Biologic and Biosimilar Naming

Clinical Perspectives and International Harmonization

Philip J. Schneider, M.S., F.A.S.H.P.
Advisory Board Chair, Alliance for Safe Biologic Medicines

September 30, 2018

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.

Biologic Naming

- Biologic medicines, like other medicines, are assigned an **International Nonproprietary Name (INN)** by the World Health Organization.
- In the US, the nonproprietary name is the "USAN" United States Adopted Name. It is often, but not always, the same as the INN.
- Since an innovator biologic and its biosimilar are different medicines, and minor differences may cause adverse effects in patients, **nonproprietary names must be distinguishable from one another.**

World Health Organization

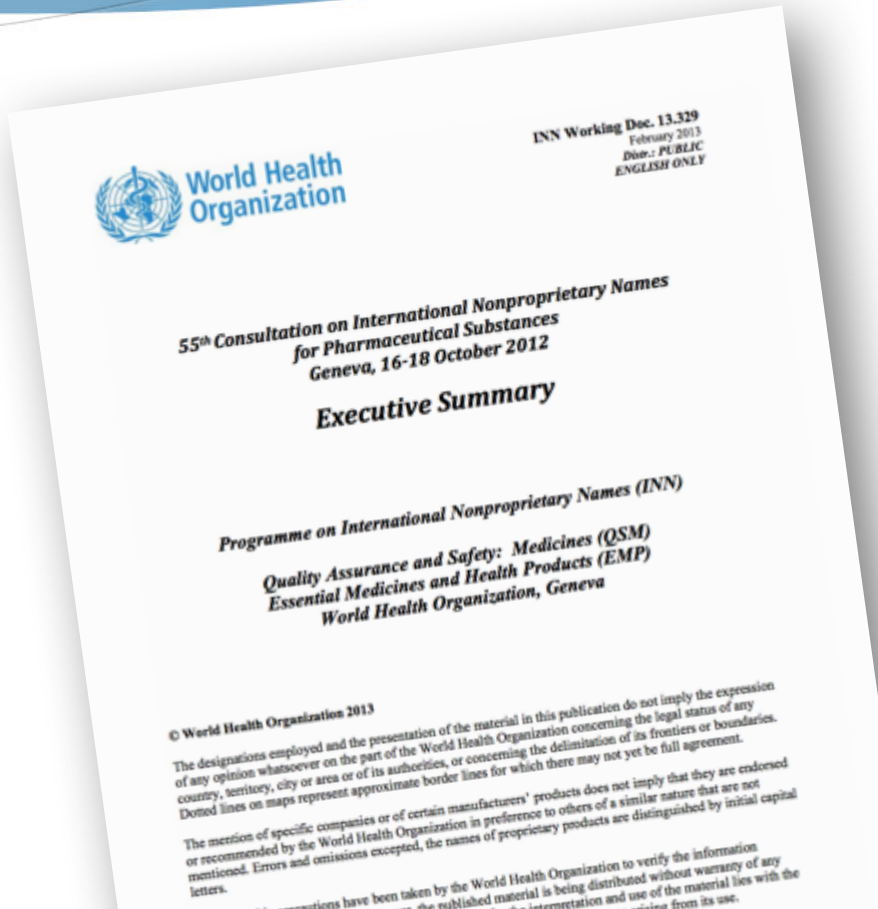
Advantages of Distinguishable Naming

- 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 - differentiating suffixes (preferably tied to manufacturer or marketing authorization holder name) will accomplish this.

An Urgent Global Health Issue… back in 2012

"The 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."

-Executive Summary, 55th INN Consultation (October 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)

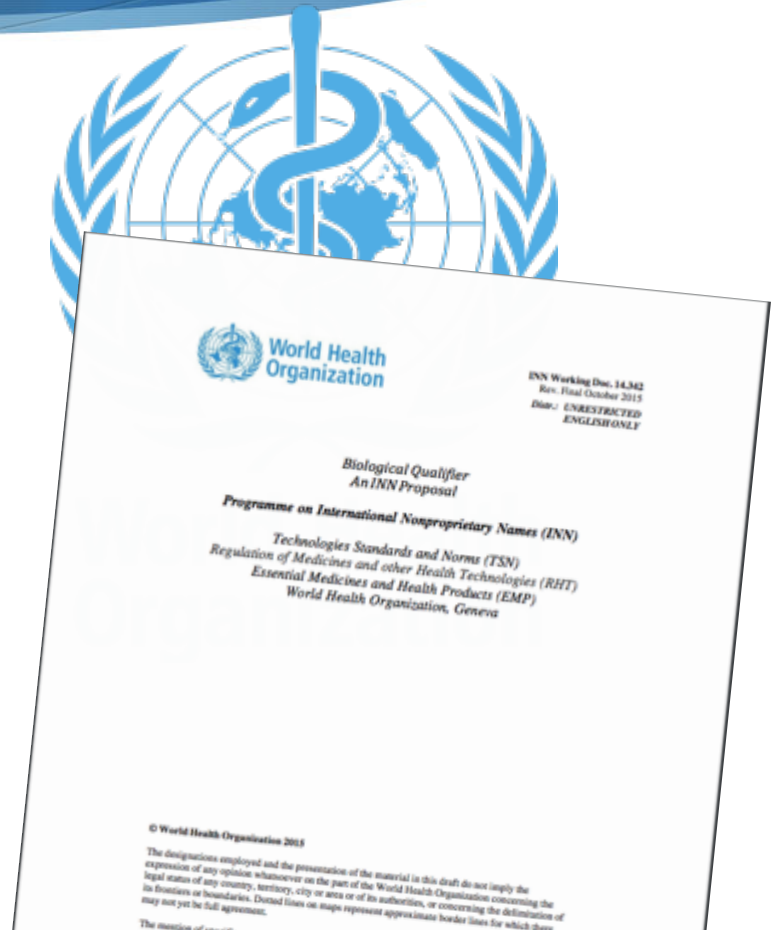
Quality Assurance and Safety: Medicines (QSM)
Essential Medicines and Health Products (EMP)
World Health Organization, Geneva

ASBM Has Been Engaged on the Naming Issue Since 2013…

- Collected physician, patient, and pharmacist perspectives worldwide, including through 8 surveys of biologic prescribers in 12 countries, a national U.S. pharmacist survey, and many forums at colleges of pharmacy nationwide.
- Participated in 10 WHO INN Consultations, the most recent on May 1st of this year.
- Met with regulators worldwide to share physician survey data, most recently TGA (Feb. 2017), Health Canada (Oct 2017).

The WHO's Solution: The Biological Qualifier (BQ)

- In 2014, the World Health Organization, which assigns international nonproprietary names (INNs) proposed a distinct naming system to ensure clear product identification.
- Biologics and biosimilars would share an INN, followed by a unique four-letter suffix.
- **Yet despite broad support, this recommendation remains unimplemented.**


World Health Organization

INN Working Doc. 14.342
Rev. Final October 2015
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

© World Health Organization 2015

The designations employed and the presentation of the material in this draft do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

WHO Meeting: April 30

- Opponents of the BQ often object to it on the grounds that it is unnecessary or redundant in countries with strong pharmacovigilance systems.
  - These reasons are typically rooted in a belief that distinct names will impede access to biosimilars- a claim that has yet to be supported with empirical evidence.

Asst. Director-General
Mariângela Simão

Head of Regulation of Medicines and other Health Technologies
Emer Cooke

INN Programme Manager
Rafaella Balocco

We believe that the opposite is true-- that the clear product identification and improved pharmacovigilance arising from distinct naming will increase confidence in biosimilars and increase their uptake.

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 remains supportive of distinct names and of international harmonization. It held a stakeholder consultation and will be announcing its own naming policy later this year.

Biosimilar Naming Around the World

filgrastim-bs1
INN plus biosimilar suffix (bs1, bs2…)

filgrastim (Zarzio)
INN plus trade name

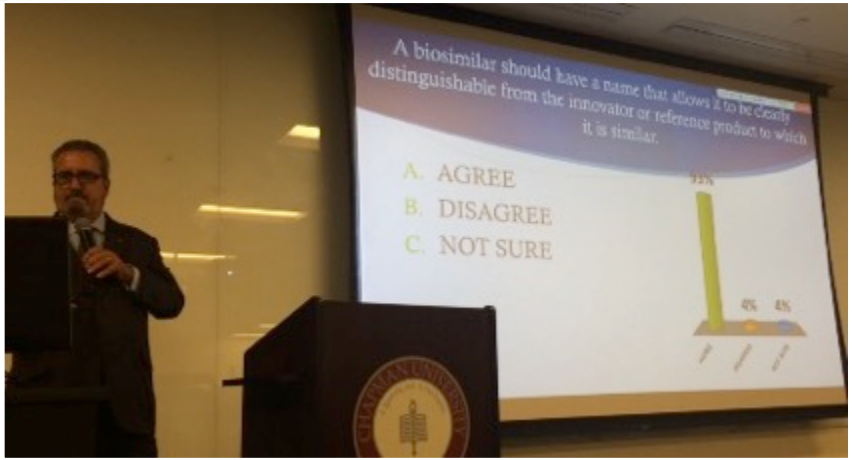
Naming System TBD,
Held Stakeholder Consultation January 2018,
willing to harmonize internationally

filgrastim-sndz
INN plus 4 letter suffix,
1st meaningful, now random

filgrasti
INN plus 4-letter suff

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 the 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?

Distinguishable Naming: ASHP Position

- The American Society of Health-System Pharmacists (ASHP) **is not opposed to the addition of a suffix, but opposes to use of prefixes, which it feels can lead to medication error.**

- Breast cancer medication KADCYLA® (ado-trastuzumab) is **dosed differently from its reference biologic** HERCEPTIN® (trastuzumab). Cases have occurred wherein a prescribing **physician has mistakenly omitted the distinguishing prefix**, resulting in a patient receiving the **wrong medication at the wrong dose**.

- ASHP is **not opposed to adding the National Drug Code (NDC) to the USAN as a suffix**, but the NDC not being used to track a product in all settings, reuse of NDCs by manufacturers, and other concerns may make this approach problematic.

ashp
pharmacists advancing healthcare

"…**We do not oppose the addition of suffixes** to the INN name if experts believe this approach is needed to facilitate pharmacovigilance,"

- Christopher Topoleski, ASHP Director of Federal Regulatory Affairs.

Distinguishable Naming: APhA Position

- **APhA does not support Unique nonproprietary names on the grounds that** it may interfere with current pharmacy safety alert systems and complicate the collection of global safety information.
- As with Human Growth Hormone and Insulin, the same nonproprietary name will not necessarily denote interchangeability, but rather be used to categorize a similar therapeutic drug.
- **APhA supports a unique identifier, such as an NDC code** that pharmacies already use to track products for identifying or tracking track the specific drug that a patient is prescribed.

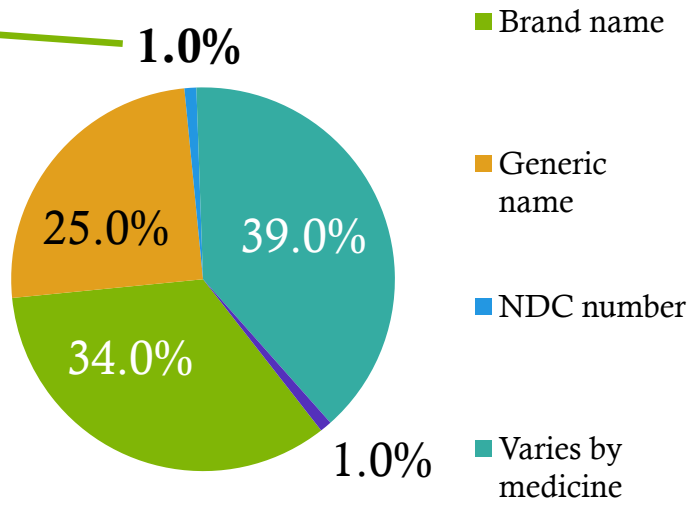
"**…a unique identifier, such as an NDC code that pharmacies already use to track products, can be used to track the specific drug that a patient is prescribed.** We recognize that non-pharmacy dispensing settings may not currently track by NDC number. "

-APhA Letter to FDA, May 2012.

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?



Distinguishable Naming: HOPA Position

- **Supports all biosimilars- interchangeable and non-interchangeable- sharing a nonproprietary name with their reference products.** Opposes FDA and WHO suffix proposals.

AMCP Academy of Managed Care Pharmacy®

"We believe that it is critically important to patients, providers, and both public and private payers that these **substantial cost savings** [of biosimilars] are not lost. By changing the established nonproprietary name of these products, these **savings are put at significant risk due to the potential for reductions in utilization."**

"**Changes will need to be made to existing software** in order to account for the addition of a suffix to INNs…These changes will add greater costs to the health care system by treating biosimilar and interchangeable biosimilar products differently from their reference products."

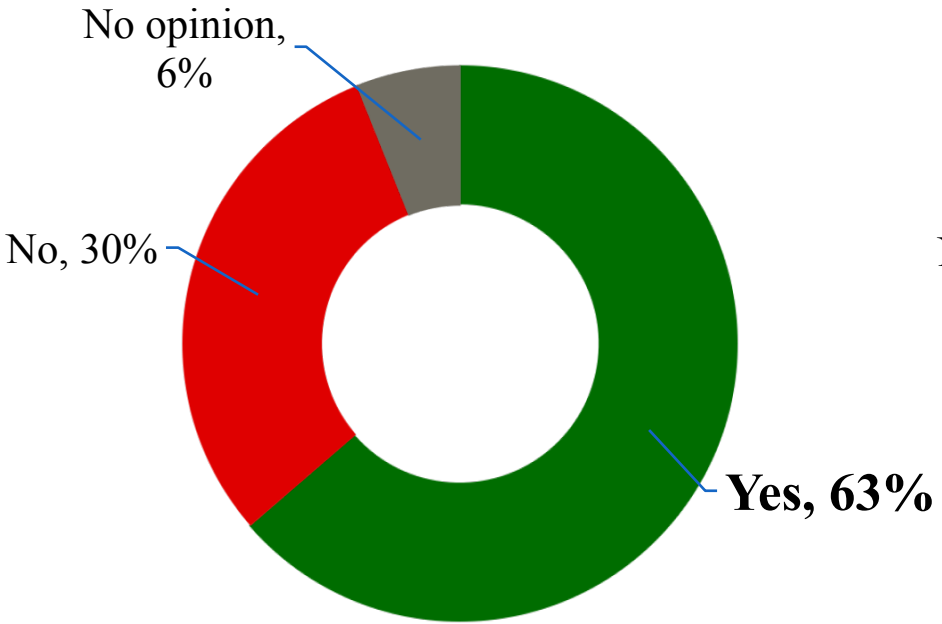
"FDA should abandon its current proposal, and instead adopt the use of standard INNs for all biosimilar and interchangeable biosimilar products."

-AMCP Comments on FDA Draft Naming Guidance, Oct. 27, 2015

ASBM 2015 U.S. Pharmacist Survey: Does a Shared INN Imply…

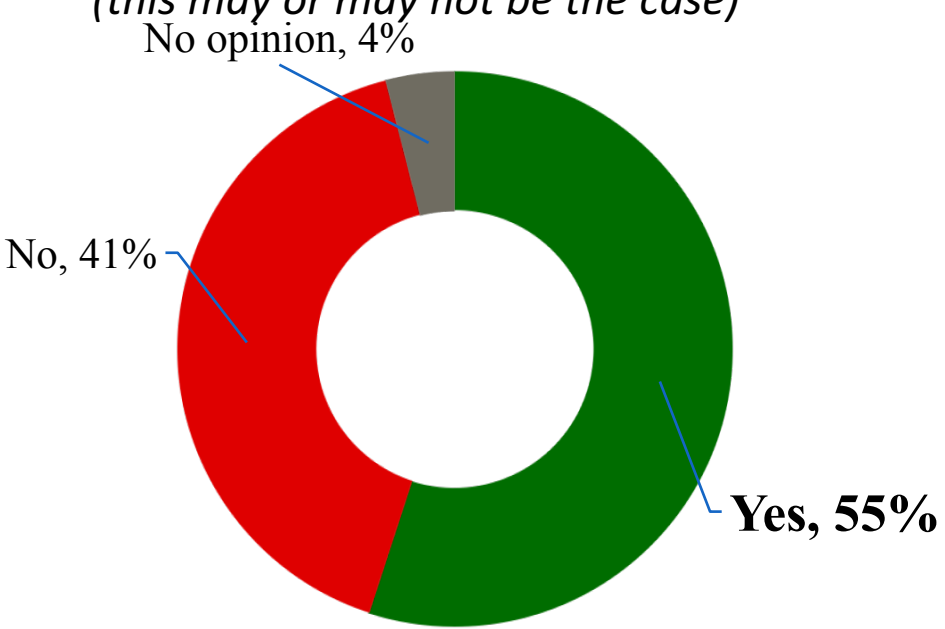
…Structural Identicality?

(this is not possible)

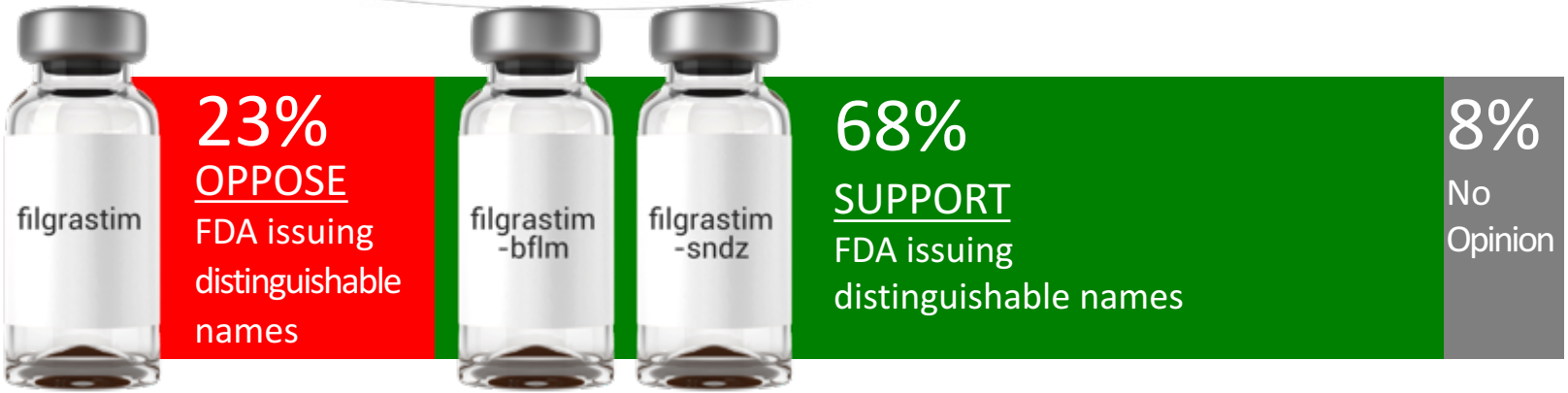


…Approval for the Same Indications?

(this may or may not be the case)



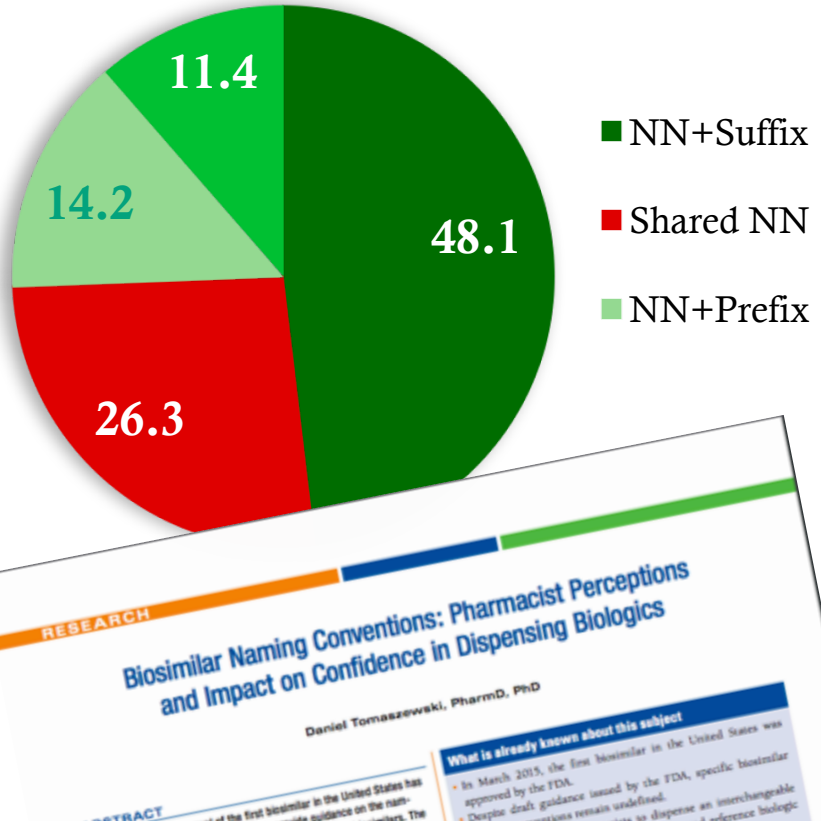
ASBM 2015 U.S. Pharmacist Survey Showed Strong Support for Distinguishable Naming



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.***



Distinguishable Naming: HOPA Position

- Prefers prefix, but supports suffix.
- Wants Suffix to be meaningful/manufacturer based, not random.

Hematology/Oncology Pharmacy Association

"HOPA's preferred naming convention would include using the current nonproprietary name associated with the reference product and modifying it **with a prefix rather than a suffix.**

'firmly believe that
the 4-character suffix proposed should be meaningful and not "devoid of meaning" for biosimilars that are not interchangeable…In theory and lacking interchangeability guidance, HOPA's position is that interchangeable products do not have to be differentiated with a suffix."

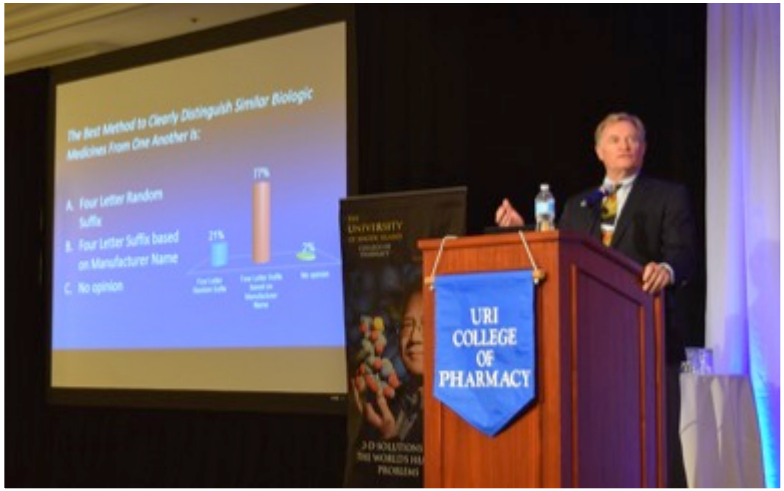
"For safety/medication error concerns as well as pharmacovigilance, this approach would make it much easier to differentiate between the biosimilar and the innovator."

-HOPA Comments on FDA Draft Naming Guidance, Oct. 27, 2015

2015 U.S. Pharmacist Survey Also Found Strong Support for Manufacturer-based suffixes.

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

Anecdotal Preference: Meaningful vs. Random Suffixes?



Newport, RI March 31st 2016
University or Rhode Island College of Pharmacy
n=150
77% support meaningful suffixes, 21% random.

Philadelphia, PA September 14th 2016
University of the Sciences, College of Pharmacy
n=50
One hand goes up in support of random suffixes.

International Harmonization Efforts

Is Suffix Implementation Feasible? ***SuffixAudit***

- A web-based method of pre-defining compliance for FDA or BQ suffixes.
- Minimizes effort demanded of both the biosimilar manufacturers and regulators.
- Establishes a reliable way of avoiding conflicts beyond the stated definition of BQ or FDA suffix compliance.
- Can remain compliant with future rules and source conflicts updates.

SuffixAudit Features

- Tests proposed suffix for compatibility with FDA Naming Guidance, WHO BQ Rules, or both.
- Detects conflicts such as duplicate suffixes, incompatible combinations, or high similarity to words, stock symbols, medical terminology, etc.
- Adds new and expanded word lists (“lexicons”) including US patents and trademarks from USPTO.
- ASBM has shared with WHO and other regulatorsas one potential implementation of a harmonized international system.

ASBM Forum on International Harmonization of Biologic Nomenclature- April 11, 2018

PARTICIPANTS INCLUDED:

- *National Regulators*
- *Physician Associations*
- *Pharmacist Groups*
- *Patient Advocacy Organizations*
- *Former Regulators*
- *Biotechnology Journals*
- *Media*

FDA U.S. FOOD & DRUG ADMINISTRATION

Health Canada

AAD AMERICAN ACADEMY of DERMATOLOGY | ASSOCIATION

American Gastroenterological Association

CSRO Coalition of State Rheumatology Organizations

Global Colon Cancer Association

SafeBiologics ALLIANCE for SAFE BIOLOGIC MEDICINES

CAPA Canadian Arthritis Patient Alliance experience · perspective · voice

International Alliance of Patients' Organizations A global voice for patients

Arthritis Foundation℠

SCIENTIFIC AMERICAN

nature biotechnology

Benefits of International Harmonization

Anthony Ridgway of Health Canada noted that pharmacovigilance is a GLOBAL CONCERN, not merely a matter of ensuring safety and efficacy for one's citizens within one's own borders.

If a Canadian travels outside of North America, they should have assurances they can get the correct medicine, and that robust and appropriate pharmacovigilance is present.

Benefits of International Harmonization

Mr. Ridgway also observed that a further benefit of a INTERNATIONAL NAMING SYSTEM vs. country-specific naming systems is the tremendous value of tracking the use of biosimilars in large populations across many countries.

July 12 Roundtable Discussion, Washington DC

- Follow-up discussion to April 11
- New participants included:
  - WHO INN Programme Manager Rafaella Balocco
  - APhA Chairman Thomas Menighan
- The representative from WHO
  - Heard the call for leadership in naming
  - Called out for support for their role
  - Confirmed that BQ is ”not dead”

APhA

FIP Meeting: 78th Congress of Pharmacy and Pharmaceutical Sciences (Glasgow, Scotland)

- On September 1st, WHO INN Programme Manager Dr. Rafaella Balocco and I were speakers at a symposium on biosimilars.
- Dr. Balocco also gave a presentation to College of Pharmacy Deans on The School of INN project that is intended to educate pharmacists and pharmacy students about non-proprietary names for medicines.
- There was a also presentation titled "Biosimilars and Biobetters: interchangeability issues for pharmacists, physicians and regulators" at which the speaker spoke in support of distinguishable non-proprietary names.
- Dr. Balocco was in attendance and was delighted; She shared that she is getting more positive about the future of the BQ proposal.

FIP Draft Statement of Policy: Therapeutic Interchange and Substitution

FIP STATEMENT OF POLICY

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

Introduction

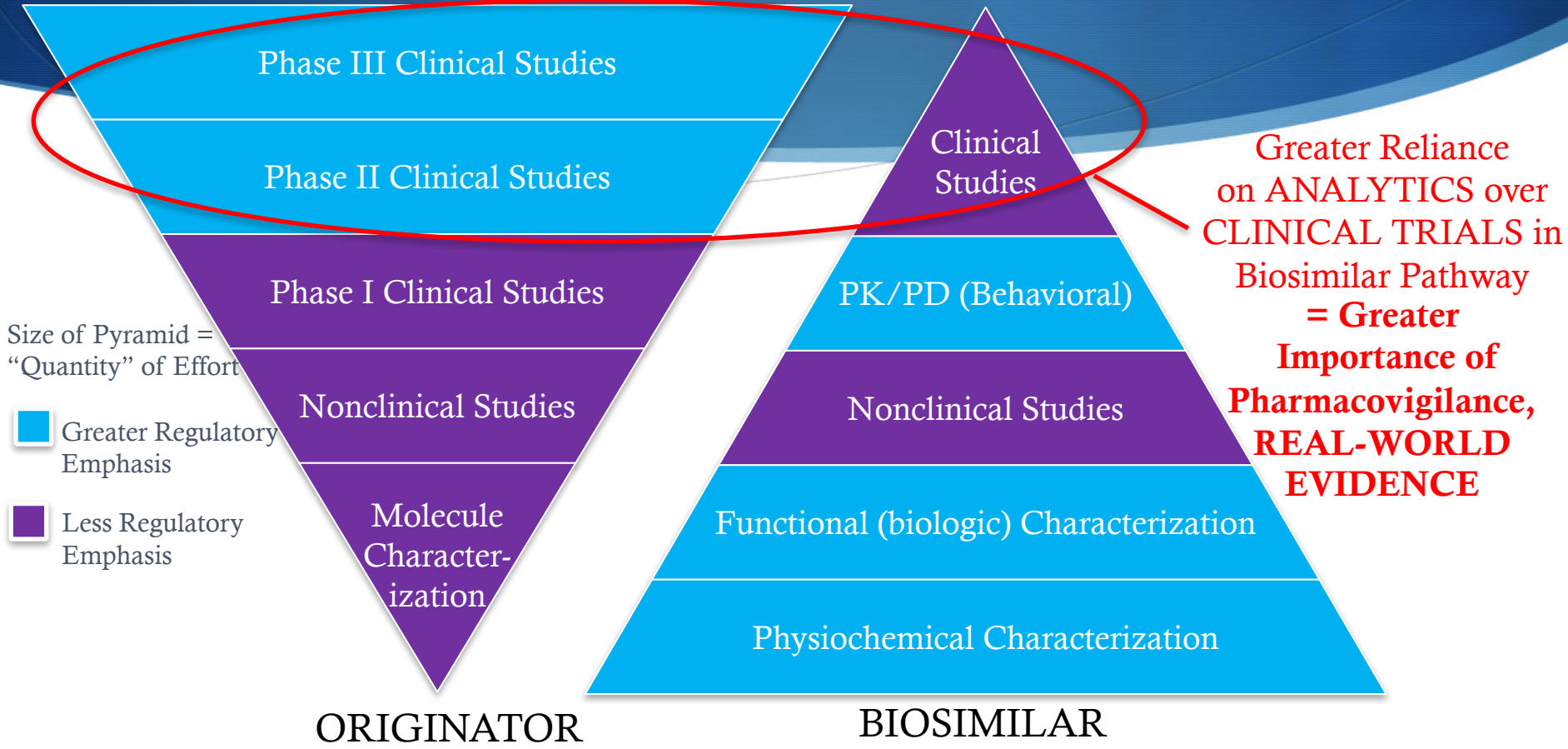
In 1992, FIP issued a statement calling on all countries to ensure the adequate quality of pharmaceutical products. Since then, countries have developed systems that guarantee that all pharmaceutical products, both manufactured locally and imported, meet satisfactory standards of quality, safety, bioavailability, 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."

Approval Process for Biosimilars: Reduced Emphasis on Clinical Trials



Thank You
For Your Attention