SafeBiologics
ALLIANCE *for* SAFE BIOLOGIC MEDICINES

# *Biosimilars: An Introduction*

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Presented to the Florida Association of Health Plans Conference
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# *The Alliance for Safe Biologic Medicines*

- Patients
- Physicians
- Scientists
- CROs
- Innovator industry

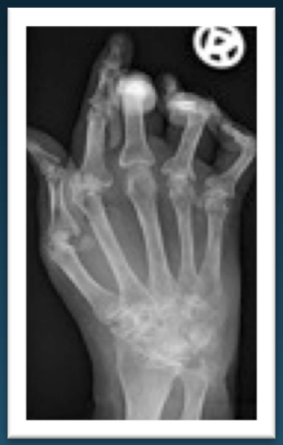
SafeBiologics
ALLIANCE *for* SAFE BIOLOGIC MEDICINES

## ASBM MEMBERS

AAPD
ACRO
AGMD
ican international cancer advocacy network
the virtual lifeline for proactive cancer patients
AMERICAN COUNCIL ON SCIENCE AND HEALTH
ABC Association of Black Cardiologists, Inc.
COLON CANCER ALLIANCE
AMGEN
MANA A National Latina Organization
RetireSafe
Standing up for America's Seniors!
NAMI
National Alliance on Mental Illness
Kidney Cancer Association®
www.KidneyCancer.org
AFPA
THE ALLIANCE FOR PATIENT ACCESS
GLOBAL HEALTHY LIVING FOUNDATION
Genentech
C3 COLORECTAL CANCER COALITION
Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

# *Role of Biotechnology in Medicine*

Advancements in science have increased the number of biotechnology products, revolutionizing the diagnosis, prevention, cure and management of many serious diseases.



**RHEUMATOID ARTHRITIS**
This disorder attacks healthy parts of the body, including its own joints, causing swelling, pain and even disfigurement. New biotech drugs target the affected area without suppressing the entire immune system.


**HIV/AIDS**
Some antiretroviral therapies like Infuvirtide (Fuzeon) stop the HIV virus from infecting cells while others treat HIV-related anemia and other complications.


**DIABETES**
Synthetically made Human insulin was made available in the 1980's. Before then, it was made from cows and pigs.

**CANCER**
Several biologics including this image of Trastuzumab (a monoclonal antibody) treat cancers.

# *Examples of Biologic Medicines*

| Product | Manufacturer | Condition |
|---|---|---|
| HumulinR (*Insulin Injection, Human Recombinant)* | Eli Lilly | Diabetes |
| Betaseron (*Interferon beta-1b)* | Bayer | Multiple Sclerosis |
| Genotropic (*Somatropin)* | Pfizer | Children with growth hormone deficiency; Prader-Willi syndrome, girls with Turner syndrome |
| Follistim (*Follitropin Beta)* | Organon | Infertility |
| NovSeven (*Coagulation Factor VIIa)* | Novo Nordisk | Hemophilia |
| Enbrel (*Etanercept)* | Amgen | Rheumatoid Arthritis, Psoriasis |
| *Epogen (Epeotin alfa)* | Amgen | Anemia caused by chronic kidney disease |
| Rituxan (*Rituximab)* | Genentech | Non-Hodgkin's lymphoma, Rheumatoid Arthritis |
| Humira (*Adalimumab injection)* | Abbot Labs | Rheumatoid Arthritis, Crone's disease, ankylosing spondylitis, psoriatic arthritis |
| Erbitux (*Cetuximab injection)* | Bristol-Meyers Squibb | Head & Neck Cancer, Colorectal Cancer |
| Pegasys (*Peginterferon alfa-2a)* | Roche | Hepatitis C, Hepatitis B |
| Herceptin (*Trastuzumab injection)* | Genentech | Metastatic Breast Cancer |
| Avastin (*Bevacizumab)* | Genentech | Colorectal Cancer, Lung Cancer, Metastatic Breast Cancer, Gliobastoma, Metastatic Kidney Cancer |

By 2014, it is projected that six out of the 10 top-selling drugs in the U.S. will be biologics, some of which may face biosimilar entry.

*Analysis Group Health Care Consulting Bulletin (Fall/Winter 2010)*

# *The differences between Chemical Drugs and Biotech Medicines you can see*

CHEMICAL DRUGS:

- Made by chemical synthesis
- Defined structure, easy to characterize
- Usually taken by mouth, prescribed by general practitioner

BIOTECH MEDICINES:

- Made by living cells-unique cell lines, from bacteria, yeast, or mammals
- Heterogenous structure, difficult to characterize
- Usually injected, prescribed by specialists

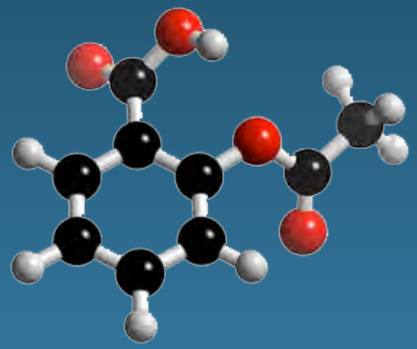
# *Biologic vs. Chemical Medicines - Differences that Matter:*

SIZE: significantly larger, more complex

STRUCTURE: Highly complex, minor manufacturing differences can cause adverse effects

DRIFT: biologics can change with time

STABILITY: Biologic medicines are sensitive to light, heat, denaturing or degradation



# *What are Biosimilars?*

- Biosimilars are often referred to as “follow-on biologics” or “follow-on proteins”.
- Biosimilars are copies of existing trade-name biological products whose patents have expired.
- While “highly similar” biosimilars are not “identical” to the reference product
- They do not utilize the same living cell line, production process, or raw material as the innovator drug.


INNOVATOR MEDICINE

**SIMILAR, BUT NOT IDENTICAL**

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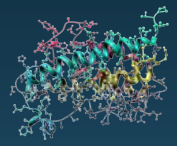
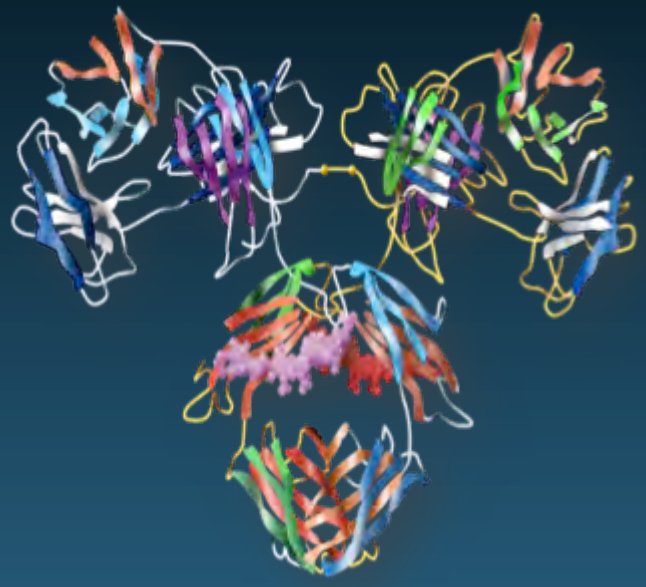
EU-APPROVED BIOSIMILAR

# *Key differences between chemical drugs and biologics*

## SIZE





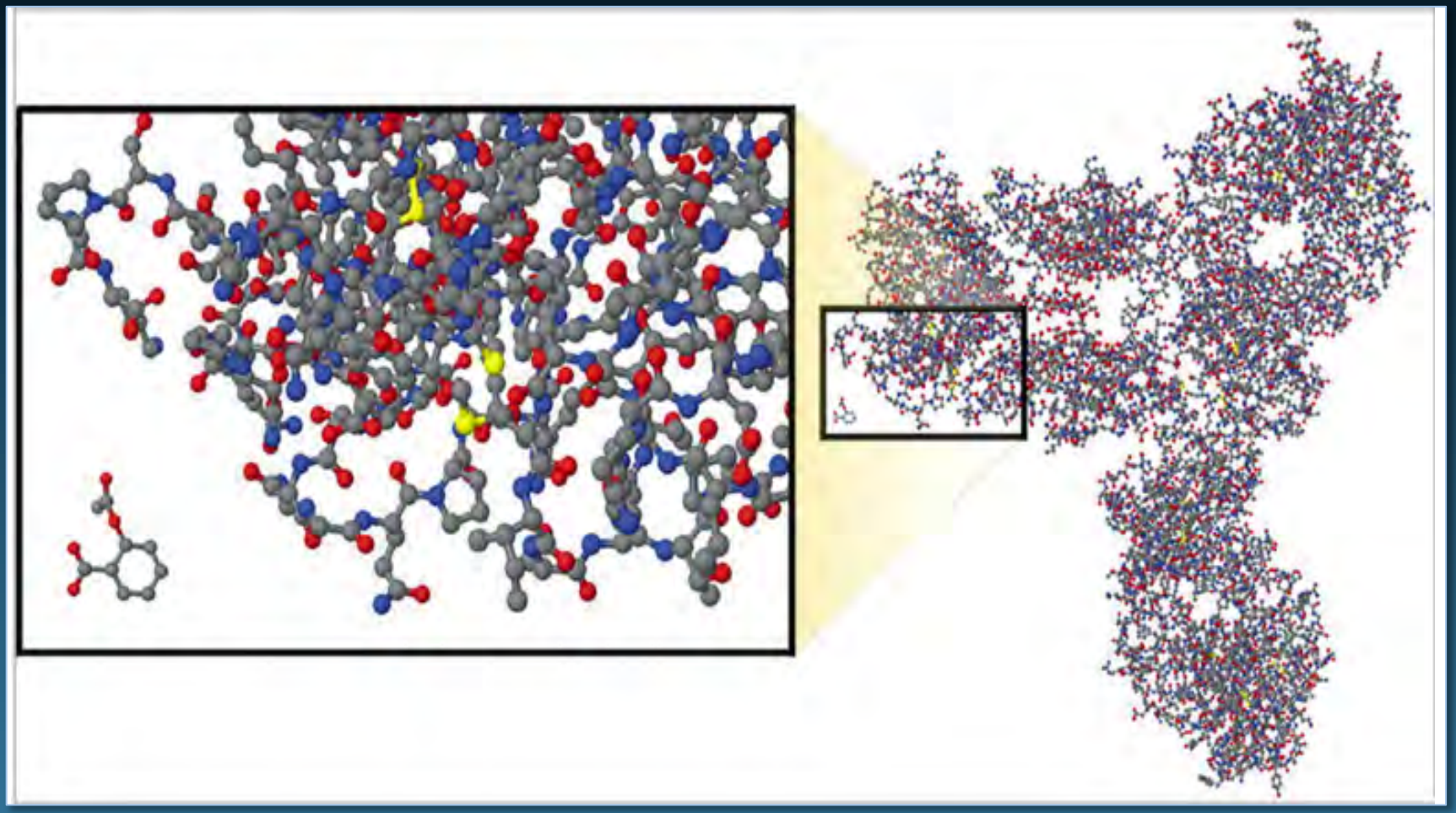
**ASPIRIN**
- ~180 daltons
- 21 atoms

**HUMAN GROWTH HORMONE**
- 191 amino acids
- ~22,000 daltons
- 3091 atoms

**lgL1 ANTIBODY**
- >1000 amino acids
- ~150,000 daltons
- >20,000 atoms

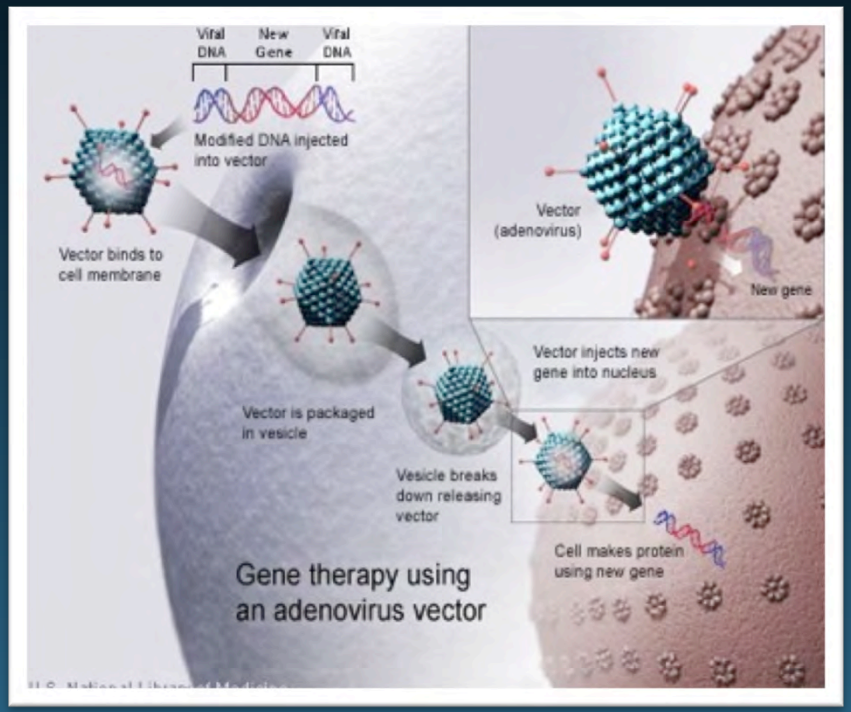
Source: Genentech

# Molecular Comparison:
## Aspirin vs. Biologic Monoclonal Antibody



Source: New England Journal of Medicines, "Developing the Nation's Biosimilars Program," August 4, 2011

# *A Highly Complex Manufacturing Process*




**Design the gene sequence**

**Place gene sequence inside a vector**

**Place vector inside a specific cell**

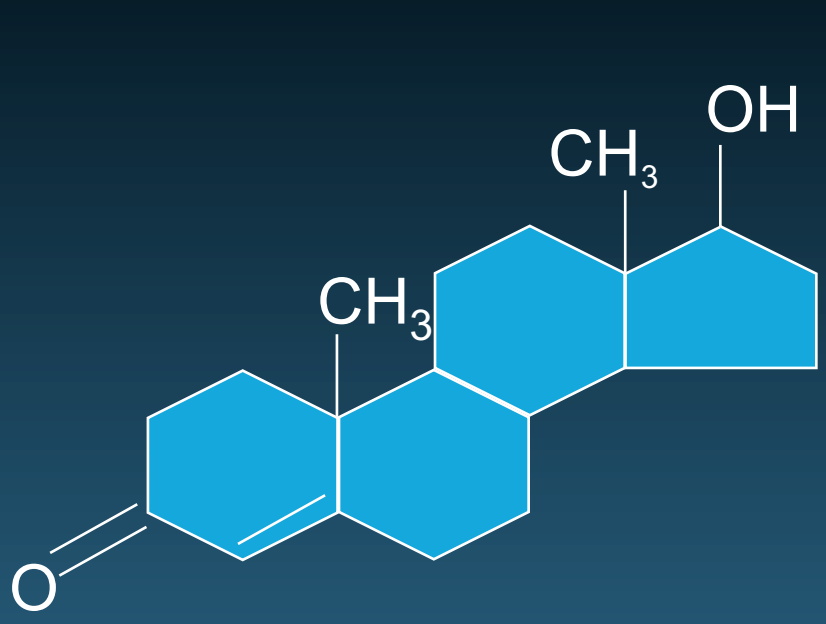
**Fermentation – cells produce the protein defined by the vector**

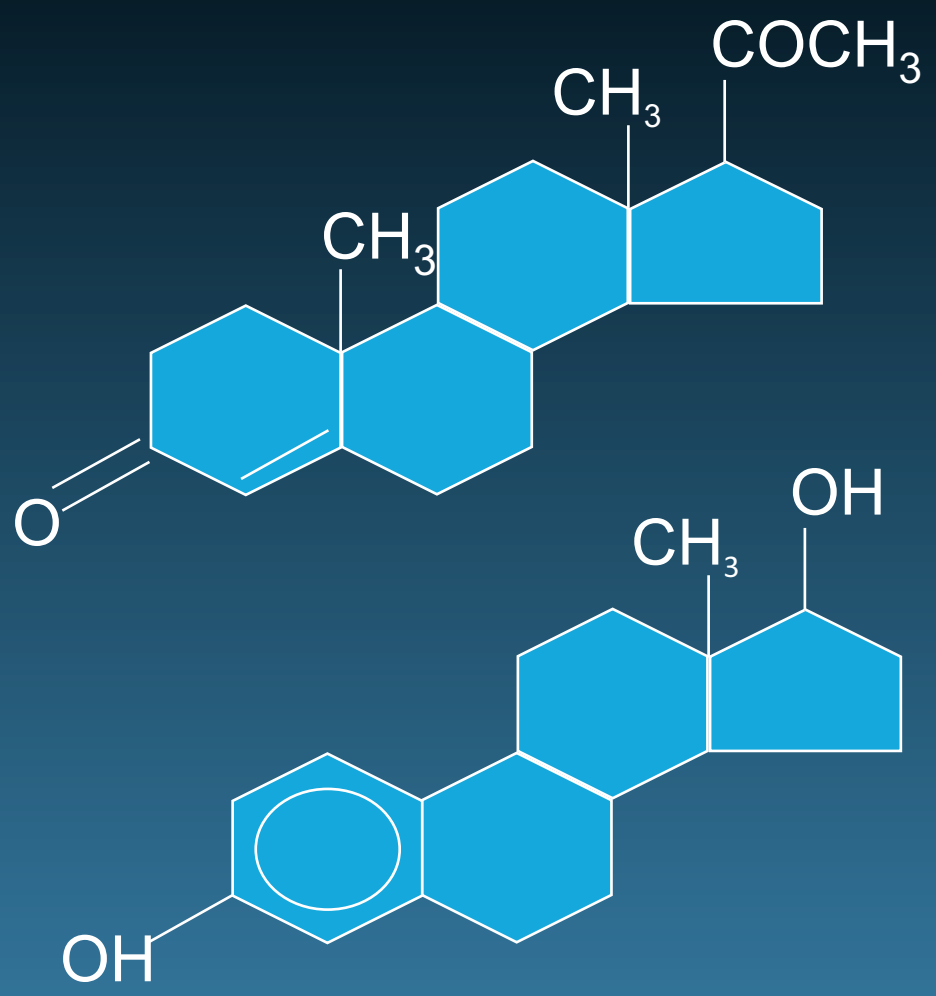
**Purification – removing the impurities**

**IgG1 antibody**
**>1000 amino acids**
**~150,000 daltons**
**>20,000 atoms**

**Highly complex protein with 3 or 4 levels of structure**

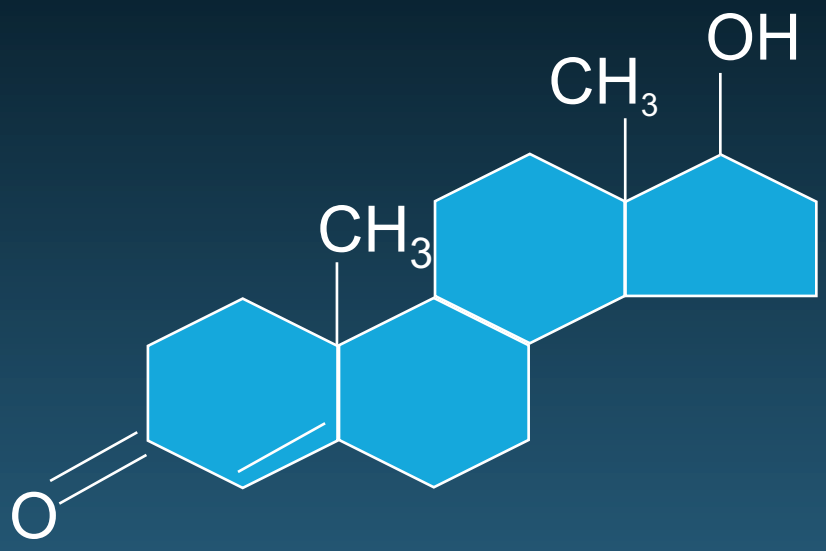
# *Small Differences = Large Impact*



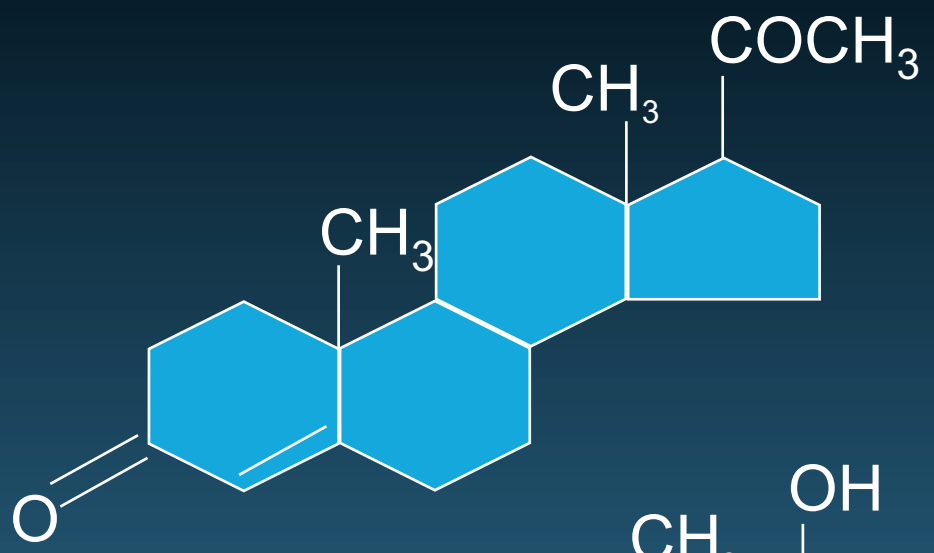




Source: Bilao LLC, 2008

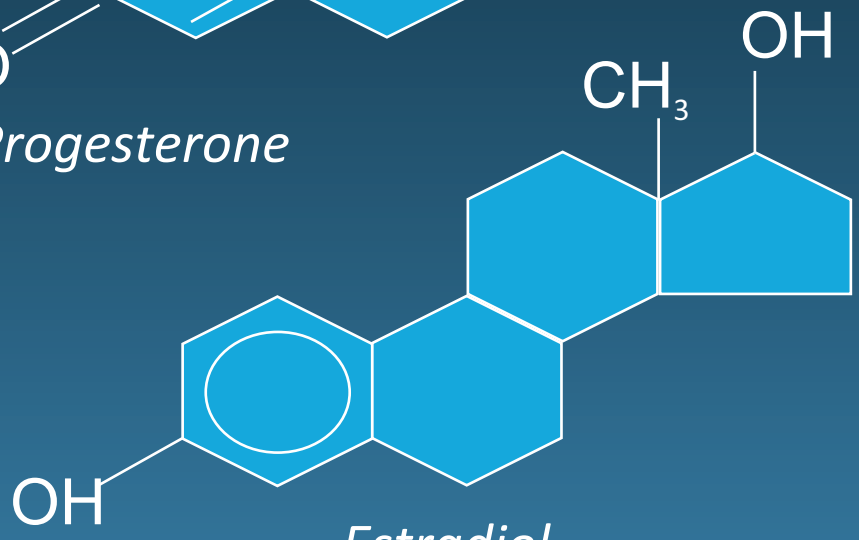
# *Small Differences = Large Impact*




*Testosterone*




*Progesterone*




*Estradiol*



Source: Bilao LLC, 2008

# *Degree of Manufacturing Change*

The degree of change determines the level of risk and thus the data required to demonstrate the product remains equally safe and effective:

**Low risk and common change = Minimal data required**

**Higher risk / less common changes = Maximal Data Required**
*(Clinical Testing, Analytical and Process)*


**It is not scientifically possible to exactly copy biologic medicines at this time.*

# *Creating a U.S. Biosimilars Pathway*

- Biologics are not covered under the 1984 Hatch-Waxman Act for generic versions of conventional drugs.
- On March 23, 2010 President Obama signed into law the Patient Protection and Affordable Care Act that included a pathway for the approval of biosimilars (also referred to as the Biologics Price Competition and Innovation Act (BPCIA).

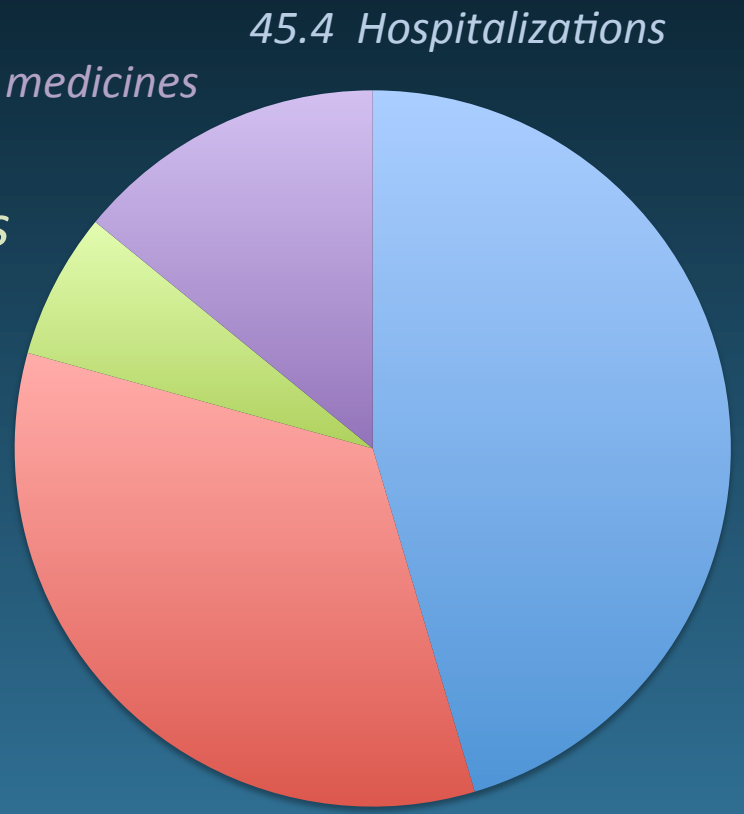
- In November 2010, the Food and Drug Administration began consulting with patient groups, physicians and industry on how to approve the first copies of biologics, known as follow-on biologics or biosimilars.
- On February 9, 2012 the FDA issued a draft guidance seeking public input.
- On May 11, the FDA held its first public hearing on the draft guidance.

# *Learning from Biosimilars Data from the EU*

- Biosimilar pathway established 2003, First biosimilar approved in 2006
- 14 approved so far
- 20% Markdown
- 15% takeup rate
- Lack of saturation
- Expected savings in U.S. market could be low initially

# *Biologic Medicines are a Small Share of Health Plan Costs*

Spending Mix for Severely Ill Patients in Top 2.5% of Health Plan Spending




For the sickest patients, who are most likely to be treated with biologic medicines, hospital costs are seven times the cost of biologic medicines.

*SOURCE: V.J. Willey, et al., "Costs of Severely Ill Members and Specialty Medication Use in a Commercially Insured Population," Health Affairs 27, no. 3 (2008): 824-834.*

# *ASBM Recommendations made at FDA May 11 Hearing*

- CLINICAL TRIALS for each new follow-on biologic, demonstration of no new side effects compared with original biologic medicine.

- A thorough EVALUATION and UNDERSTANDING of biosimilars will be needed before interchangeability is allowed


- Treatment decisions are the purview of the physician and patient, FDA must BAR AUTOMATIC SUBSTITUTION of biologics by pharmacist, insurer, or other third party.

- UNIQUE PROPRIETARY NAME for each biological product for clarity during prescription and monitoring.

- TRACKING/TRACING SYSTEM- label with unique names and lot numbers, to quickly identify source of any potential adverse effects.

## *Summary*

- Biosimilars are not generics.
- The FDA released a 'biosimilars pathway' earlier this year.
- The FDA will decide what analytical, preclinical and clinical data will be needed for approval.
- Prior to biosimilars' market entry, key policy questions must be addressed with a science-based, transparent approach that seeks the input of major stakeholders and puts patients first.