SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES

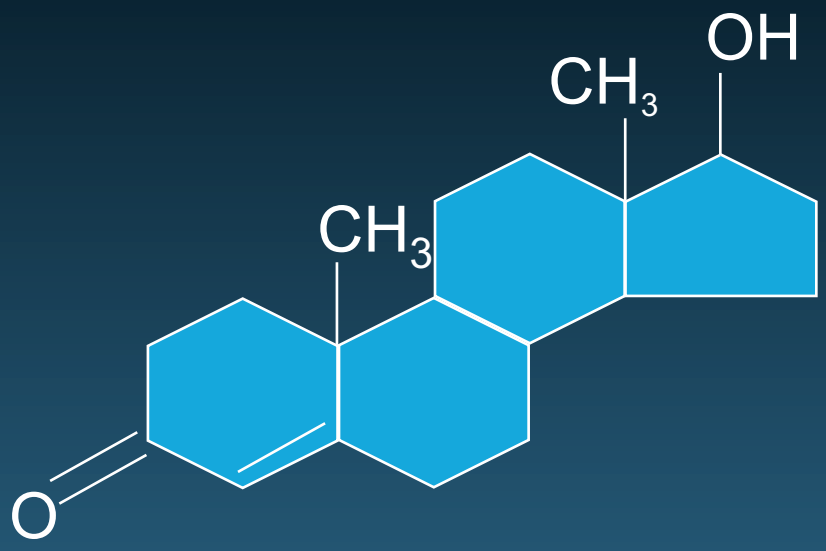
Interchangeabilty of Biosimilar Medicines: A Clinical Perspective

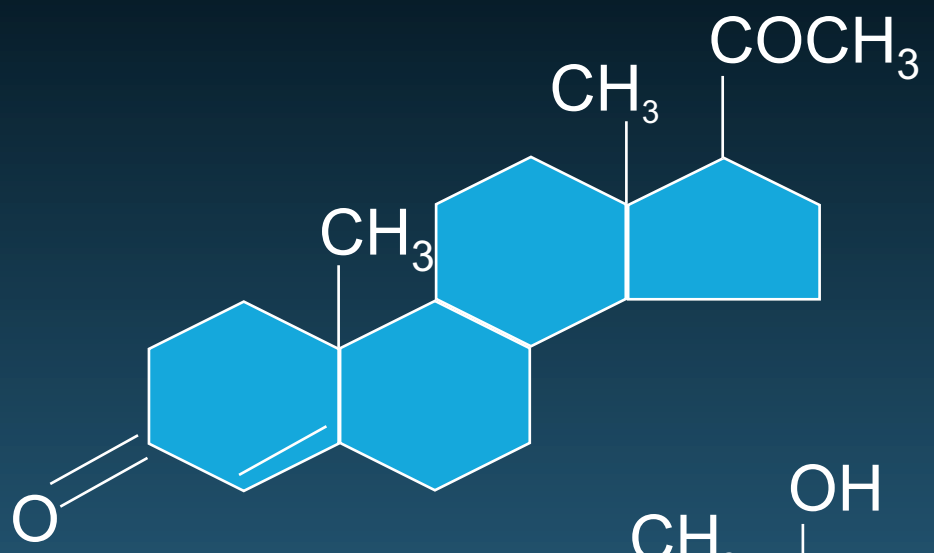
Richard Dolinar, MD
Endocrinologist, Chairman of the Alliance for Safe Biologic Medicines
Presented to the FDA/DIA Biosimilars Conference
September 13, 2012

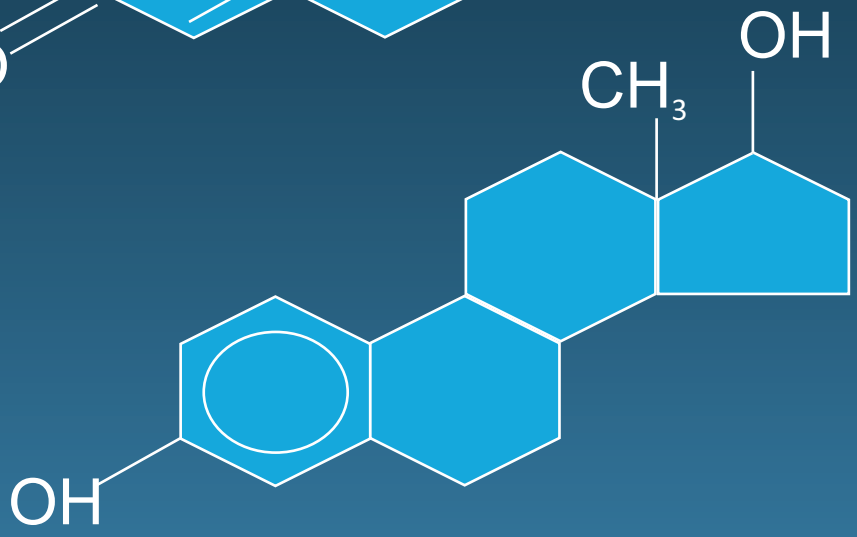
Any designation of interchangeability must be about patient safety first

… because small differences can matter.

Small Differences

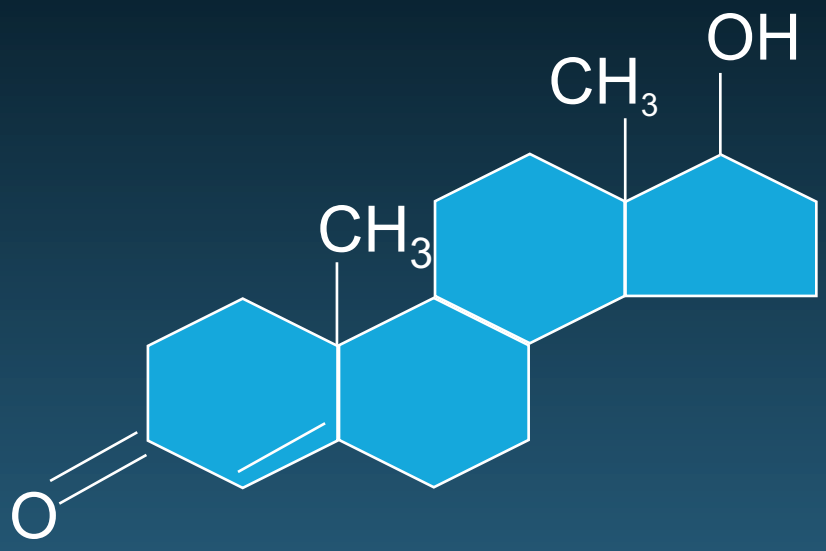




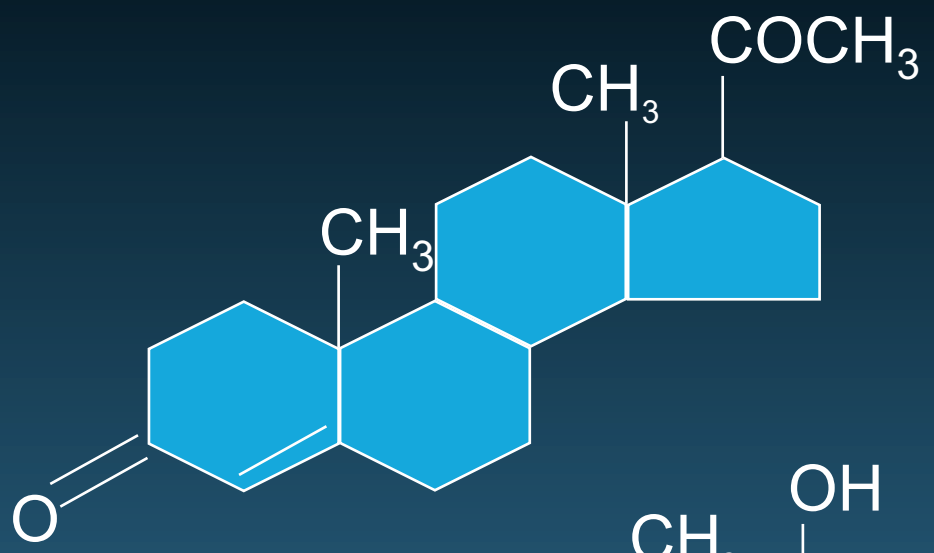


Source: Bilao LLC, 2008

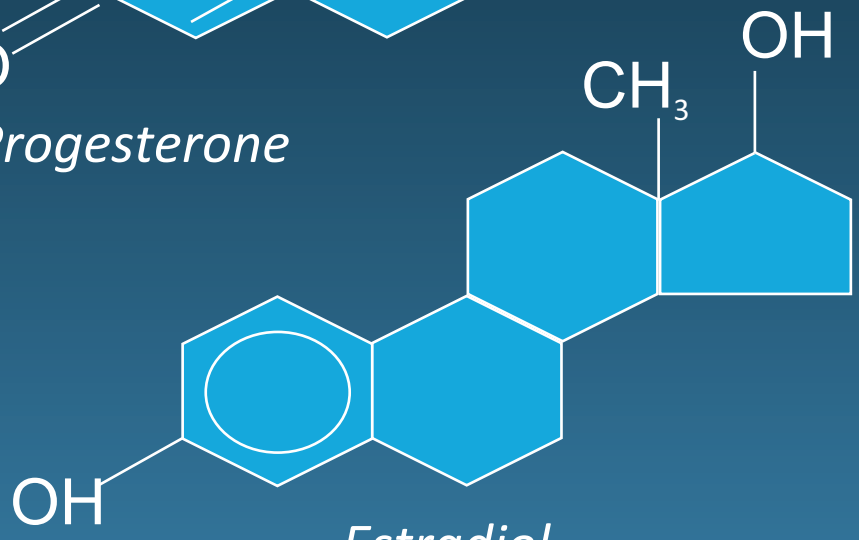
Small Differences = Large Impact



Testosterone



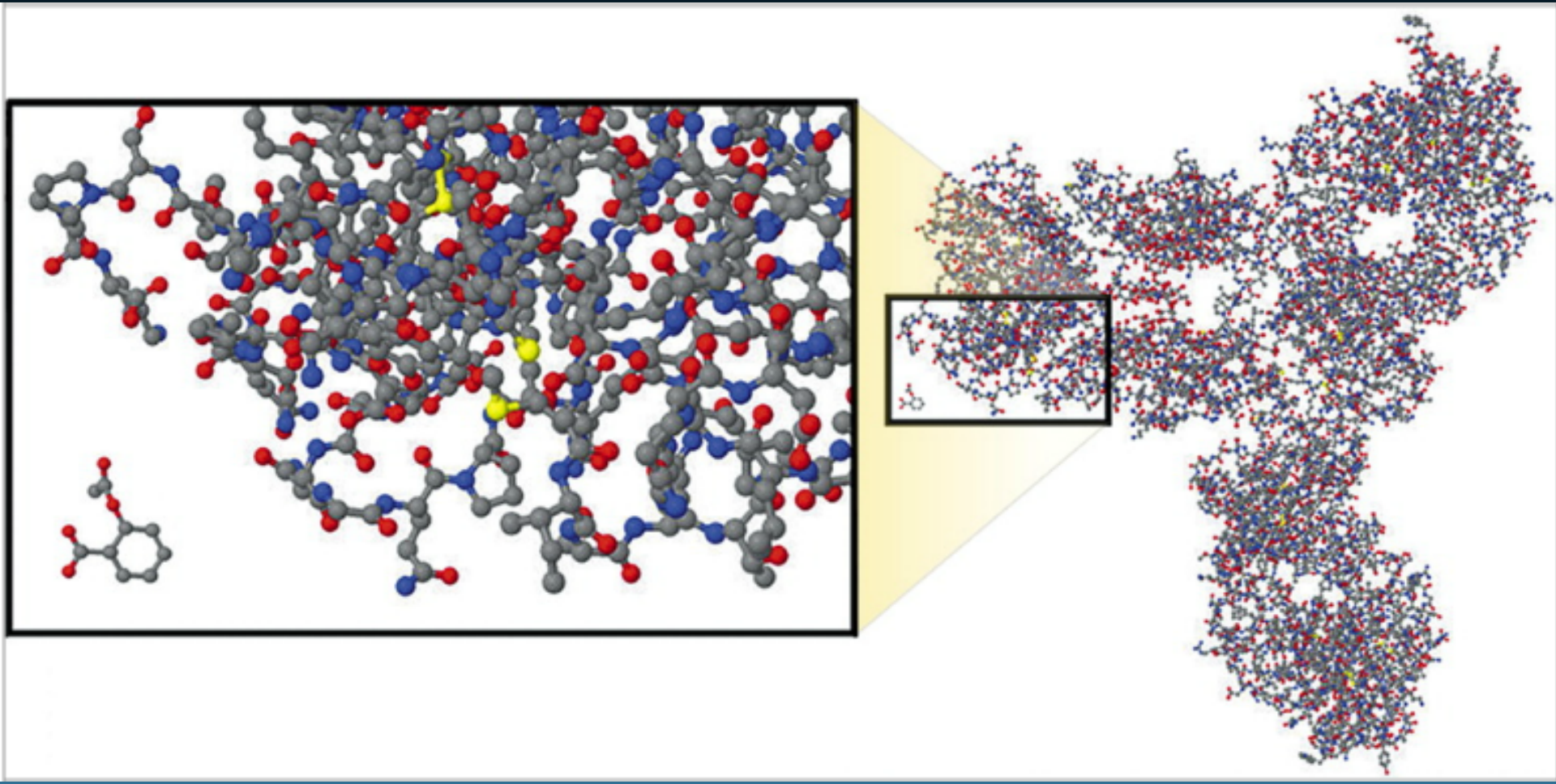
Progesterone



Estradiol

Source: Bilao LLC, 2008

The molecular complexity of biologics makes interchangeability a challenging aspiration



For these reasons Canada and 18 EU countries
DO NOT ALLOW Automatic Substitution

ASBM Working Group Meeting on Interchangeability

DATE: May 24, 2012

Agenda: *Biosimilars and interchangeability*

- Meeting of ASBM National Advisory Board members, most of whom are practicing physicians.

- Overwhelming concern about harm to patients if prescribed product is substituted.

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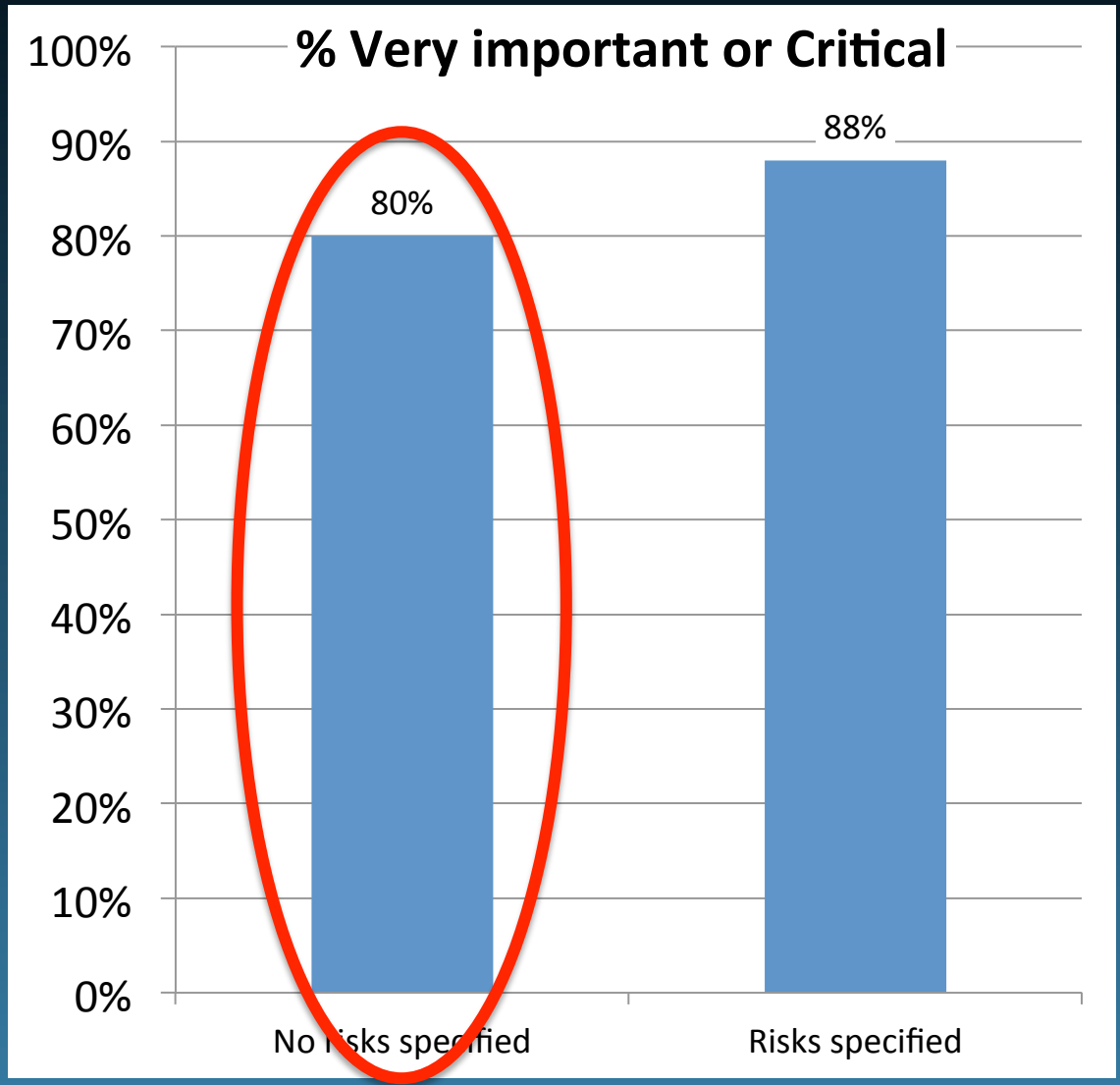
Survey Methodology

- 376 U.S. physicians, distributed equally across
  - Endocrinology
  - Dermatology
  - Oncology
  - Rheumatology
  - Nephrology
  - Neurology
- Confidence interval is + or - 5%

Importance of Notification of Medication Switch: With and Without Known Risks

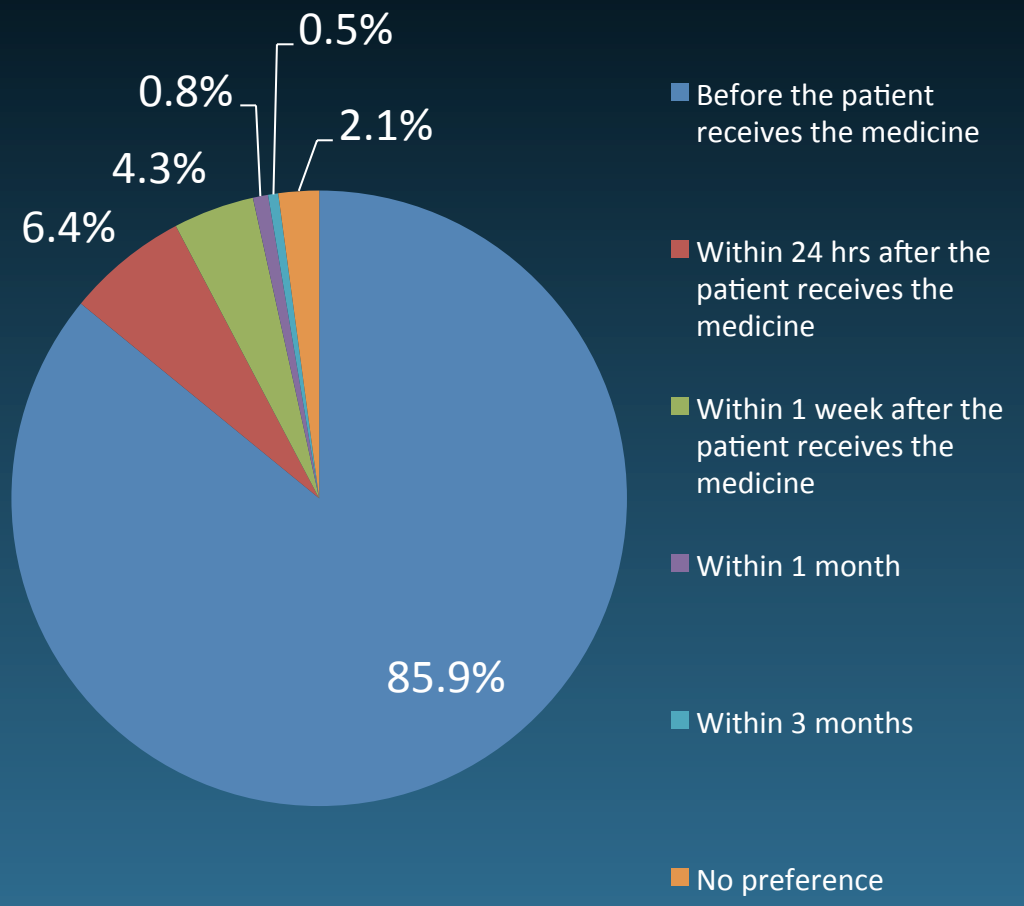
Question: How important would it be for you to be notified by the pharmacist that your patient has received a biologic other than the one you prescribed

…if you were aware that the product could cause an unwanted immune response in some patients or that small differences between brands could have clinical implications for patients?



Timeline for Notification (n=376)

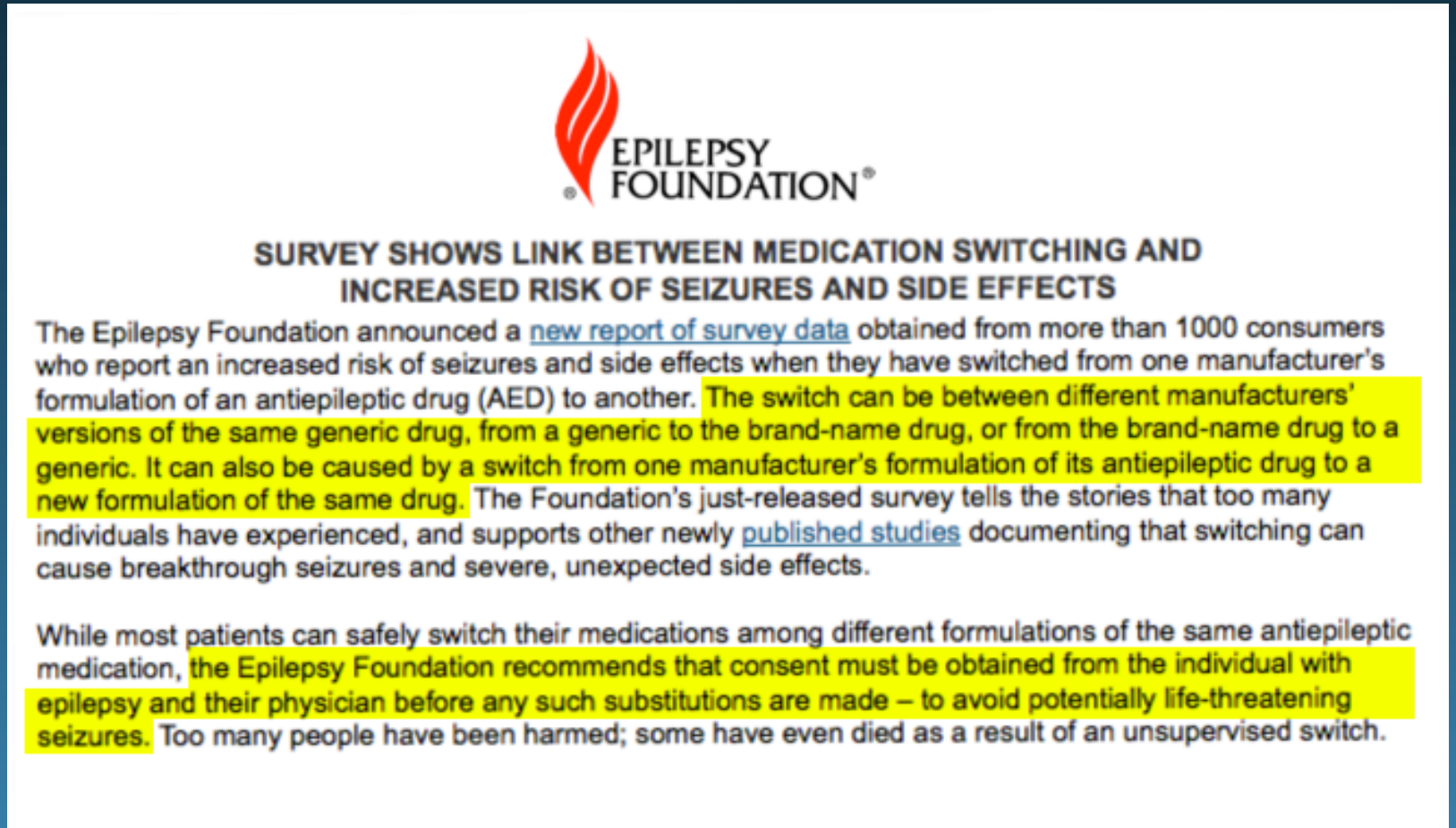
Question: At what point would you prefer to be notified of a change in the biologic medicine dispensed?



- Respondents held clear preferences for their timelines for notification.
- About 85% would prefer to be notified “Before the patient receives the medicine.”

Medication Switching and Side Effects

Even CHEMICALLY IDENTICAL medicines can have different effects when a patient is switched from one to the other, such as increased risk of seizure in epileptic patients.



EPILEPSY FOUNDATION®

SURVEY SHOWS LINK BETWEEN MEDICATION SWITCHING AND INCREASED RISK OF SEIZURES AND SIDE EFFECTS

The Epilepsy Foundation announced a new report of survey data obtained from more than 1000 consumers who report an increased risk of seizures and side effects when they have switched from one manufacturer's formulation of an antiepileptic drug (AED) to another. The switch can be between different manufacturers' versions of the same generic drug, from a generic to the brand-name drug, or from the brand-name drug to a generic. It can also be caused by a switch from one manufacturer's formulation of its antiepileptic drug to a new formulation of the same drug. The Foundation's just-released survey tells the stories that too many individuals have experienced, and supports other newly published studies documenting that switching can cause breakthrough seizures and severe, unexpected side effects.

While most patients can safely switch their medications among different formulations of the same antiepileptic medication, the Epilepsy Foundation recommends that consent must be obtained from the individual with epilepsy and their physician before any such substitutions are made – to avoid potentially life-threatening seizures. Too many people have been harmed; some have even died as a result of an unsupervised switch.

Growth Hormone brands

PRODUCT	MANUFACTURER
Genotropin	Pfizer
Humatrope	Eli
Norditrop	
Nutropin	
Omnitrope	
Saizen	
Tev-Tropin	

8% of switches resulted in growth deceleration

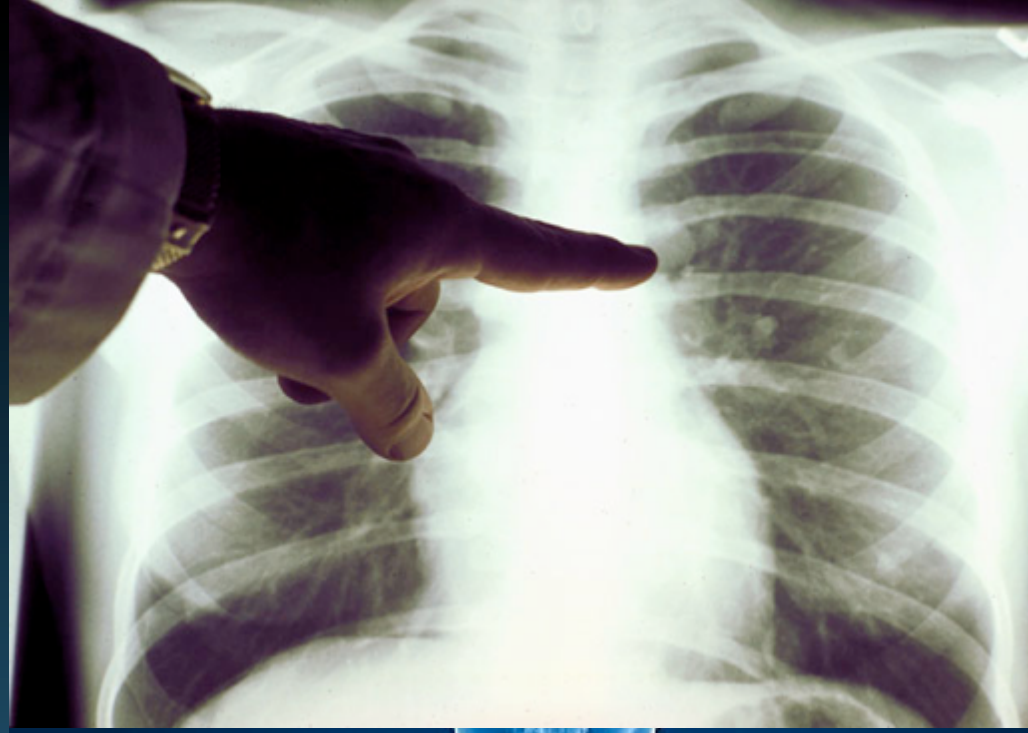
Source: GH Brand Switches, Endocr Pract. 2012;18 (No. 3) p. 310, 2012 AACE

ORDERS are to be clear and precise and followed exactly.

Orders are not POETRY open to individual interpretation.

Ground lost is GROUND LOST.

-ASBM Physician Notification Working Group Meeting, May 24, 2012




PROCEED
WITH
CAUTION

Interchangeability designations require more information

- *FDA Draft Guidance on Biosimilars wisely calls for more information before allowing interchangeability*

- May 11 hearing made it clear that the FDA's draft guidance will proceed cautiously, but that there is pressure to speed up the process – especially with regard to interchangeability.

FDA NEWS RELEASE

For Immediate Release: Feb. 9, 2012
Media Inquiries: Sandy Walsh, 301-796-4669; sandy.walsh@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA ISSUES DRAFT GUIDANCE ON BIOSIMILAR PRODUCT DEVELOPMENT

The U.S. Food and Drug Administration today issued three draft guidance documents on biosimilar product development to assist industry in developing such products in the United States.

"When it comes to getting new biosimilar products on the market, FDA has taken an innovative approach to supporting their development at every step of the process," said Janet Woodcock, M.D., director of FDA's Center for Drug Evaluation and Research. "These draft documents are designed to help industry develop biosimilar versions of currently approved biological products, which can enhance competition and may lead to better patient access and lower cost to consumers."

The Patient Protection and Affordable Care Act, signed into law by President Obama on March 23, 2010, amended the Public Health Service Act to create an abbreviated approval pathway -- under section 351(k) -- for biological products that are demonstrated to be highly similar (biosimilar) to or interchangeable with an FDA-licensed biological product.

Biological products are therapies used to treat diseases and health conditions. They include a wide variety of products blood and blood components, gene therapies, tissues, and proteins. Unlike most prescription biological products generally are made from human and/or animal

The FDA understands that when balancing Cost Reduction against Patient Safety…

…<u>Safety must always win.</u>

In summary: Interchangeability policy Must account for:

- Products drift over time.
- Accurate tracking and tracing of adverse events
- Rare adverse events not frequent enough to be detected in clinical trials

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