professional communications should be encouraged. **Prescribers should be recommended to use the INN** to avoid medication errors in prescribing/dispensing and to ensure patient's safety/benefits. The national legislation of the country should be taken into account. Along with the Good Pharmacy Practice principles, **clarity with regard to the pharmaceutical product supplied such as tradename, batch number and expiry date should be provided by the pharmacist."**

WHO Identified International Harmonization of Biologic Nomenclature as an Urgent Need… back in 2012.

- **That year, the WHO's Executive Summary of the INN Consultation said:**

åThe naming of SBPs **needs to be addressed globally and soon** while the number of registered SBPs remains relatively small and with the INN programme being the best forum to achieve this.ç

-Executive Summary, 55th INN Consultation (Oct. 2012) Published Feb. 2013



World Health Organization

INN Working Doc. 13.329
February 2013
Distr.: PUBLIC
ENGLISH ONLY

55th Consultation on International Nonproprietary Names for Pharmaceutical Substances
Geneva, 16-18 October 2012

Executive Summary

Programme on International Nonproprietary Names (INN)
Quality Assurance and Safety: Medicines (QSM)
Essential Medicines and Health Products (EMP)
World Health Organization, Geneva

Health Organization 2013

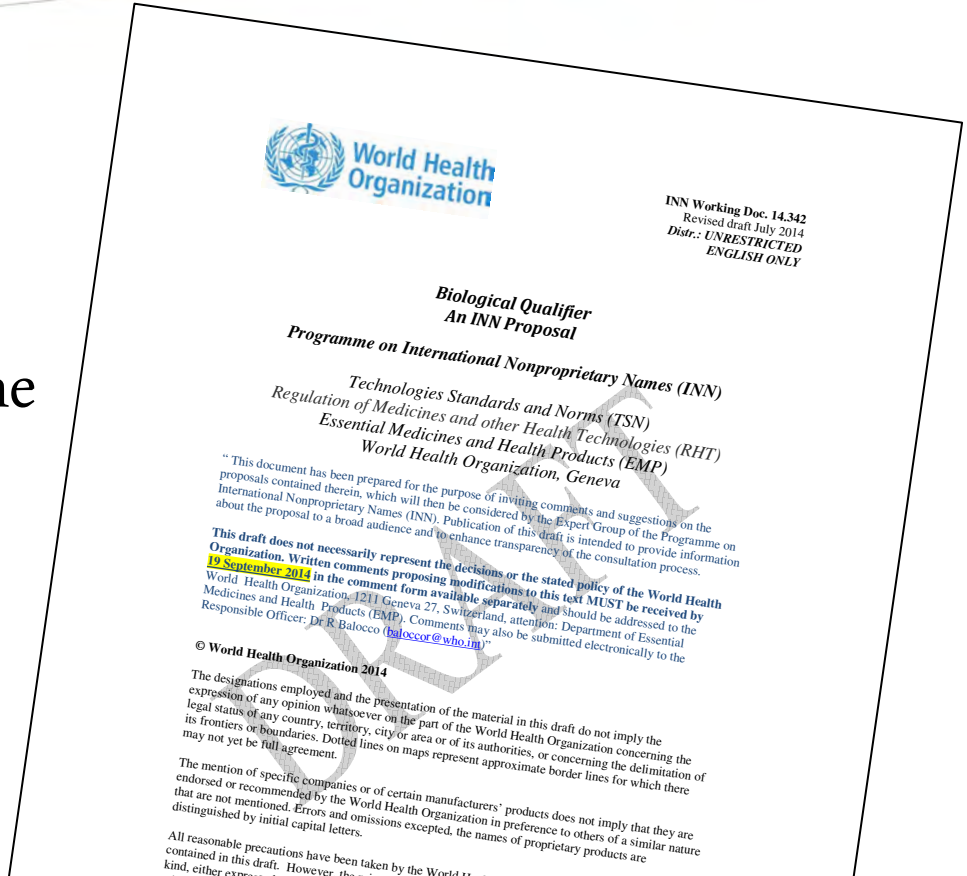
material in this publication do not imply the expression concerning the legal status of any boundaries.

ASBM Has Been Engaged on the Naming Issue Since 2013…

- Collected physician, patient, and pharmacist perspectives worldwide, including through multiple surveys of biologic prescribers across 13 countries, a national U.S. pharmacist survey, and many forums at colleges of pharmacy nationwide.
- Participated in 13 WHO INN consultations, the most recent on October 22nd of last year.
- Met with numerous regulators worldwide to share physician survey data, including the European Commission, FDA, Health Canada, the Italian and Spanish Health Ministries, and TGA.

The INN Expert Group Made its Recommendation in 2014…

- Requested by regulators "to avoid proliferation of separate and distinct national qualifier systems".
- Yet after years of research on the problem; and after consultation with regulators and other stakeholders; **the INN Expert Group recommendation remains unimplemented.**



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)"

WHO Solution: The Biological Qualifier (BQ)

- Similar biologics will be differentiated from each other by use of a random 4-letter code known as a "Biological Qualifier" (BQ).

- Codes will be appended to an INN shared by multiple products.

- Codes will be tied to the manufacturer/marketing authorization holders – the entities responsible for product's safety and efficacy.


World Health Organization

Biological Qualifier
An INN Proposal

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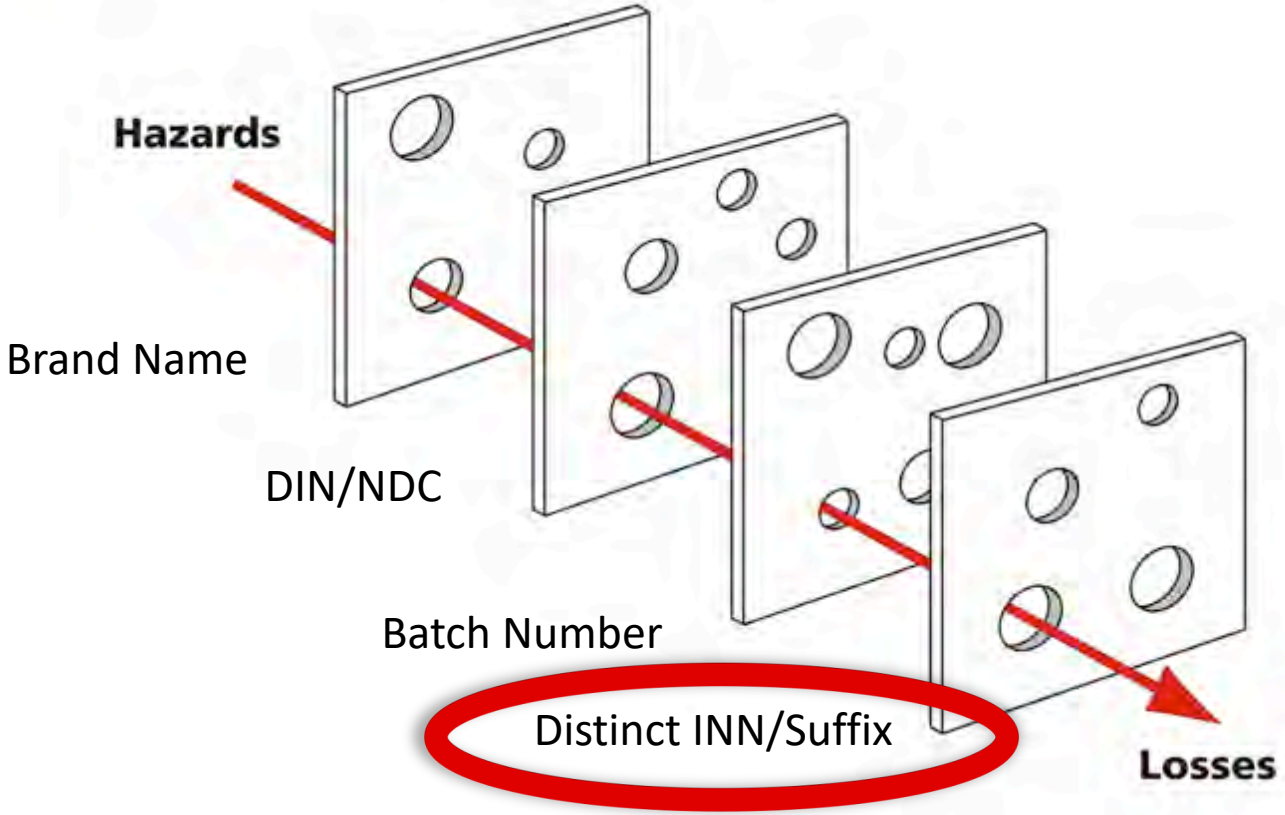
Essential Medicines and Health Products (EMP)
World Health Organization, Geneva

Distinct INN as a "Defense" in Identification of Biologic Medicines



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

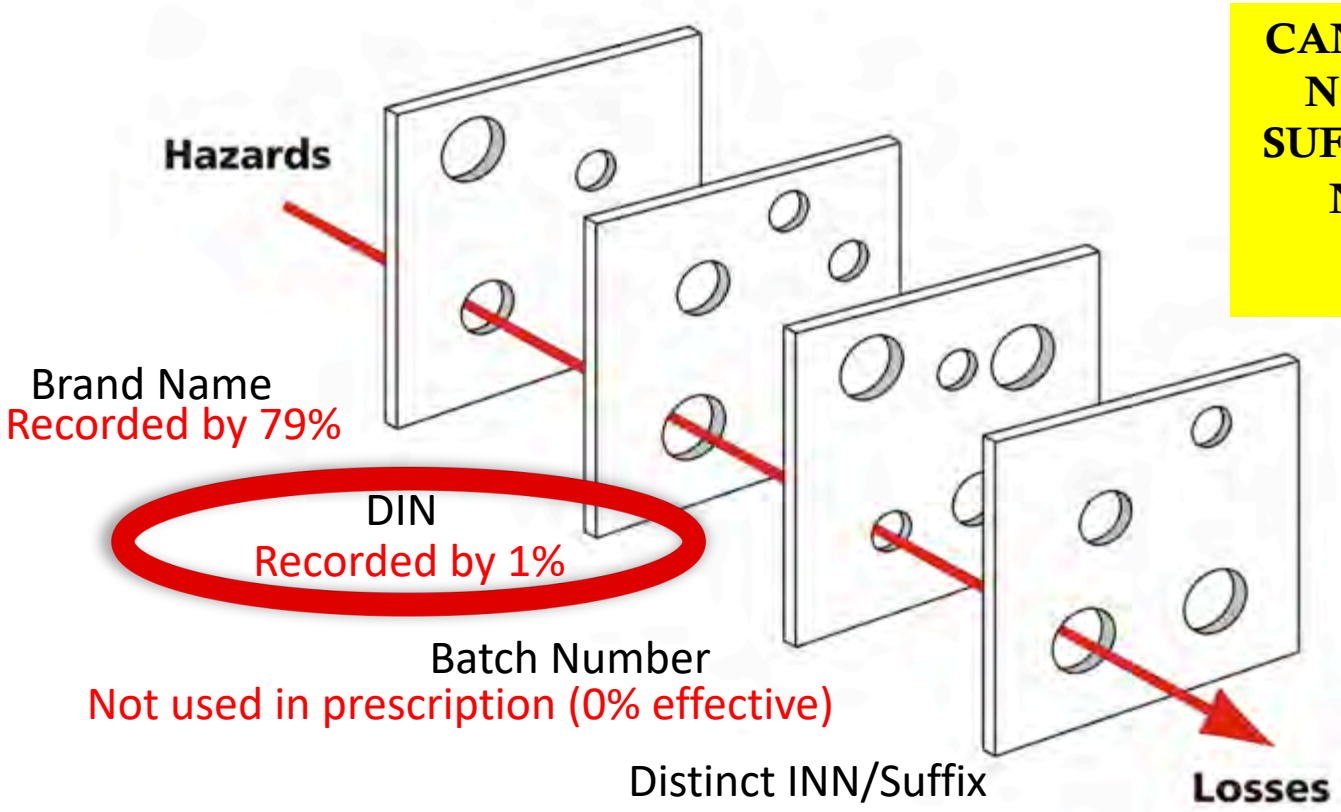
- TGA, initially supportive of WHO, has reversed itself.
- FDA has proposed and implemented its own BQ-like suffix system.
- Health Canada attempted to harmonize with US, but eventually went with a system based on Shared INN + Drug Identification Number (DIN).

February 14, 2019: Health Canada Announces Its Naming Policy

- No distinct nonproprietary names or suffix
- No harmonization with FDA/"North American approach"
- Shared INNs covering multiple products
- Reliance on Drug Information Number (DIN) used primarily by pharmacists
- **Identifies lack of WHO Action implementing of an international standard** as a factor in the decision:

  "There is no internationally adopted naming scheme to distinguish among biologics that, based on active ingredient, will be assigned the same International Nonproprietary Name (INN) by the World Health Organization"

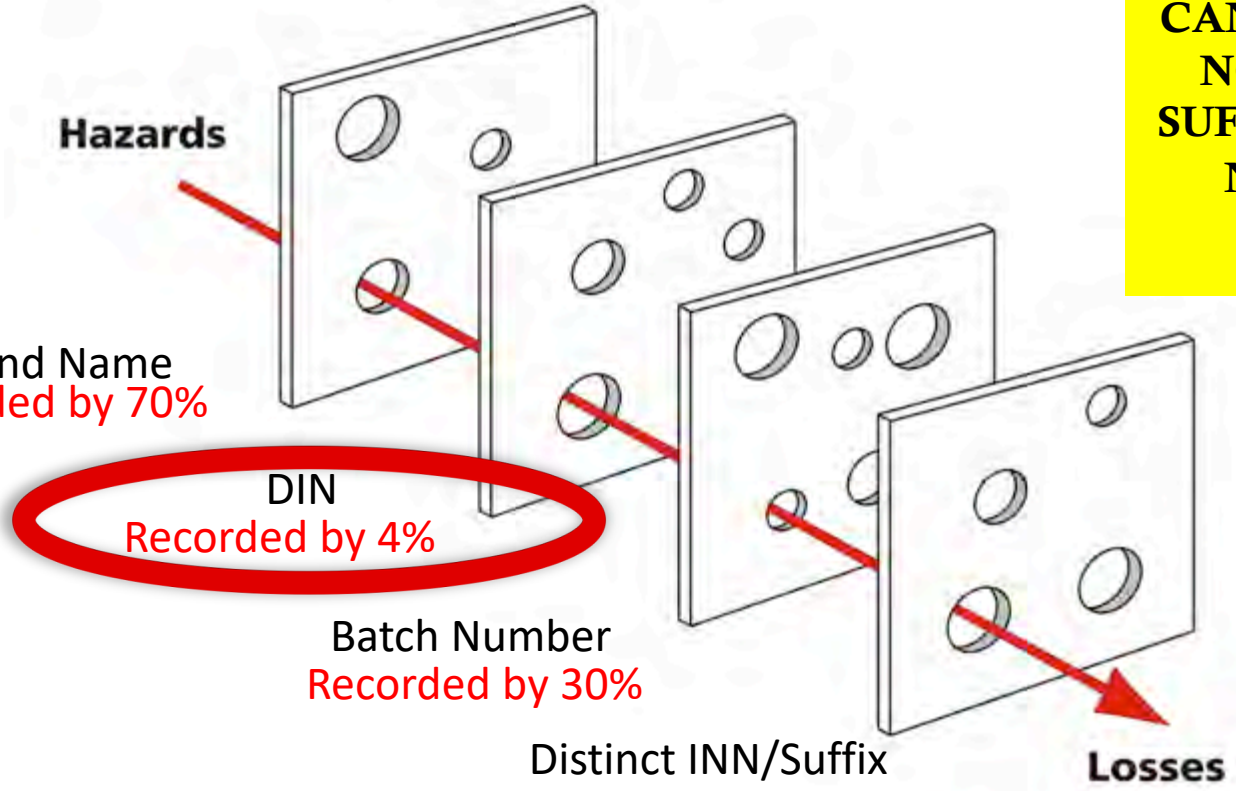
Modeling from Canadian Survey Data (n=403): Identification in Patient Record



CANADIAN APPROACH: NO DISTINCT INN or SUFFIX, Reliance on Brand Name and/or DIN =

~20% loss

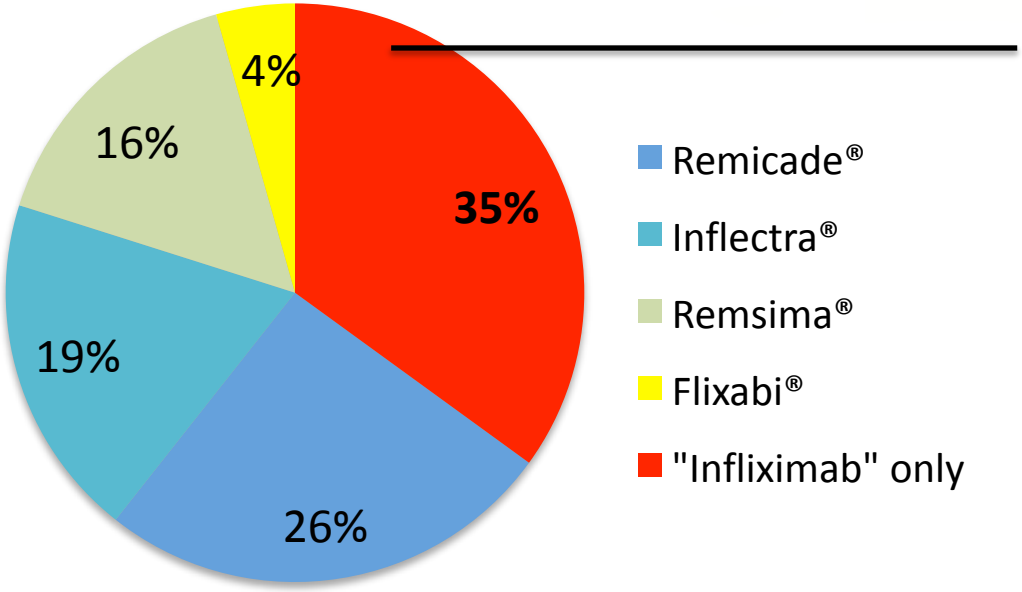
Modeling from 2017 Canadian Survey Data (n=403): Identification, Adverse Event Reporting



CANADIAN APPROACH: NO DISTINCT INN or SUFFIX, Reliance on Brand Name and/or DIN =

~20% loss

Inadequacy of Reliance on Brand Name is Borne Out by Adverse Event Reporting Data in EU



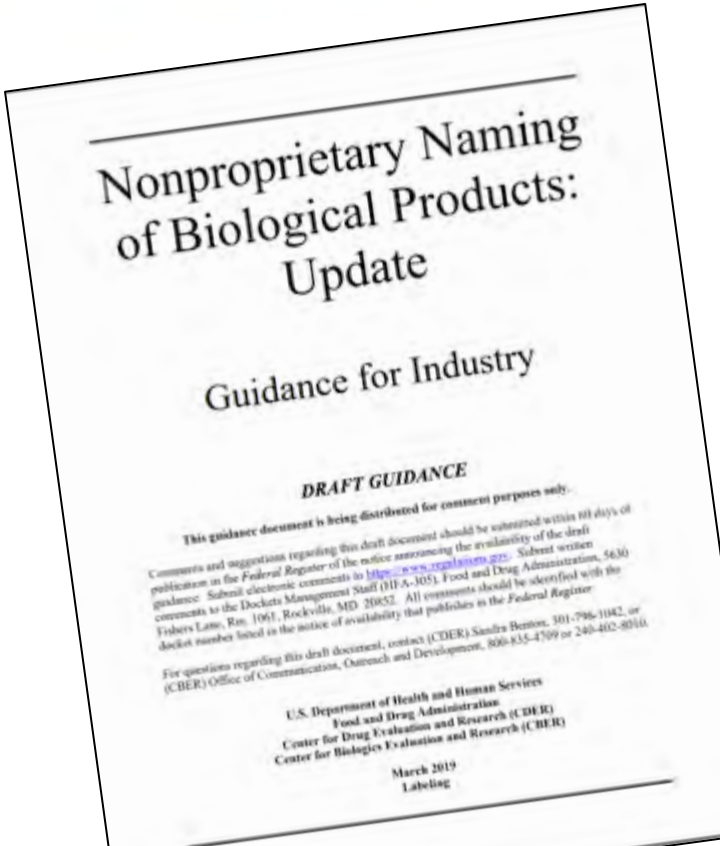
- **35%** of EU adverse event reports for infliximab in 2018 **did not specify brand name.**
- Note that this is **despite the fact** that reporting by brand name has been **required by law** since 2012.

Source: EudraVigilance- European database of suspected adverse drug reaction reports. www.adrreports.eu ; accessed May 3, 2019.

FDA Updated Naming Guidance

Shortly after the Health Canada decision, FDA announced that it was dropping the requirement to retrospectively apply suffixes to existing biologic products, including originator biologic and follow-on/biosimilar insulins. **All products- innovator and biosimilar- will receive suffixes going forward.**

Health Canada explicitly cited these costs in their "What We Heard" document as a reason they did not ultimately choose to harmonize with FDA's system.



Nonproprietary Naming of Biological Products: Update

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

March 2019
Labeling

ASBM Meetings with FDA, Health Canada, WHO

Over the past two years, ASBM has hosted three meetings with FDA and Health Canada to discuss the benefits, and importance of:

- Increasing biosimilar uptake
- Building confidence in safe use of biosimilars
- Distinct naming as a tool to address pharmacovigilance challenges, increase confidence
- International harmonization as a tool to promote safety and collect data
- **The importance of WHO leadership on these issues**

World Health Organization

FDA U.S. FOOD & DRUG ADMINISTRATION

Health Canada

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)

pmda

Shared INN plus distinct suffix (bs1, bs2…)
Willing to harmonize with WHO

EUROPEAN MEDICINES AGENCY

Australian Government
Department of Health
Therapeutic Goods Administration

Health Canada

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

Conclusions

- Distinct naming of biologics provides many benefits including reduces chance of inadvertent substitutions, improved pharmacovigilance, and greater manufacturer accountability.
- While pharmacy societies have opposed distinct naming schemes and some prefer to use NDC/DIN, **when surveyed, US pharmacists are generally supportive of distinct naming.**
- **Lack of timely WHO leadership on the naming issue** has resulted in regulators forging their own paths.
- Individual country-specific systems are not a substitute for a global pharmacovigilance system for biologics; **they do not adequately address safety and tracking challenges, nor address patient and physician concerns.**
- In particular, adverse event reporting data from jurisdictions reliant on consistent use of brand names by practitioners shows that **this approach has not proven to be an effective solution**, despite having been required by EU law since 2012.

Thank You
For Your Attention