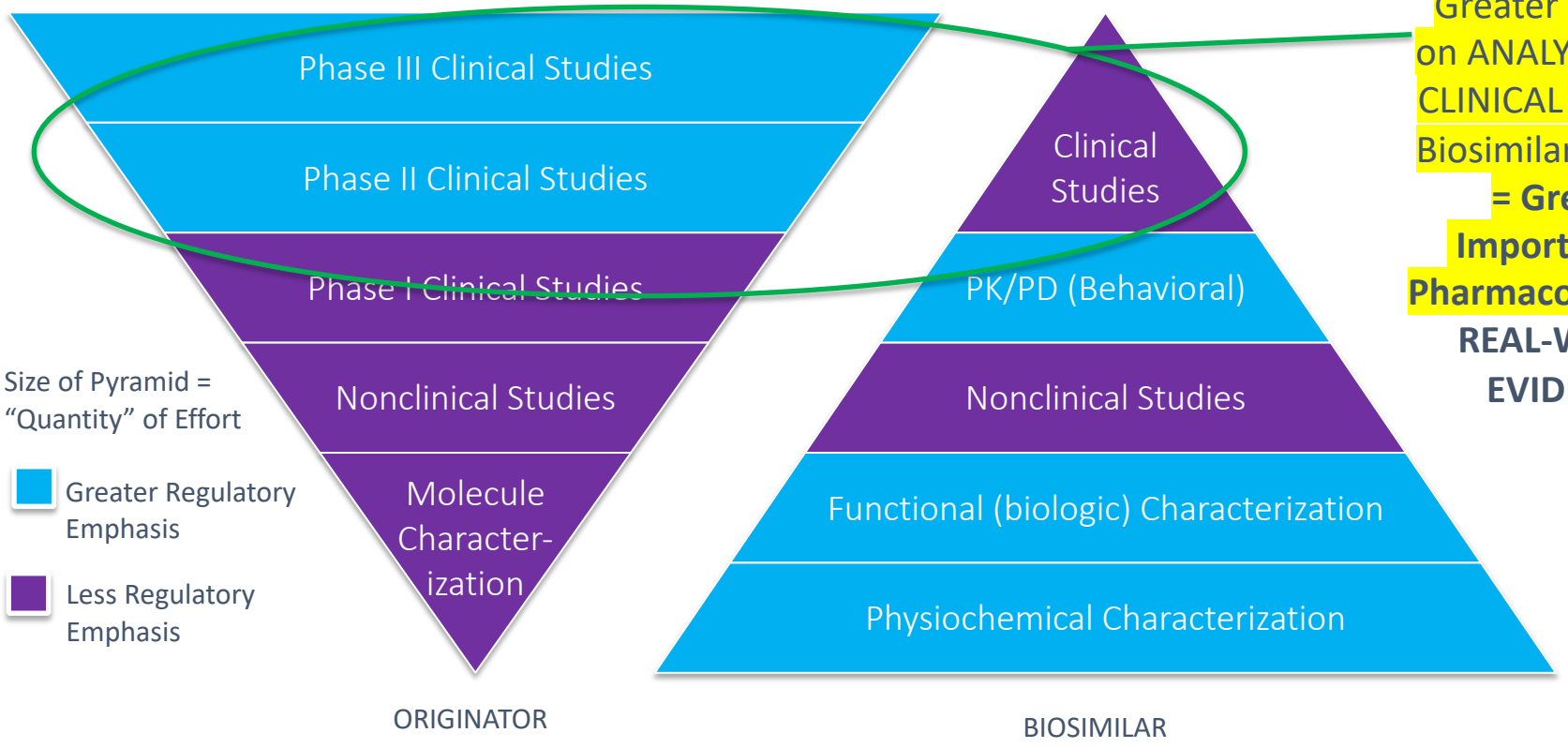
II. Nomenclature and the Importance of Non-Proprietary Names

Approval Pathway: Originator vs. Biosimilar



Greater Reliance on ANALYTICS over CLINICAL TRIALS in Biosimilar Pathway **= Greater Importance of Pharmacovigilance, REAL-WORLD EVIDENCE**

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

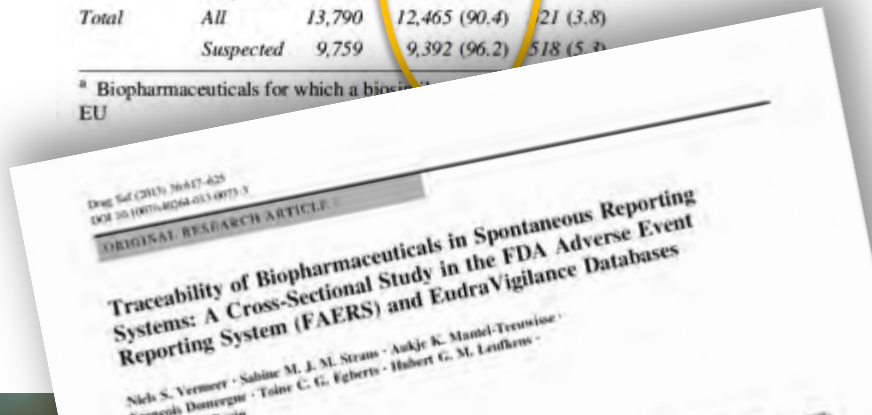
An early (2013) study of biosimilar identifiability in EudraVigilance ADR reports found a range of 76-96%.

- "Of the six currently approved biosimilars in Europe (sold under 12 different trade names), five contain the same INN as the innovator. It has therefore been recognized **that the INN system, although playing an important role in global pharmacovigilance, cannot be relied upon for product identification of biosimilars.**"
- As the number of biosimilars on the market is expected to increase at a rapid pace, and a road for biosimilar registration is currently been paved in the US, **traceability of biosimilars will only become more important.**

Table 3 Identifiability of biosimilars[a] in EudraVigilance

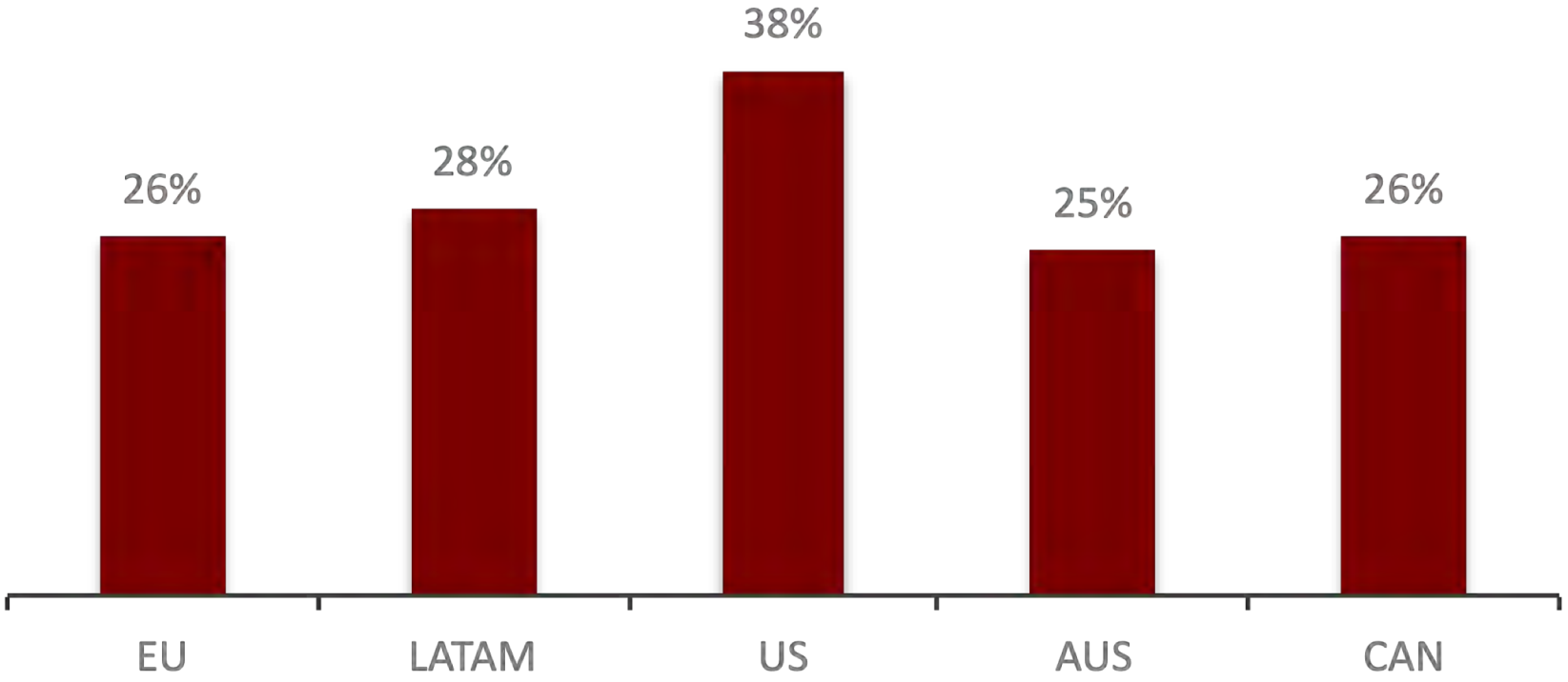
Biopharmaceutical, role code		Total number of drugs	Drugs with identifiable product name [*n* (%)]	Drugs with identifiable product name and traceable batch number [*n* (%)]
Epoetin alfa	All	9,125	8,615 (94.4)	320 (3.5)
	Suspected	6,903	6,829 (98.9)	318 (4.6)
Filgrastim	All	2,227	1,702 (76.4)	73 (3.3)
	Suspected	706	600 (85.0)	72 (10.2)
Somatropin	All	2,438	2,148 (88.1)	128 (5.3)
	Suspected	2,150	1,963 (91.3)	128 (6.0)
Total	*All*	*13,790*	*12,465 (90.4)*	*521 (3.8)*
	Suspected	*9,759*	*9,392 (96.2)*	*518 (5.3)*

[a] Biopharmaceuticals for which a biosi...
EU


Drug Saf (2013) 36:617–625
DOI 10.1007/s40264-013-0075-3
ORIGINAL RESEARCH ARTICLE
Traceability of Biopharmaceuticals in Spontaneous Reporting Systems: A Cross-Sectional Study in the FDA Adverse Event Reporting System (FAERS) and EudraVigilance Databases
Niels S. Vermeer · Sabine M. J. M. Straus · Aukje K. Mantel-Teeuwisse · François Domergue · Toine C. G. Egberts · Hubert G. M. Leufkens

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

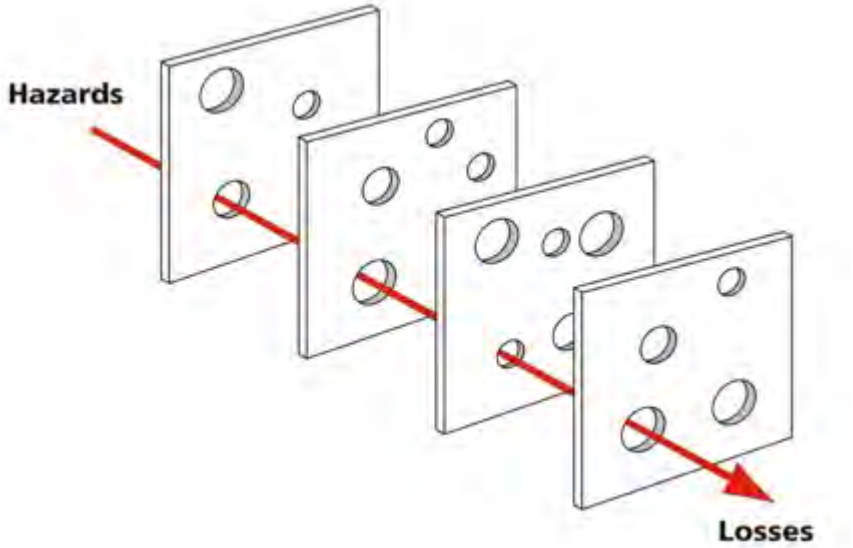
(This could result in improper attribution or pooling of adverse events.)



Safety Science: High Reliability Systems

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

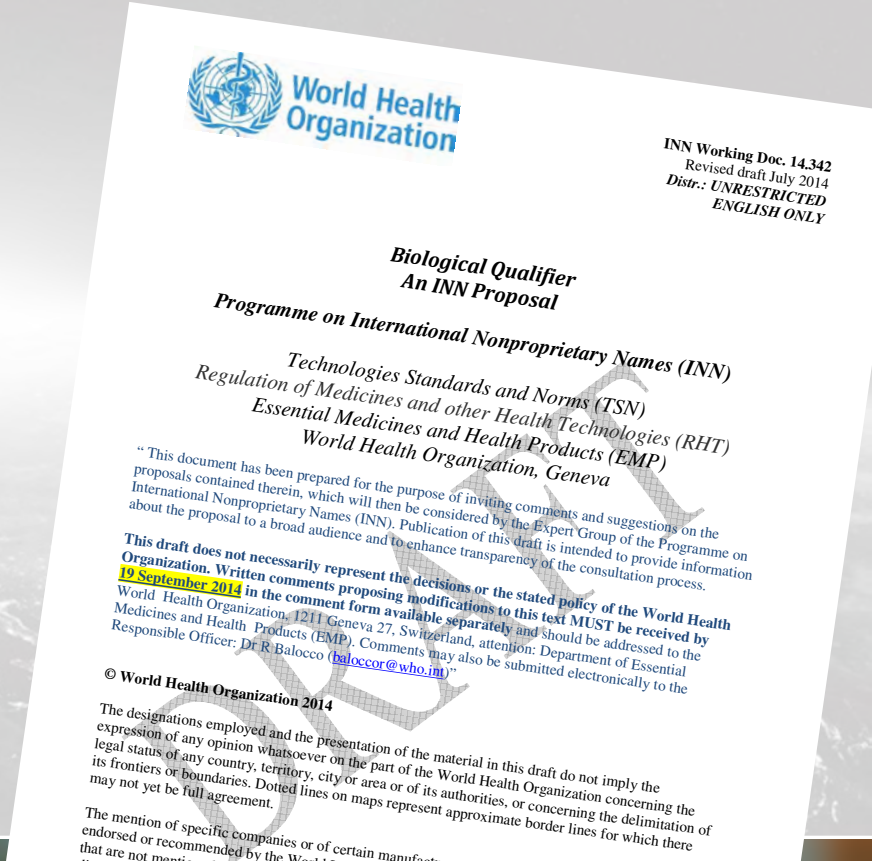
- The “Swiss cheese model” from industrial psychologist James Reasons is used worldwide to design high reliability safety systems.



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

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

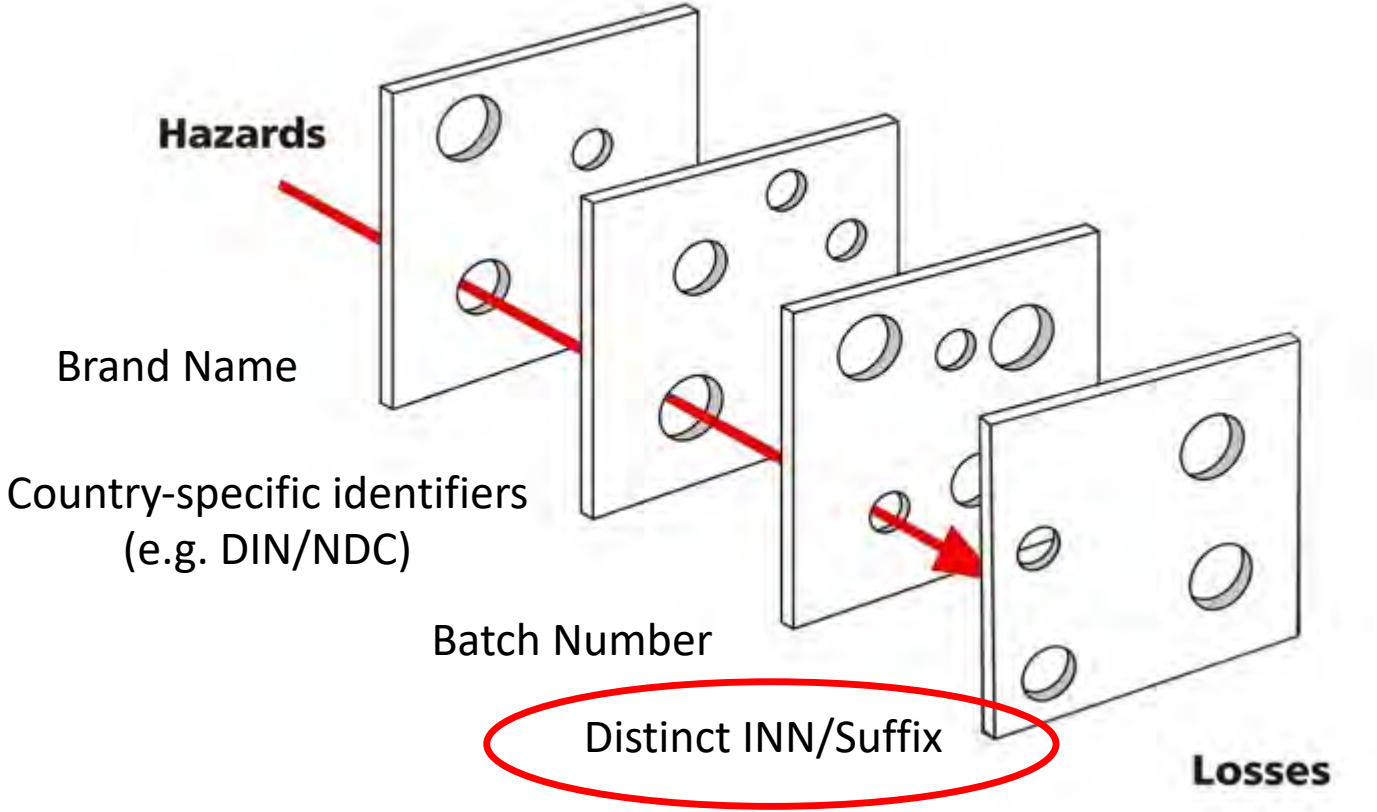
Programme on International Nonproprietary Names (INN)

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



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

Health Canada

pmda

MINISTRY OF PUBLIC HEALTH

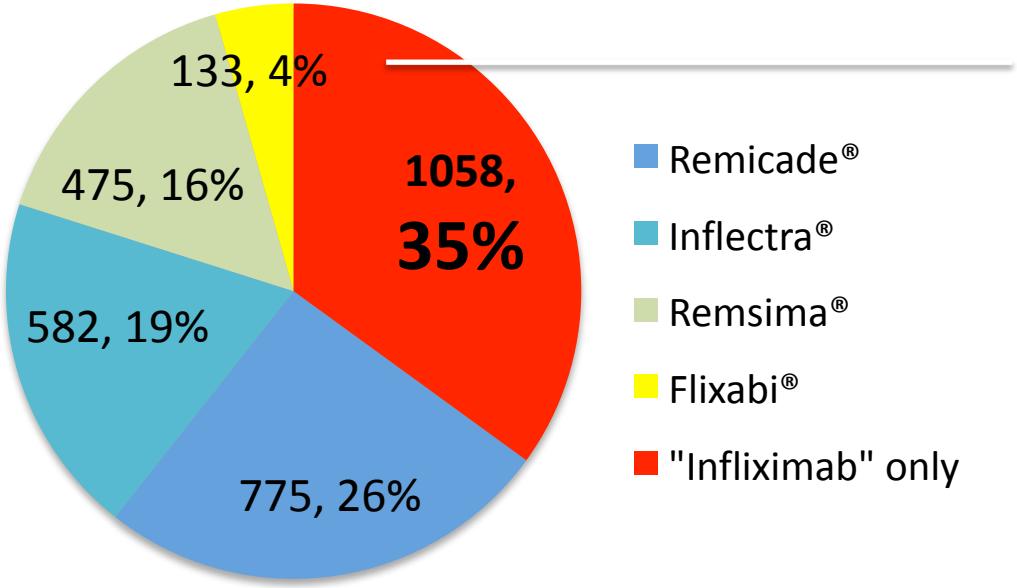
PERÚ Ministerio de Salud

Ministry of Health Malaysia

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

2018 EudraVigilance data shows that brand name is not being consistently recorded.



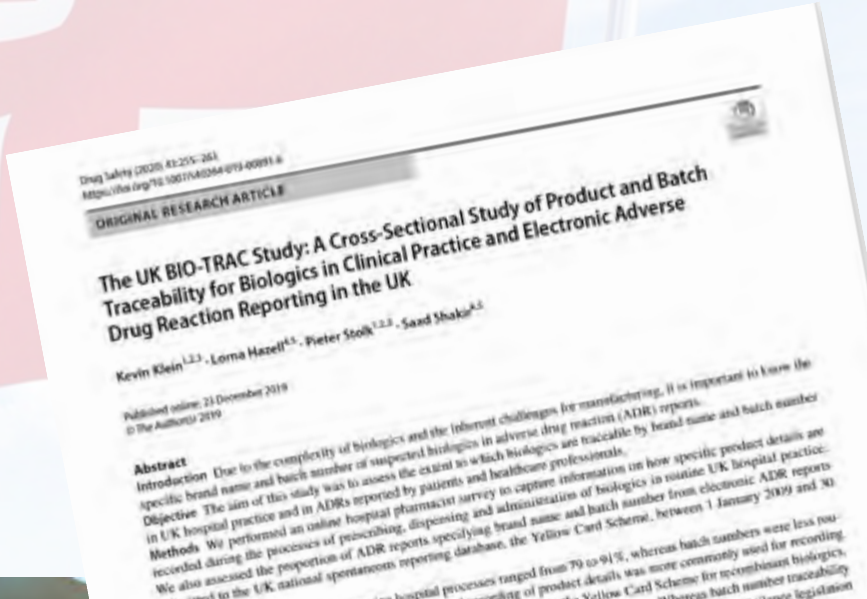
35% of EU adverse event reports for infliximab in 2018 did not specify brand name.

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.

These findings are consistent with those of the UK-BIOTRAC Study (Dec 2019)

- The study revealed that brand name recording in routine hospital processes ranged from 79% to 91%.
- But among the ADR reports analyzed, **only 38% had an identifiable brand name.**
- The authors conclude: "Whereas batch number traceability in electronic ADR reports improved slightly after the implementation of the European Union pharmacovigilance legislation in 2012, **no improvement of brand name traceability was observed in the UK."**



Drug Safety (2020) 43:255–263
https://doi.org/10.1007/s40264-019-00891-6

ORIGINAL RESEARCH ARTICLE

The UK BIO-TRAC Study: A Cross-Sectional Study of Product and Batch Traceability for Biologics in Clinical Practice and Electronic Adverse Drug Reaction Reporting in the UK

Kevin Klein[1,2,3] · Lorna Hazell[4,5] · Pieter Stolk[1,2,3] · Saad Shakir[4,5]

Published online: 23 December 2019
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Abstract

Introduction Due to the complexity of biologics and the inherent challenges for manufacturing, it is important to know the specific brand name and batch number of suspected biologics in adverse drug reaction (ADR) reports.

Objective The aim of this study was to assess the extent to which biologics are traceable by brand name and batch number in UK hospital practice and in ADRs reported by patients and healthcare professionals.

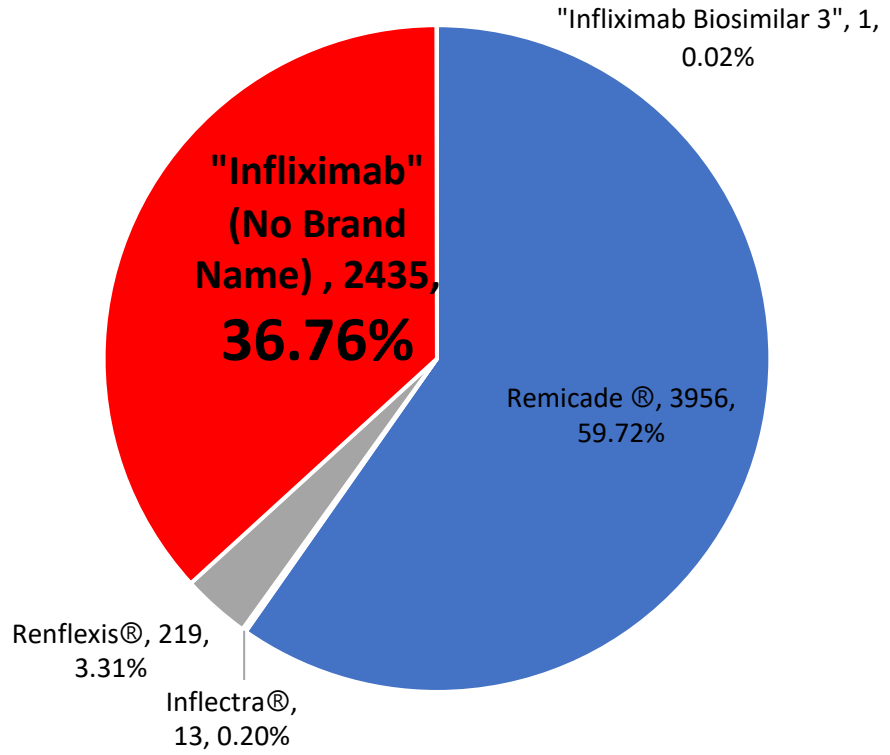
Methods We performed an online hospital pharmacist survey to capture information on how specific product details are recorded during the processes of prescribing, dispensing and administration of biologics in routine UK hospital practice. We also assessed the proportion of ADR reports specifying brand name and batch number from electronic ADR reports in the UK national spontaneous reporting database, the Yellow Card Scheme, between 1 January 2009 and 30

2020 Canadian ADR Reports for Infliximab contain brand name only 63% of the time.

An analysis of Canadian ADR reports for infliximab in 2020 shows **37%** did not specify brand name.

This is a near-identical figure to that seen in EU (35%).

There are now 7 approved infliximab products in Canada.



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 is inadequate to consistently identify the biologic in ADR reports- the only question is to what degree.
- Reliance on brand name to differentiate between products with shared INN has been shown to create anywhere from a 5% to 38% ambiguity. This appears to vary by country and by setting, including within a country.
- 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. This problem appears to increase as the number of biosimilars grows.
- WHO has identified lack of a naming standard as a regulatory challenge that undermines the strong pharmacovigilance needed for biologics and biosimilars.

SafeBiologics

ALLIANCE *for* SAFE BIOLOGIC MEDICINES

Thank You For Your Attention