Biologic and Biosimilar Medicines
Their Purpose, Development, Structure, and Effects

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Introduction
Previously directed the Pharmacy Residency program at Ohio State University, led an interprofessional program to improve the medication use system to reduce adverse drug events.

Past president of the American Society of Health System Pharmacists (ASHP).

Former Chairman of the Board of Pharmaceutical Practice of the International Pharmaceutical Federation (FIP), current Vice President and Fellow of FIP.

Published more than 180 articles and abstracts in professional and scientific journals, 38 book chapters, edited seven books and given more than 500 contributed or invited presentations in 22 countries and the US.

Recipient of Donald E. Francke Medal for significant international contributions to health-system pharmacy. (2006); Harvey A.K Whitney Award, known as health-system pharmacy's highest honor (2008).

2012 recognized as a Fellow of the American Society for Parenteral and Enteral Nutrition (FASPEN).

2014 Advisory Board Chair of the Alliance for Safe Biologic Medicines, a group of physicians, pharmacists, patient advocates and others which educates and advises policymakers working on biosimilar policy.
Biosimilars Pop Quiz
How familiar are you with BIOLOGIC medicines?

1. Very Familiar-complete understanding,
2. Familiar-basic understanding,
3. I have heard of them but could not define
4. I have never heard of them
How familiar are you with BIOSIMILAR medicines?

1. Very Familiar-complete understanding,
2. Familiar-basic understanding,
3. I have heard of them but could not define
4. I have never heard of them
Have any biosimilars been approved by the FDA for use in the U.S.?

1. YES
2. NO
“Biosimilars are structurally identical to the reference biologic product upon which they are based.”

1. TRUE
2. FALSE
“A biosimilar is by definition interchangeable with its reference biologic product.”

1. TRUE
2. FALSE
Does a biosimilar having the same nonproprietary/scientific name as its reference product imply identical chemical structure?

1. YES
2. NO
3. NOT SURE
Does a biosimilar having the same nonproprietary/scientific name as its reference product imply approval for the same indications?

1. YES
2. NO
3. NOT SURE
Does a biosimilar having the same nonproprietary/scientific name as its reference product imply that a patient can be safely switched between it and its reference product with the same result and no additional risks?

1. YES
2. NO
3. NOT SURE
“As a pharmacist, I believe I will have a role in making decisions about the choice of biologics for specific indications.”

1. YES
2. NO
3. NOT SURE
“I believe the safe use of biosimilars will reduce healthcare costs.”

1. YES
2. NO
3. NOT SURE
Which of the following tools will you use to realize the potential cost benefits of biosimilars:

1. The formulary system
2. Clinical practice guidelines that specify the choice of drugs
3. Therapeutic interchange policy
4. Patient-specific dialog with the prescriber on a case-by-case basis
5. All of the above
“I need and plan to learn more about biologics to prepare myself for a role in the safe use of biosimilars.”

1. TRUE
2. FALSE
Biologics and Biosimilars: Overview
What is a Biologic Medicine?

A **biologic medicine** is a **substance** that is made **from** a **living organism** or its products and is used in the prevention, diagnosis, treatment, or cure of a disease. Biologic medicines include:

- antibodies
- vaccines
- interleukins (these can regulate immune responses)
- hormones
- blood and blood products

At a molecular level, biologic medicines are often 200–1000 times the size of a chemical drug molecule and are far more complex structurally. They are highly sensitive to handling and their environment.

Biologics are more difficult to characterize and manufacture than chemical drugs.

Due to their size and sensitivity, biologic medicines are almost always injected into a patient’s body.
Developing a biosimilar requires reverse-engineering an innovator biologic. **Biosimilars are often mistakenly referred to as “generic” biologics.**

Unlike with generic copies of chemical medicines, the fact that they are made using living cells means biologic medicines cannot be copied exactly. It can only ever be “similar” to its reference biologic.

FDA is in the process of drafting guidance on how similar a biosimilar must be to earn a designation of “interchangeable”, meaning that the biosimilar has the **same clinical effects in a patient without additional risks.** Bruce Babbitt of PAREXEL Consulting, a former U.S. Dept. of Health & Human Services official, will present a regulatory overview later today.

“Interchangeable” biosimilars are those which pharmacists will potentially be able to substitute. Biosimilar substitution will be discussed in more detail later today.
How Are Biologics Used?
Benefits of Biologic Medicines

- Biologic medicines have made a significant difference in the lives of patients with serious illnesses, including cancer, blood conditions, auto-immune disorders such as rheumatoid arthritis (RA) and psoriasis, and neurological disorders like multiple sclerosis (MS).

- By understanding the mechanisms of diseases, companies have developed biologic medicines to target and modify the underlying causes of disease, potentially altering the course of the disease rather than simply treating symptoms.

- The development of new biologic medicines may be the best hope for effectively treating diseases for which there are currently no cures.
Advances in the understanding of RA over the last 20 years have led to a new treatment paradigm, where reducing disability and achieving remission are now possible goals. Once researchers understood the underlying inflammatory mechanisms of RA, scientists developed disease-modifying biologic medicines to target the proteins that regulate inflammation. Biologic medicines have proved effective in slowing down disease progression and joint damage, helping to improve daily function.

Dr. Harry Gewanter, chairman of the Alliance for Safe Biologic Medicines, and a practicing pediatric rheumatologist, will explain this later in more detail.
Investigating cancer pathways and determining the molecular basis of cancer has led to the development of new targeted diagnostics and treatments. Traditionally, cancer has been treated with surgery, radiation, and chemotherapy. Biotechnology has contributed to significant advances in cancer treatment, including hormone therapies, biologics, and targeted therapies such as monoclonal antibodies.

Some kinds of colorectal cancer are caused by the overexpression of epidermal growth factor receptors (EGFR), causing the overly rapid cell growth associated with most cancers. There are several EGFR inhibitors available to patients.

Patient advocate Andrew Spiegel, executive director of the Global Colon Cancer Association, will provide a patient perspective on biologic medicines later today.
Two Sources of Biologic Medicines

NATURAL:
- Eggs
- Pigs
- Cows
- Humans

RECOMBINANT:
- Bacteria
- Yeast
- Mammalian Cells
- Transgenic Plants
- Transgenic Animals
Two Types of Biologic Therapy

REPLACEMENT therapy:
A patient is administered an *endogenous* (i.e., naturally occurring) protein or hormone to compensate for the loss, due to disease, genetic or otherwise, or surgery of a gland or tissue that would normally produce the substance.

INTERVENTION therapy:
A novel biologic molecule is designed to specifically bind a chosen target.
### Biologic Medicine Source and Therapy Types

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<tr>
<th>NATURAL SOURCE</th>
<th>RECOMBINANT SOURCE</th>
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<td>REPLACEMENT THERAPY</td>
<td><strong>NATURAL SOURCE</strong></td>
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<td>insulin from pigs and cows</td>
<td>Recombinant technology has made possible the synthesis of insulin and granulocyte colony-stimulating factor (used to assist in minimizing the immunosuppressive effects of chemotherapy)</td>
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<td>human blood for Factor VIII (clotting factor), Immunoglobulin G antibodies, and Albumin</td>
<td>Yeast has also become a source of recombinant forms of insulin and human growth hormone (HGH).</td>
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<td>INTERVENTION THERAPY</td>
<td>Flu Vaccine grown within egg</td>
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Education on Biosimilars is a Top Priority for Pharmacist Organizations

Pharmacists and health systems prepare to add biosimilars to formularies

January 01, 2015

Pharmacists can help address many unknowns among health systems, prescribers, and patients. Prescription drug spending is increasing while most other areas of health care spending are slowing down. In 2013, the most recent year for which CMS data are available, prescription drug spending increased by 2.5%—a staggering leap from the 0.5% increase in 2012. "Many in health care are pinning their hopes on biosimilars to help slow the quick clip of rising drug costs.

The first two biosimilars, versions of filgrastim (Neupogen—Amgen) and infliximab (Remicade—Janssen), could hit the U.S. market in the first or second quarter of 2015. Because biosimilars are not identical copies of their biologic counterparts to the degree that generics are copies of small-molecule drugs, there are many unknowns among health systems and prescribers. Pharmacists can help address these issues as health systems add the new drugs to their formularies.
FDA Approval of the More Biosimilars is Expected Shortly

- On March 17, FDA’s Arthritis Advisory Committee will meet to review Remisma, a biosimilar to Remicade (infliximab) – used to treat rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn’s disease and ulcerative colitis.

- This is the first monoclonal antibody (MaB) to seek approval from FDA under its approval pathway. Approved in EU and Canada, although for different indications.

- FDA approval is sought for all indications for which the innovator product has approval.
Evolution of Biologic Therapies
History of Biologic Medicines
Early 20th Century

- 1920s: Biologics derived from Animal Sources- insulin from cow and pig pancreas.
- 1940s: influenza vaccines manufactured within eggs.
- 1950: human blood-derived proteins used in treatment of hemophilia and primary immune deficiency.
1953: Drs. Watson and Crick reveal structure of DNA, commencing era of modern biotechnology.

1960s: scientists fully understand the genetic code.

1973: Bacterial genes used to insert recombinant DNA into a cell for replication.

1973: “Southern blot” technique developed to study DNA structure.
1975: Colony hybridization and Southern blotting developed for detecting specific DNA sequences.

1975: first **monoclonal antibody** developed by fusing immortal tumor cells with antibody-producing B-lymphocyte cells to produce hybrid cells (hybridomas) that synthesize identical (or “monoclonal”) antibodies.
1977: Long sequences of DNA can now be sequenced. Genetically engineered bacteria used to synthesize peptide hormone somatostatin.

For the first time a synthetic recombinant gene had been used to clone a protein. Many consider this the beginning of the Age of Biotechnology.
History of Biologic Medicines
Late 20th Century

1982: Insulin becomes first-ever approved human therapeutic manufactured using recombinant technology in *E. coli* bacteria, rather than mammal cells.

Today, recombinant insulin is made within both bacteria and yeast.
1987: FDA approves genetically engineered plasminogen activator to treat heart attacks.

1989: FDA approves Erythropoietin (EPO), a complex glycoprotein used to treat anemia in patients with cancer or kidney damage.
Nearly 200 biologic and recombinant biotechnology medicines are helping 800 million patients worldwide.

907 medicines and vaccines targeting more than 100 diseases are in human clinical trials or under FDA review.

This includes 338 monoclonal antibodies, 250 vaccines, 93 recombinant proteins, 60 cell therapies, 46 gene therapies and 30 antisense medicines.
How Do Biologics Differ From Chemical Medicines?
Differences Between Biologic and Chemical Medicines

- **SIZE**: Chemical compounds are generally much smaller in size than biologics and are generally unseen by the human immune system.

- **STRUCTURE**: The structure and function of a chemical compound are simple and straightforward, but a biologic protein has a complex three-dimensional structure. Some of the proteins have post-translational modifications in the form of sugar attachments (called glycosylation) at specific sites, or they may have chemical modifications. Due to the structural complexity of biologics, the relationship between structure and function is often unclear (as explained on the subsequent slide under characterization).
**STABILITY:** Chemical drug structure is defined by rigid and stable covalent bonds, whereas a protein’s structure is defined by the sequence (relatively stable covalent bonds) AND the three-dimensional folding into a structure stabilized by weak non-covalent bonds. The interactions of many weak bonds give proteins a three-dimensional structure and functional flexibility but also make it **sensitive to chemical and physical degradation.**

**VARIABILITY:** While an active pharmaceutical ingredient of a drug consists of a single, well-defined structure, a biologic medicine exhibits a diversity of structures due to being prone to weak non-covalent bonds as well as the diversity of enzymatic and chemical modifications that can occur. Consequently, a biologic medicine is a heterogeneous mixture of product and its related components as well as impurities from the manufacturing process.
MANUFACTURING: Chemical compounds are manufactured using chemical reactions that are predictable and robustly reproducible, so an identical copy can be made. However, biotechnology medicines are made using living cells. Therefore, an identical copy of a biologic medicine using a different cell line and/or different manufacturing process is not possible.

CHARACTERIZATION: Chemical compounds are easy to fully characterize. In addition, since the structure of the active ingredient in the chemical drug is precisely known, we can expect to see the same pharmaceutical function in vivo.
CHARACTERIZATION (continued): Characterization of biologic medicines requires multiple, orthogonal, advanced analytical methods. While many biologic products have been well-characterized, complete characterization to the last atom is impossible. In addition, correlating the diverse structures in a biologic medicine to function is quite difficult.

IMMUNOGENICITY: Immunogenicity is the reaction of the body’s immune system to a foreign substance. Chemical compounds have a lower potential while biologics have higher potential for immunogenicity.
Proteins: Size, Structure & Complexity

**Small Molecule Drug**
- Aspirin
  - 21 atoms

**Large Molecule Drug**
- hGH
  - ~3000 atoms

**Large Biologic**
- IgG Antibody
  - ~25,000 atoms

**Size**
- Bike
  - ~20 lbs
- Car
  - ~3000 lbs

**Complexity**
- F16 Jet
  - ~25,000 lbs (without fuel)

Source: Genentech
Advantages of Large Size/Complexity of Biologic Medicines

- More precise fit to a large target (disease)
- Can interact with multiple targets (such as binding to two receptors) simultaneously
- Large molecule can stay in body longer
One Disadvantage of Large Size/Complexity: Immunogenicity

- Biologics have provided new options in the prevention and treatment of diseases in which previous therapies treated only the symptoms. However, because of their complexity, biologics are associated with additional risks. The most important of these risks is the potential to cause immunogenicity.

- Immunogenicity occurs when the immune system in the human body mounts an attack when a foreign substance enters the body. For example, when we catch a common cold (i.e. rhinovirus) or the flu (i.e., influenza virus), our body responds by attacking these viruses, thereby neutralizing them.
All biologic medicines are fairly large molecules, sometimes resembling a virus, and have the potential to induce unwanted antibody responses (i.e., be immunogenic).

The unwanted immune response may be of no consequence for a patient or of serious consequence.

- Immunogenicity may neutralize the medicine, minimizing or eliminating the intended effect of the medicine.
- One of the main concerns is that the immune system may attack the endogenous protein, making the patient’s condition worse than before the medicine was introduced.
Many biologic products are engineered and manufactured to be as similar as possible to an already existing endogenous protein in the body. However, if there is some small difference that allows the body to differentiate or discriminate between the drug and the endogenous protein, the immune system may develop an antibody or immunogenic response against that protein. In addition, that immunogenic response may broaden and actually cross-react with the endogenous protein.

In many cases the presence of antibody may not cause clinical consequences, but in some cases it can result in significant consequences. One such example is a condition called Pure Red Blood Cell Aplasia (PRCA), a syndrome characterized by severe anemia and absence of erythroblasts from an otherwise normal bone marrow.

The immune reaction neutralizes the endogenous protein necessary for red blood cell product and the patient needs blood transfusions to address the anemia.
Antibody reactions cannot be predicted via other means (e.g., animal studies), which is why **clinical data are necessary**.

Processes and conditions could influence molecular structures in unexpected ways, leading to an unwanted immunogenic reaction.

**Monitoring patients for an immune reaction to the biologic is important both before and after regulatory approval.**
Approval Process of Biologics
Researchers look for potential new compounds to treat targeted diseases.

Toxicology is tested in animals and living tissue.

During this phase researchers look for:
- a correct dosage level
- appropriate frequency of administration
- the best delivery system (oral, topical, intravenous, etc.)
- short- and long-term survival of animals

Following animal testing, manufacturer files an Investigational New Drug Application (IND) or Clinical Trials Application (CTA) with FDA.
After the approval of the IND/CTA, the experimental drug then moves into Phase I: human testing.

In this phase, the drug is tested in a small number (under 100) of healthy participants.

Researchers look to see how well the drug is tolerated, how it is processed by the human body, and what the correct dosing is.
Approval Process: Phase II
Human Testing

- Once determined to be tolerated by healthy individuals, the medicine is **tested in** (100-300) **patients** to determine if it actually works.

- Manufacturer conducts dose range finding studies to estimate patient response for dose given to analyze safety/efficacy.
A large-scale study of effectiveness and side effects is conducted, medicine is tested in larger population (1000-3000) patients.

FDA looks at these data to determine safety and efficacy.

Manufacturer tests the biologic medicine’s viability and determines the logistics of scaling up to a large supply.

Following Phase III a **Biologics License Application (BLA)** or **Marketing Authorization** are filed with FDA. These are typically 100,000 pages long and contain animal and human trial results and manufacturing data. Approval typically takes 1-2 years.
Once approved, a biologic medicine is then marketed to the general population.

Short- and long-term side effects are monitored.

This can result in revision of labeling or manufacturing changes.
Approval of Post-Marketing Changes

- Risk to product quality, safety, and efficacy vary based on the nature of the process change.
- Major changes to the process may require additional clinical studies.
Sensitivity of Biologics to Structural Modifications can Result in Immunogenicity
Several modifications will always occur in production of the protein.

Manufacturing conditions can have an impact on the molecule’s structure.
Structural Modification: Aggregation

UNALTERED IgG MOLECULE
(simplified model of desired product)

AGGREGATION

- When two or more protein molecules (monomers) bind together.
- Considered undesirable because small aggregates may cause immunogenic reaction, while larger particulates may cause adverse events on administration.
UNALTERED IgG MOLECULE
(simplified model of desired product)

FRAGMENTATION

- When an intact protein breaks apart due to manufacturing, processing, or handling conditions.
- Fragments can cause immunogenic reaction since part of protein that is normally unexposed when intact is exposed. Incomplete molecule impacts efficacy.
**Structural Modification: Oxidation**

**UNALTERED IgG MOLECULE**
(simplified model of desired product)

**OXIDATION**

- Specific amino acids in the protein molecule can become oxidized.
- Oxidized products may result in loss of efficacy, or aggregation (which in turn may lead to immunogenic reactions, or adverse events upon administration).
Composition of Biologic Medicine: Structural Modification: Deamidation

UNALTERED lgG MOLECULE (simplified model of desired product)

DEAMIDATION

- Protein molecules could lose an amine group (-NH$_3$) due to enzymes or due to manufacturing conditions (such as heat), resulting in a deamidated protein, and reduced efficacy.
Composition of Biologic Medicine: Structural Modification: Glycation

**UNALTERED IgG MOLECULE**
(simplified model of desired product)

**GLYCATON**
- Uncontrolled or random addition of sugars (e.g., glucose or fructose) to a protein.
- Can cause aggregation (which in turn may lead to immunogenic reactions, or adverse events upon administration) or reduced efficacy.
Many different types of sugars get linked to a protein during glycosylation, a common post-translational modification to improve therapeutic efficacy.

Even minor changes in these structures can have major impact on safety and efficacy.

On occasions, some sugars not natural to humans (e.g., galactose-alpha,1, 3 galactose) that can be found in therapeutic proteins have been reported to cause anaphylaxis.
These modifications (see list below) can occur at multiple sites on protein, for example this IgG molecule has 9600 possible variations. **Unlike a chemical drug, a biologic medicine will contain many of these variations.**

- Pyro-Glu (2)
- Deamidation (3 x 2)
- Methionine oxidation (2 x 2)
- Glycation (2 x 2)
- High mannose G0, G1, G1, G2 (5)
- Sialylation (5)
- C-term Lys (2)

\[(9600)^2 \approx 10^8\]

\[2 \times 6 \times 4 \times 4 \times 5 \times 5 \times 2 = 9600\]
While chemical medicines are relatively stable, biologics can undergo many modifications during storage, and their composition (which of the molecule’s variations are present) will change over time.
Complete Characterization is Impossible

- The complexity and sensitivity of biologics, their heterogenous nature, and their propensity to change over time, make characterization to the last atom impossible with current scientific knowledge and tools.

- To learn more about characterization of biologics, please consult *International Journal of Pharmaceuticals, 2003, November, 266, 3-16*
Degradation During Storage, Handling, and Preparation of Biologic Medicines
Contributing Factors to Degradation During Storage and Handling of Biologics

- Temperature Change
- Dilution
- Filtration
- Shaking
- Adsorption
- Shearing Forces
- Leaching
- Oxygen Exposure
- Metal Exposure
- Silicon Exposure
Potential for Degradation During Preparation

- **TEMPERATURE CHANGE:**
  Removing product from refrigeration can cause aggregation, precipitation.

- **ADDING DILUTENT:**
  Introduction of metal ions, silicon, oxygen can result in oxidation, catalysis, aggregation.

- **RECONSTITUTING:**
  Shaking, interaction with container, shearing forces can result in denaturing, unfolding, aggregation, hydrolysis, deamination.

- **INTRODUCTION TO INFUSION BAG:**
  Absorption, exposure to oxygen, silicon, and metal ions, leaching, shearing forces, etc., can result in denaturing, unfolding, aggregation, hydrolysis, deamination.
Minimizing Degradation of Biologics

- Avoid rapid temperature change- increase temperature gradually.
- Avoid multiple temperature cycles.
- Avoid excess force (shaking, shearing forces).
- Be aware of device composition (needle gauge, potential for contamination).
- Consult manufacturer stability data.
Biosimilars: How Close is “Close Enough”?
Biosimilars cannot be, and thus are not expected to be, direct copies of originator (also known as “reference”) biologics.

FDA defines a biosimilar as “a biological product that is highly similar to the reference product notwithstanding minor differences in clinically inactive components.”

Minor differences are expected and permitted but must be demonstrated not to be “clinically meaningful” in regards to safety, purity, or potency.
GenZyme, a biologic manufacturer made a manufacturing process change when scaling up production of its FDA-approved biologic.

Even though made from the same cell line, the resulting molecule was different enough that new clinical trials were required and a new International Nonproprietary Name (INN) was assigned to it- which was in effect a new product- a biosimilar to its reference molecule.
The U.S. is still in the process of developing its Biosimilar Approval Pathway.

Existing and upcoming FDA Guidance on biosimilar approval will be discussed in more detail later today.
Biosimilar Naming
Biosimilar 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 Assigned 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**.

- **Distinguishable naming** allows an accurate, unambiguous patient record, and correct attribution of adverse events to the precise product, not a general category of similar medicines.
Pharmacists and Distinguishable Naming

- Pharmacists have traditionally avoided look-alike, sound-alike drug names.
- Even if a drug is considered similar, it should be easily identified.
- Industry has been asked in the past to change drug names to avoid confusion and errors.

SOME SUGGESTED WAYS OF DISTINGUISHING BIOSIMILARS:

- Unique USAN?
- Same USAN + Suffix?
- Same USAN + NDC Code
- Prefix + Same USAN?
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.

“...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.
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, 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.

“...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.
ASBM 2012 Survey of 376 U.S. physicians who prescribe biologics showed that NDC codes were **not used by physicians to identify in patient record** (0.5%).

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**.
The WHO has proposed adding a unique, random 4-letter code called a Biological Qualifier (BQ) to the INN of all biologics, including biosimilars, to differentiate them.

Adherence to the BQ System is voluntary. A similar system is already in place in Japan. FDA has not yet weighed in.

ASBM chairman Dr. Harry Gewanter and I will be presenting our perspectives at a meeting of the WHO’s Consultation on International Nonproprietary Names later this year.

Dr. Gewanter will discuss in more detail ASBM’s work with the WHO in developing international naming standards.
Thank You
For Your Attention