

**MOMENTA**



# Anti-Competitive Deterrents to Investment and Innovation in Biosimilars and Interchangeable Biologics

*Follow-On Biologics Workshop*

*Bruce A. Leicher, Sr. Vice President and General  
Counsel, Momenta Pharmaceuticals Inc.*

*Federal Trade Commission February 4, 2014*

# Corporate Overview

- Biotech company founded 2001 based on technology developed at the MIT for the precise understanding of complex mixture medicines
- 250+ employees located in Cambridge, MA
  - Substantial Growth (100+ ) in Employment due to new Biosimilar Pathway
- Expertise in high-resolution analytics, biological characterization, and process engineering



# Introduction

- Biosimilar and Interchangeable Biologics policy should be driven and measured by how it:
  - Promotes Innovation and Attracts Investment
  - Addresses Patient Needs and Patient Safety
  - Avoids using the least innovative and most anti-competitive solutions to achieve these objectives
- The opposition to Biosimilar and Interchangeable Biologic Competition:
  - Is the central factor that motivates restrictions on substitution of Interchangeable Biologics
  - Undermines the attractiveness of investment in, and access to, safer, more affordable biologics
- The related commercial campaigns to require different non-proprietary names, and to restrict access to brand product for FDA-regulated biosimilarity and interchangeability testing are designed to impede investment in, development of, and competition by, safe and affordable Biosimilars and Interchangeable Biologics.

# A Long Established Campaign Against Biosimilar Innovation and Competition

Tactic	Message	Barriers to Competition
BIO CP - 2003	<ul style="list-style-type: none"> <li>• Generic Biologics are Impossible</li> </ul>	<ul style="list-style-type: none"> <li>• Prevent Regulatory Approval</li> <li>• Prevent/Deter Legislative pathway</li> </ul>
Oppose Biosimilar Pathway - 2	<ul style="list-style-type: none"> <li>• Biosimilars are unsafe even if possible</li> <li>• Interchangeable biologics are impossible/different</li> </ul>	<ul style="list-style-type: none"> <li>• Prevent/Deter pathway</li> <li>• Incorporate legislative features that prevent/deter use of the pathway               <ul style="list-style-type: none"> <li>• Mandatory Clinical Trials</li> <li>• Complex IP exchange</li> </ul> </li> </ul>
Influence FDA Guidance - 2011	<ul style="list-style-type: none"> <li>• Same messages</li> </ul>	<ul style="list-style-type: none"> <li>• Emphasize differences (Eg. Naming)</li> <li>• Mandate Unnecessary Clinical trials</li> <li>• Freeze scientific standards for similarity and interchangeability</li> </ul>
Abbvie CP	<ul style="list-style-type: none"> <li>• Same messages</li> </ul>	<ul style="list-style-type: none"> <li>• Delay Biosimilars for 10 years</li> </ul>
Naming Campaign InJ Citizen Petition	<ul style="list-style-type: none"> <li>• Biosimilars are different and raise safety concerns</li> </ul>	<ul style="list-style-type: none"> <li>• Amplifies anti-biosimilar commercial campaign with providers, payors, patients and regulators</li> </ul>
Restricted Access to Reference Products	<ul style="list-style-type: none"> <li>• Biosimilar companies are irresponsible</li> </ul>	<ul style="list-style-type: none"> <li>• Prevents/Delays initiation of development</li> </ul>

# The State Substitution Campaign is the Next Tactic to Prevent and Restrict Competition from Interchangeable Biologics

- Interchangeable Biologics were adopted and embraced in the BPCIA
- The opposition failed at the Federal Level and now seeks to use the same anti-competitive messages to enact laws that will deter or prevent investment in Interchangeable Biologics
- The BPCIA is clear, and is even clearer than Hatch-Waxman, in that it expressly provides:

*“the [interchangeable] biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product” (emphasis added).*

- Yet, the States are being asked, in effect, to join in a commercial marketing campaign to
  - Disparage Interchangeable Biologics
  - Restrict substitution; and
  - Provide notice to doctors to intervene and be concerned about FDA approved biologics

# Why is Substitution so Important?

- Substitution eliminates the need for sales and marketing to physicians and payors
  - Note that some biosimilar companies now support a so-called “compromise”
  - Note also that each of these biosimilar companies
    - May not be seeking to develop interchangeable biologics, and/or
    - May plan to market their biosimilars and interchangeable biologics with a sales force, and
    - Thus benefits from preventing substitution to protect pricing and profits in their branded and “marketed” biosimilar business
- Substitution provides for the highest level of access and affordability to medicines after patents and exclusivity expire
- Substitution enables a return on investment for the substantial innovation needed to develop Interchangeable Biologics that match the reference product

# Anti-Biosimilar déjà vu: State Substitution Restrictions are Designed to Restrict Competition, Not Improve Safety or Knowledge

- Notice Provisions are designed to deliver a message that Interchangeable Biologics are “different” or “suspect” and give marketed products a competitive advantage
  - E.g., BIO appropriately opposes GMO labelling for just this reason
- Special notice and recordkeeping burden pharmacists to deter substitution and promote branded biologics and branded biosimilars
- This matters
  - To patients, who cannot access or afford life saving biologics
  - To physicians, who want transparent and reliable information from biologics manufacturers about all products
  - To payors, who cannot pay for biologics and other critical care
  - To novel developers, who rely on headroom in payor budgets from generics to pay for novel new medicines
  - To regulators, who want to promote quality by design innovation

# Legislation Against Biosimilars: Brand Company-supported Bills Were Appropriately Questioned

## The New York Times

Tuesday, January 29, 2013 Last Update: 8:44 AM ET

### Billions at Risk, Firms Lobby States to Limit Generics

By ANDREW POLLACK

The biotechnology industry's lobbying effort could blunt new competition to its products and reduce the savings anticipated in the federal health care overhaul.

## Los Angeles Times | OPINION

### Battle over 'biosimilars'

States shouldn't stand in the way of cheaper versions of biologic drugs the FDA deems safe.

## The New York Times

Editorial: Improper Efforts to Limit Competitive Drugs  
February 9, 2013

### Hamburg Defends Biosimilar Substitution, Says Efforts to Undermine Trust Are 'Worrisome'

ORLANDO — FDA Commissioner Margaret Hamburg defended the substitutability of interchangeable biosimilars, saying that attempts to undermine trust in the products are "worrisome and represent a disservice to patients who could benefit from these lower-cost treatments."

Drug Industry Daily

Feb. 25, 2013 | Vol. 12 No. 39



# Why Innovative Biosimilar and Interchangeable Biologics Matter For Patient Access

- **Brand Biologics are Expensive**
  - The average daily cost of a brand name biologic product is approximately 22 times greater than a traditional drug.
  - Biologics can cost as much as \$10,000 to several hundred thousand dollars per year.
- **Biologics are the Future of Medicine**
  - By 2016 it is predicted that eight of the top 10 products on the market will be biologics.
- **The Price of Brand Biologics Continues to Increase**
  - U.S. average annual spending growth from 2002 to 2007 was 16% for biologics, compared with 3.7% for drugs.

# Anticipated Annual Changes in U.S. Spending on Traditional Drugs

Therapy Class	2013	2014	2015	3-Year Compounded Total
DIABETES	8.9%	6.8%	6.7%	24.1%
HIGH BLOOD CHOLESTEROL	-6.9%	-4.0%	-5.3%	-15.4%
HIGH BLOOD PRESSURE /HEART DISEASE	-7.2%	-5.9%	-6.0%	-17.9%
ASTHMA	-7.3%	0.8%	1.3%	-5.4%
ULCER DISEASE	-5.6%	-6.4%	-13.2%	-23.3%
DEPRESSION	-4.7%	-8.7%	-6.5%	-18.6%
ATTENTION DISORDERS	4.4%	10.0%	8.6%	24.8%
MENTAL/NEUROLOGICAL DISORDERS	-7.4%	-1.8%	-5.7%	-14.2%
PAIN	-3.3%	-4.5%	-4.2%	-11.6%
INFECTIONS	-6.9%	-6.8%	-6.0%	-18.4%
<b>OVERALL TRADITIONAL</b>	<b>-1.0%</b>	<b>-1.7%</b>	<b>-1.4%</b>	<b>-4.1%</b>

# Anticipated Annual Changes in U.S. Spending on Specialty Drugs (Many are Biologics)

Therapy Class	2013	2014	2015	3-Year Compounded Total
INFLAMMATORY CONDITIONS	25.1%	17.2%	17.4%	72.2%
MULTIPLE SCLEROSIS	19.8%	18.5%	16.8%	65.6%
CANCER	21.3%	20.9%	21.0%	77.4%
HIV	9.2%	9.6%	9.4%	30.9%
HEPATITIS C	33.0%	58.5%	168.4%	465.8%
GROWTH DEFICIENCY	6.2%	5.9%	6.5%	19.9%
ANTICOAGULANT	-0.3%	-0.2%	0.0%	-0.6%
PULMONARY HYPERTENSION	11.0%	11.1%	10.5%	-14.2%
RESPIRATORY CONDITIONS	24.8%	29.5%	27.9%	36.3%
TRANSPLANT	-2.2%	1.0%	-1.2%	-2.4%
<b>OVERALL SPECIALTY</b>	<b>17.8%</b>	<b>19.6%</b>	<b>18.4%</b>	<b>66.8%</b>

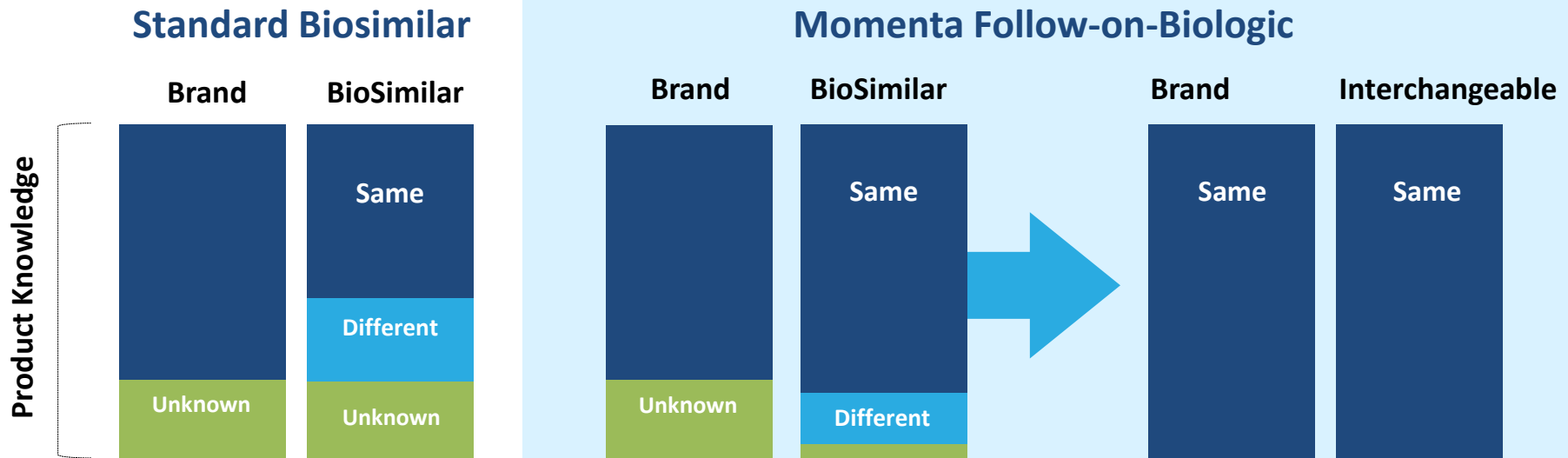
5.21.13 | Glen Stettin, MD

Specialty Drug Spending to Jump 67% by 2015

**HEALTHCARE INSIGHTS**  
FROM THE EXPRESS SCRIPTS LAB

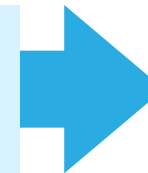
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# Innovation is the Best way to Create Access to Safe, Affordable Interchangeable Biologics



**Remove uncertainty. Qualify differences. Demonstrate equivalence.**

- Thorough Product Characterization
- Manufacturing Process Design
- Product Control and Quality



- Increased POS for approval
- Targeted clinical requirements
- Opportunity for interchangeability
- Improved commercial differentiation

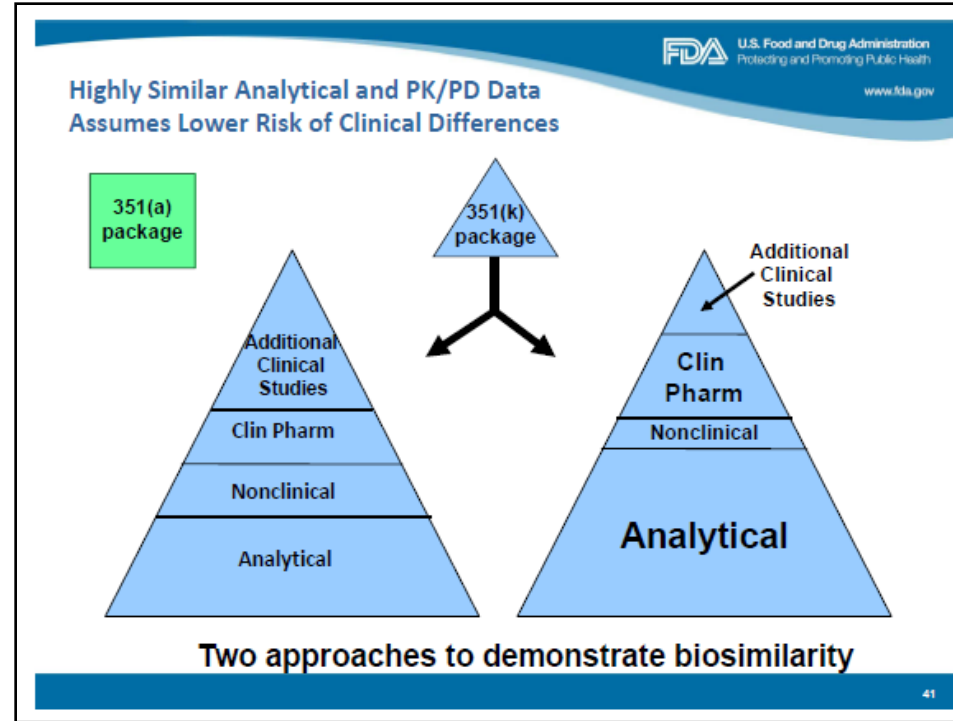
**No Need for Reliance on Brand Trade Secrets**

# The FDA Spurs Investment by Promoting Innovation

## Approval Standards are Rigorous

- Biosimilars must:
    - Be Highly Similar to the Reference Product
    - Not have clinically meaningful differences
  - Interchangeable Biologics must also:
    - Be expected to perform the same in any given patient
    - Have the same risk associated with switching as the reference product
- And Most Importantly:
- Are By Statutory Definition, Substitutable at the Pharmacy without the Intervention of a Physician

## Approach Drives Understanding of what Biologics Are: The Product is not Merely the Process



# The Experience with Generic Lovenox is Relevant to the Development of Biosimilars



The NEW ENGLAND JOURNAL of MEDICINE

Perspective  
AUGUST 4, 2011

## Developing the Nation's Biosimilars Program

Steven Kozlowski, M.D., Janet Woodcock, M.D., Karen Midthun, M.D., and Rachel Behrman Sherman, M.D., M.P.H.

## PERSPECTIVE

### Scientific considerations in the review and approval of generic enoxaparin in the United States

Sau Lee<sup>1</sup>, Andre Raw<sup>1</sup>, Lawrence Yu<sup>1</sup>, Robert Lionberger<sup>1</sup>, Naiqi Ya<sup>1</sup>, Daniela Verthelyi<sup>2</sup>, Amy Rosenberg<sup>2</sup>, Steve Kozlowski<sup>2</sup>, Keith Webber<sup>1</sup> & Janet Woodcock<sup>3</sup>

VOLUME 31 NUMBER 3 MARCH 2013 NATURE BIOTECHNOLOGY

“Although it [Momenta’s generic Lovenox] is ... regulated under [the Food, Drug and Cosmetic Act], it was perhaps one of the most complex reviews imaginable, and it’s a superb example of how physiochemical studies could let us approve a generic drug,” Sherman maintained. “We still needed [non-clinical] immunogenicity studies, so we still needed some information, *but that’s about as complex probably as we expect that our average biosimilar application is going to be, and I think it’s a great illustration of the current state of the science and what we hope to be able to do with these applications.*”

– Rachel Sherman MD, Director of the Office of Medical Policy, CDER

Elsevier  
BusinessIntelligence

Friday, February 10, 2012

**Biosimilars: Similarities to Enoxaparin and the Elephant in the Room**

# Innovation is the Pro-Competitive Way to Provide Substitution Transparency

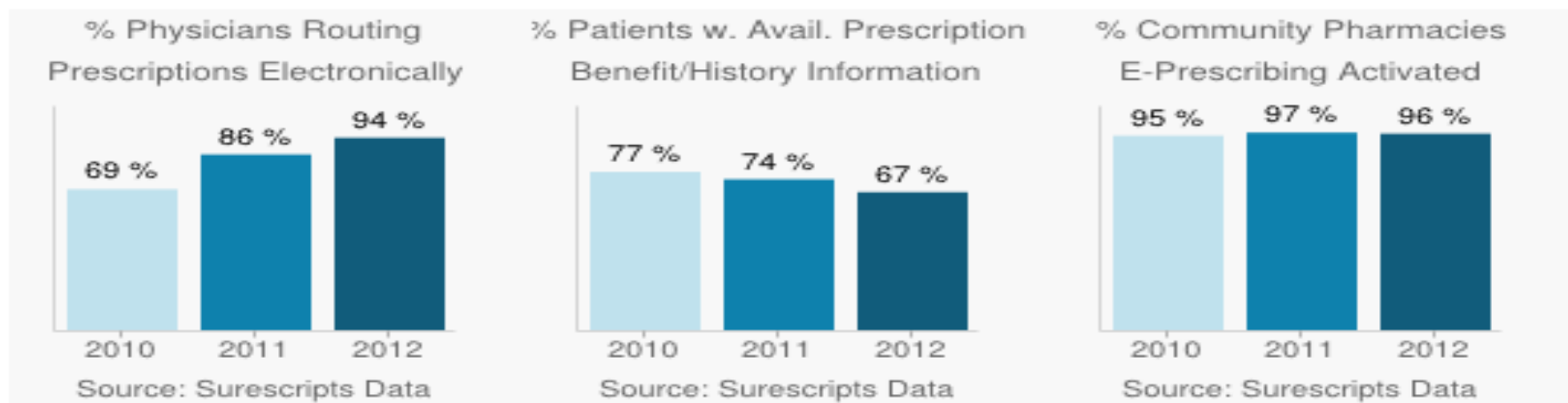
- Special notification proponents argue for special notice under the guise of transparency - Why? Special Notice
  - Favors marketed brand and biosimilar products
  - Restricts and disparages substitutable Interchangeable Biologics
- Nationwide ePrescribing networks provide comprehensive transparency without restricting competition
  - Surescripts provides real time access to all dispensed medications and improves patient safety without discouraging substitution
  - Surescripts access is free to all physicians through the National ePrescribing Patient Safety Initiative
    - Any doctor can access and see what was dispensed
    - It reduces prescription conflicts and errors as well
  - ePrescribing is universally available and can be used even if a physician writes a prescription on paper



# Massachusetts E-Prescribing Adoption

	2010	2011	2012
Physicians Routing Prescriptions at Year End <sup>2</sup>	11,005	13,608	14,929
Community Pharmacies Activated for E-Prescribing at Year-End <sup>3</sup>	1,038	1,064	1,075

## Massachusetts Adoption Percentages





# National ePrescribing Patient Safety Initiative



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is Now.

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EACH YEAR.



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## FREE electronic prescribing... for every physician in America.

The **National ePrescribing Patient Safety Initiative (NEPSI)** is a joint project of dedicated organizations that each play a unique role in resolving the current crisis in preventable medication errors.

Electronic prescribing (ePrescribing) is a viable solution to counter shortcomings of the current paper-based prescribing processes that are in large part responsible for these errors. However, accessibility and cost barriers have slowed adoption of ePrescribing by providers.



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# State Pharmacy Substitution Bill In Massachusetts

- Encourages Investment and Innovation in Safe and More Affordable Interchangeable Biologics:
  - Authorizes Pharmacist Substitution of Interchangeable Biologics
  - Relies on Electronic Medical Records to ensure Physicians aware of the biologic their patient receives
  - Avoids “disparagement” of biosimilars and interchangeable biologics
    - No physician intervention required
    - No prior notice required
    - No special record keeping is required
    - Substitution is handled in the same manner as generic substitution
  - Promotes Cost Effective Patient Access
  - Uses Innovation to develop Interchangeable Biologics and to Inform Physicians
  - Avoids Anti-Competitive practices
- Today’s science allows for demonstration that biologics are the “same”. (*Professor William S. Hancock, Barnett Institute of Chemical and Biological Analysis, Northeastern University, MassBio Policy Leadership Breakfast (January 23, 2013)*).

# CA Bill Vetoed



OFFICE OF THE GOVERNOR

OCT 12 2013

To the Members of the California State Senate:

Senate Bill 598 would effect two changes to our state's pharmacy law. First, it would allow interchangeable "biosimilar" drugs to be substituted for biologic drugs, once these interchangeable drugs are approved by the federal Food and Drug Administration (FDA). This is a policy I strongly support.

Second, it requires pharmacists to send notifications back to prescribers about which drug was dispensed. This requirement, which on its face looks reasonable, is for some reason highly controversial. Doctors with whom I have spoken would welcome this information. CalPERS and other large purchasers warn that the requirement itself would cast doubt on the safety and desirability of more cost-effective alternatives to biologics.

The FDA, which has jurisdiction for approving all drugs, has not yet determined what standards will be required for biosimilars to meet the higher threshold for "interchangeability." Given this fact, to require physician notification at this point strikes me as premature.

For these reasons, I am returning SB 598 without my signature.

Sincerely,

  
Edmund G. Brown Jr.

GOVERNOR EDMUND G. BROWN JR. • SACRAMENTO, CALIFORNIA 95814 • (916) 445-2841

“Senate Bill (SB) 598 would affect two changes to our state’s pharmacy law. First, **it would allow interchangeable “biosimilar” drugs to be substituted for biologic drugs**, once these interchangeable drugs are approved by the FDA. **This is a policy I strongly support.**

....Second, it requires pharmacists to send notifications back to prescribers about which drug was dispensed. ....**to require physician notification at this point strikes me as premature.**

....I am returning SB 598 without my signature.”

—Edmund G. Brown Jr., Governor of California

# The FTC Should Adopt a Policy Opposing Anti-Competitive State Substitution Laws

- State Substitution Conflicts with the BPCIA and Restricts Competition when they require:
  - Prior intervention by physician for substitution
  - Prior notice to provoke intervention by physician before substitution
  - Subsequent notice to provoke intervention by physician and discourage substitution
    - Notice would be used by brand sales representatives to say Interchangeable products are different (code for an unproven safety risk)
    - Interchangeable Products would need sales and marketing support to compete (causing increased costs for consumers)
- Restrictions will deter critical investment required to Innovate and Develop Interchangeable Biologics
  - We should not pass laws that put a ceiling on innovation
- Special Notification is unnecessary and will discourage use of ePrescribing that appropriately ensures access to transparent dispensing information by physicians
- The FTC should encourage the FDA or HHS to Adopt a Preemption Policy to Preclude State Substitution Conflicts and Promote Consistency with the Definition of Interchangeability under the BPCIA

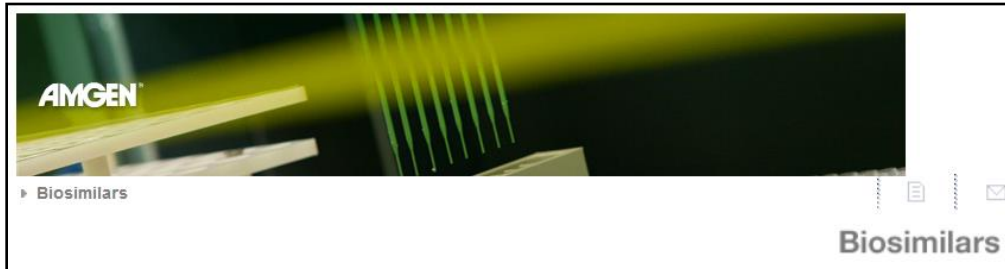
*“[an interchangeable] biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product” (emphasis added).*

# Biosimilar and Interchangeable Biologic Non-Proprietary Naming

- Biosimilars are carefully reviewed and approved by the FDA
  - Biosimilars must be highly similar and have been shown not to have clinically meaningful differences
  - Interchangeable Biologics must also be demonstrated to be capable of being substitutable at the pharmacy without the need for intervention of a physician.
- There is no defensible basis for different Non-Proprietary Names other than to restrict competition
- Like State Substitution Restrictions, the effort to seek distinct non-proprietary names is primarily a commercial effort to make biosimilars and interchangeable products appear different to physicians and patients
- If successful, it will impair investment, innovation and the competitive savings expected from biosimilars and interchangeable biologics

# “Biosimilar” or “Biodifferent”? The Real Purpose of the Naming Proposal...

In order to maximize benefits of the pathway, as policies and laws are developed and implemented, should we be emphasizing similarities or differences?



“Unlike generic medicines where the active ingredients are identical, **biosimilars are not likely to be identical to the originator biologic**. Biosimilar development requires significant expertise, infrastructure and investment to demonstrate **safety** and equivalent efficacy and to ensure **safe, reliable** supply of therapies for patients.”



## Why is Patient Safety A Concern in the Biosimilars Debate?

“**Safety is a priority for the development of all medicines, but biologics raise safety considerations above and beyond those of chemical drugs.** This is because biologics are more structurally complex medicines than chemical drugs, and even slight changes in their manufacture can cause undetected changes in the biological composition of the product. These changes can in turn affect the safety and effectiveness of the product in patients. **The EPREX example provides a further rationale for not considering a follow-on product to be interchangeable with an innovative product.**”

A screenshot of the Genentech website. The top left features the Genentech logo and the text 'A Member of the Roche Group'. Below the logo is a navigation menu with options: 'for SCIENTISTS', 'for MEDICAL PROFESSIONALS', 'for PATIENTS', 'for MEDIA', and 'for GOOD'. The main content area is titled 'Biosimilars' and includes a sub-header 'Views On Public Policy'. The text on the page states: 'The term biosimilar refers to products that are marketed after expiration of patents, which are claimed to have similar properties to existing biologic products. Due to the complexity of biologics, a product can only be made that is similar, but not identical.' Below this, it says 'With patient safety as a priority, Genentech believes that:'. The page also features a sidebar with a menu containing 'Views On Public Policy', 'Our View on Pricing', 'Biosimilars', and 'Clinical Trial Transparency'. The word 'Patient Safety' is prominently displayed in a large, bold font.

### Patient Safety

We believe that because of the differences between biologics, challenging issues exist relating to the development, approval and marketing of biosimilar products. We further believe that patient safety must be of paramount consideration when evaluating these issues.

## Biosimilars in rheumatology: the wind of change

Christian K Schneider

**Correspondence to** Dr C K Schneider, Danish Health and Medicines Authority, Medicines Assessment and Clinical Trials, Copenhagen 2300, Denmark, and Twincore Centre for Experimental and Clinical Infection Research, Hanover, Germany; [chsc@dkma.dk](mailto:chsc@dkma.dk)

....no batch of any reference product is ‘identical’ to the previous one—‘non-identity’ is a normal feature of biotechnology that has to be controlled by tight specifications of critical product attributes, within current technical and scientific limitations (inherent variability). The ‘art’ for a biosimilar is to demonstrate that the biosimilar is as close as possible to its reference product in all relevant functional and structural aspects.

...What is often not mentioned is that originator mAbs/cepts have undergone changes after their approval—this is what regulators call the ‘life cycle’ of a medicine.

*Ann Rheum Dis* March 2013 Vol 72 No 3

# Pharmacovigilance Does not Justify Unique Names

- Safety Reporting is not dependent on Non-Proprietary Names
  - NDC Number and its bar code is used to track and record products at the pharmacy and is unique to the product and manufacturing batch
  - Manufacturer name is on the product
- Alleged Pharmacovigilance concerns relate to all Medicines and Pharmacovigilance Generally, not Biosimilars
  - If there is a problem, fix it for all medicines, not just biosimilars
  - The Innovative Medwatcher smartphone APP is available and should be re-launched
  - ePrescribing also records NDC number which is the most useful identifier



# Pharmacovigilance Does not Justify Unique Names

- Safety reporting could be impaired by balkanization of Non-Proprietary Names
- Rare signals across biosimilar products could be missed if brand and biosimilar product data is treated as unrelated and are used to differentiate products

# Pharmacovigilance Does not Justify Unique Names

- Brand Products that are sold Interchangeably and Have the Same Name Despite:
  - Product Drift
  - Manufacturing Changes
  - Is the quality issue really with products that are not thoroughly tested to assure they are biosimilar or interchangeable?
    - EPREX
    - Heparin
- Competing Brand Products Also share the same Non-Proprietary Name, E.g.,
  - Kogenate antihemophilic factor (Recombinant) vs. Recombinate antihemophilic factor (recombinant)
  - Xyntha antihemophilic factor (Recombinant) plasma/albumin-free) vs. Advate antihemophilic factor (Recombinant) plasma/albumin-free)
  - Avonex Interferon Beta-1A vs. Rebif Interferon Beta-1A

# Restricted Access Programs

- Biosimilarity and Interchangeability Testing requires access to Brand Comparator Products
- Restrictive Distribution Networks and REMs Programs are increasingly used to track and potentially prevent comparative testing of biosimilar products, Cf., Actelion
  - Restricted Access programs are used to monitor, prevent and delay competitive development
  - Vertical restrictions with distribution chain prevent or restrict the re-sale of product to biosimilar competitors
- FTC should confirm that it is unlawful to restrict or delay access to reference product for FDA regulated biosimilar testing

# Conclusion

- Biosimilar and Interchangeable Biologic policy should be driven and measured by how it:
  - Promotes Innovation and Attracts Investment
  - Addresses Patient Needs and Patient Safety
  - Avoids using the least innovative and most anti-competitive solutions to achieve these objectives
- The opposition to Biosimilar and Interchangeable Biologic Competition:
  - Motivates restrictions on substitution of Interchangeable Biologics; and
  - Undermines the attractiveness of investment in, and access to, safer, more affordable biologics
- The FTC should encourage the FDA or HHS to adopt a Preemption Policy to ensure State Substitution legislation is:
  - Consistent with the BPCI; and
  - Facilitates investment to promote the use of innovation to provide patient access to safe and affordable Interchangeable Biologics
- The FTC should oppose as anti-competitive, efforts to:
  - Require different non-proprietary names; and
  - Restrict access to reference product for biosimilarity and interchangeability testing.