Biosimilars: The Impact on Academic Pharmacy

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Learning Objectives

- Review the accreditation standards and licensure requirements for doctor of pharmacy graduates.
- Discuss important educational challenges for professional and post-graduate education related to biosimilars and potential impact on patients.
- Understand the issues surrounding proposed processes for FDA regulatory approval of biosimilars.

Application for Approval New Drug

- Submit NDA or BLA
  - NDA (New Drug Application) for drug with chemically synthesized active pharmaceutical ingredient (API)
  - BLA (Biologics License Applications) for drug manufactured using biological systems
- ANDA (Abbreviated New Drug Application) is an application for a U.S. generic drug approval for an existing licensed medication or approved drug.

Requirements for a Generic Drug

- Same active ingredient(s)
- Same route of administration
- Same dosage form
- Same strength
- Same conditions of use

Compared to reference listed drug (RLD) - (brand name product)

Hatch-Waxman Amendments to FFD&C Act - 1984

- Created the generic drug industry
- Increased availability of generics
  - 1984 12% generic
  - 2000 44% generic
  - 2010 75% generic
  - 2012 80% generic
- Biologics Price Competition and Innovation Act (BPCI) of 2009
- Increased availability of biosimilars……

Top 10 Products by Sales

Rank 2008	Rank 2014
1 atorvastatin	**bevacizumab**
2 clopidogrel	**adalimumab**
3 fluticasone/salmeterol	**rituximab**
4 **etanercept**	**etanercept**
5 valsartan	**insulin glargine**
6 **rituximab**	**trastuzumab**
7 **infliximab**	rosuvastatin
8 esomeprazole	tiotropium
9 **epoetin alfa**	**infliximab**
10 **bevacizumab**	imatinib

40% of new products in the pipeline are specialty pharmaceuticals

Adapted from: Noonan K. Future Drug Sales Predictions Highlight Importance of Follow-on Biologics Legislation. Patent Docs 2009

Biologics Price Competition and Innovation Act (BPCI) of 2009

- The BPCI Act was enacted as part of the Affordable Care Act on March 23, 2010. The BPCI Act creates an abbreviated licensure pathway for biological products demonstrated to be biosimilar to, or interchangeable with, a reference product.
- The BPCI Act, sets forth the requirements for an application for a proposed biosimilar product and an application or a supplement for a proposed interchangeable product.
- PHS Act defines *biosimilarity* to mean "that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components" and that "there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. The BPCI Act also amended the definition of biological product to include "protein".

What Are Biologics?

- Drugs manufactured from living cells or micro-organisms by biotechnology methods
- Biologics replicate the natural enzymes, antibodies, or hormones found in our bodies
- Classes of biologics include: Hormones, Vaccines, recombinant DNA proteins (rDNA), Monoclonal antibodies (MAb), Immunomodulators, Enzymes
- Properties:
  - Large, complex molecules
  - Stability issues
  - Injectables (SC, IV)
  - Risk of immunogenicity

In 2012, Americans spent $325.8 billion on prescriptions (~$60 billion was on biologics)

Demonstrating Biosimilarity

- To obtain licensure of a proposed product under section 351(k) of the PHS Act, a sponsor must demonstrate that the proposed product is biosimilar to a single reference product that previously has been licensed by FDA.

- To demonstrate biosimilarity, a sponsor must provide sufficient data and information to show that the proposed product and the reference product are highly similar notwithstanding minor differences in clinically inactive components and that there are no clinically meaningful differences between the two products in terms of safety, purity, and potency. Evidence may include:
  - **Structural Analysis,**
  - **Functional Assays,**
  - **Animal Data,**
  - **Clinical Studies**

Key Points to Biosimilars

- Biosimilars are unique products and not generic versions of innovator biologics
- Biosimilars cannot be substituted for brand name biologics with without prescriber approval
- Currently, no approval pathway in the United States for the regulation of biosimilars
  - Europe has an advanced framework in place
- Development and approval of biosimilars are associated with more costs time comparability issues and costs, time, issues, regulatory hurdles than that of small molecule generics
- Differences in protein glycosylation can result in immunogenicity, a significant concern for biosimilars

Vision for Pharmacy Practice (2015) *

Pharmacists will be the health care professionals responsible for providing patient care that ensures optimal medication therapy outcomes.

Optimize Medication Therapy

Manage Health Resources

Promote Wellness

Pharmaceutical Education Outcomes **

Pharmacy Graduate in the US should be capable of:

Pharmaceutical Care

Provide patient-centered as well as population-based care

Systems Management

Manage human, physical, medical, informational, medication use systems and technological resources

Public Health

Assure the availability of effective health and disease prevention services and policy

* Joint Commission of Pharmacy Practitioners; [November 2004]

** AACP Center for the Advancement of Pharmaceutical Education (CAPE) [adopted 2004]

Center for the Advancement of Pharmacy Education (CAPE) 2013 Educational Outcomes

Four broad domains to guide the academy in educating pharmacists who possess:

1) foundational knowledge that is integrated throughout pharmacy curricula;

2) essentials for practicing pharmacy and delivering patient-centered care;

3) effective approaches to practice and care; and

4) the ability to develop personally and professionally.

ACPE Standards & Guidelines

Immunology

- human immunity and immune response
- principles of antigen-antibody relationships
- molecular biology of immune response
- genetic basis for antibody synthesis, development, function, and immunopathology

Molecular Biology/Genetics

- cell structure and components
- ion channels and receptor physiology
- mitosis and meiosis
- chromosomes and DNA
- gene transcription and translation processes
- recombinant DNA technology

ACPE Standards & Guidelines

Pharmacogenomics/genetics

- genetic basis for disease and drug action
- genetic basis for alteration of drug metabolism
- genome and proteomic principles in relation to disease and drug development
- genetic basis for individualizing drug doses

Pharmacist-Provided Care for Special Populations

- pathophysiologic and pharmacotherapy alterations specific for special population patients for prescription & nonprescription meds
- dosage calculation and adjustments in special-population patients
- drug monitoring for positive/negative outcomes in special-population patients

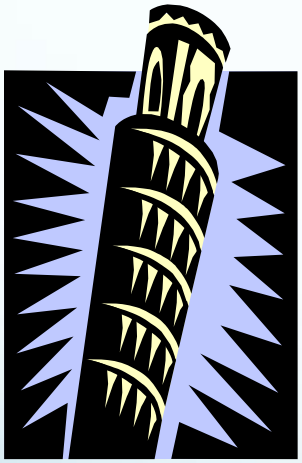
Instruction-Centered Paradigm

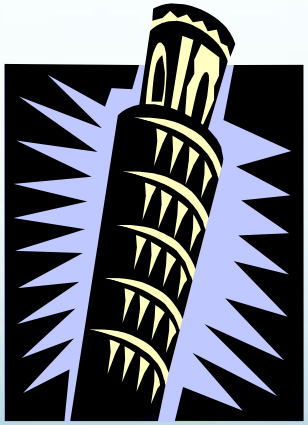
"Academic Silo Mentality"

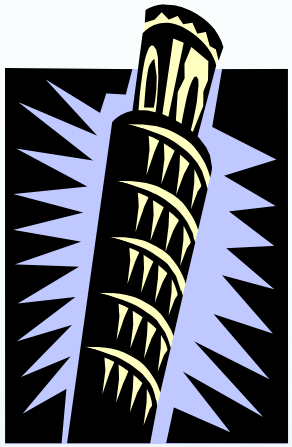
Pharmacology

Basic Sciences

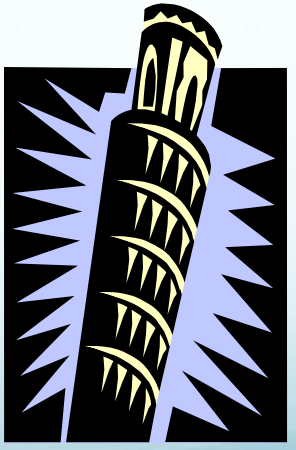
Pharmacotherapeutics

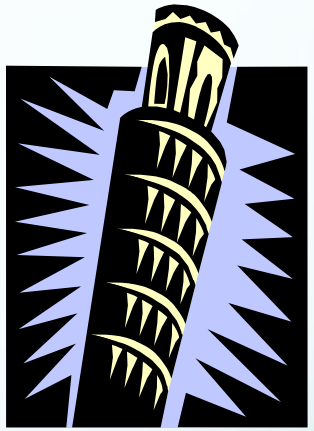






Pharmaceutics

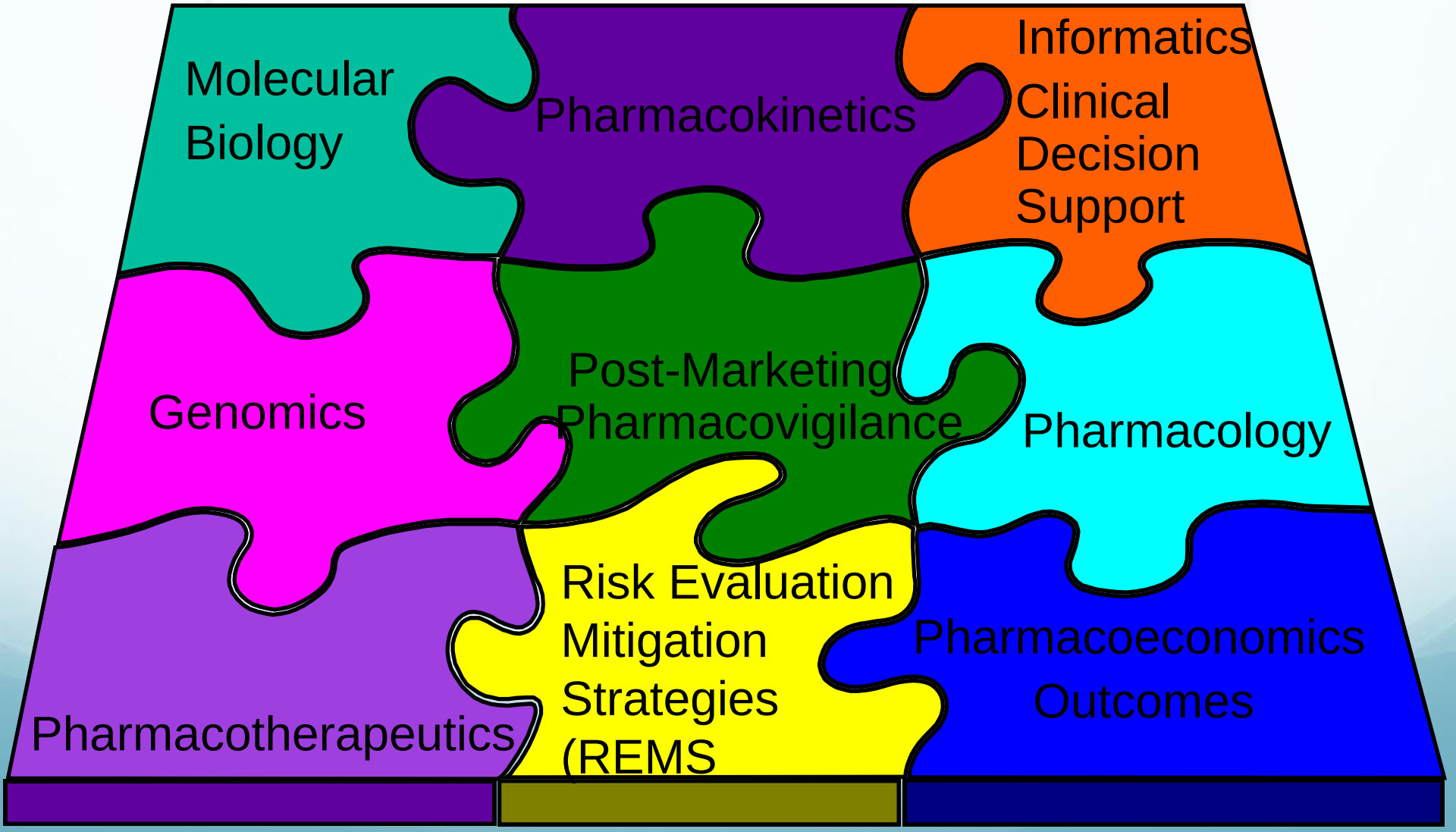




Medicinal Chemistry

Pharmacy Administration

Integration of Academic Disciplines Around Biologics



Health Professions Education: A Bridge to Quality

All Health Professionals Should be able to:

- Deliver patient-centered care
- Work in interdisciplinary teams
- Employ evidence-based practice
- Apply quality improvement approaches
- Utilize informatics

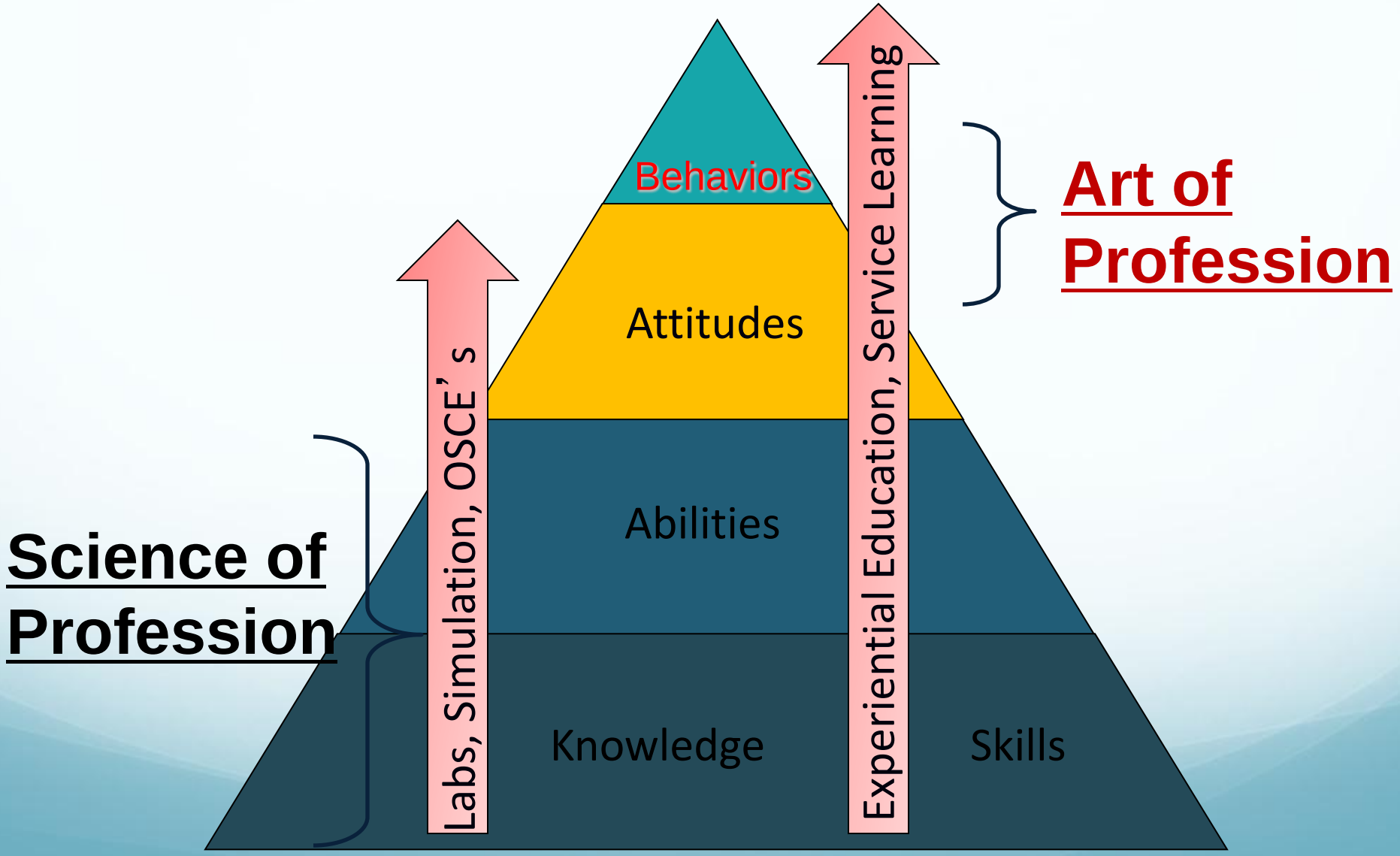
Health Professions Education: A Bridge to Quality (2003) Institute of Medicine (IOM). National Academy of Sciences. www.nap.edu/openbook,

Approaches Learning

- Various Pedagogical Approaches
  - Self-Directed Learning
  - Group-Based/Active Learning
  - Problem-Based Learning (PBL)
  - Distance Education
- Workshops/Laboratory
  - Case-Based, Hands-on Experiences
  - Objective Structured Clinical Examinations (OSCE's)

- Use of Technology
  - Web-based, Podcasts
  - Computer Assisted Instruction
  - Synchronous and Asynchronous modes
- Process of Formative and Summative Feedback
  - "Minute Papers"
  - "Milestone Assessments"
  - "High Stakes" Exams

Taxonomy of Education



Academic Technologies and Online Learning

Teaching >> Learning >> Assessment @ RU_COP

On-line (Synchronous, Asynchronous)

Step 1 Construction

Step 2a Implementation: **ON-Campus Synchronous**

Step 2b Implementation: **OFF-Campus Asynchronous**

Step 3 Post-Evaluation by Students

Step 4 Post-Evaluation by Faculty

Step 5 Validation

Follow Standard Operating Procedures

On-line Moodle/Respondus, Others)

Test Item Analysis, Student Input

Debrief and Review of Results

NAPLEX Blueprint

The NAPLEX Competency Statements

- Area 1 Assess Pharmacotherapy to Assure Safe and Effective Therapeutic Outcomes (56% of Test)
- Area 2 Assess Safe and Accurate Preparation and Dispensing of Medications (33% of Test)
- Area 3 Assess, Recommend, and Provide Health care Information that Promotes Public Health (11% of Test)

Tips for Navigating Forward

- Avoid the NIH mentality
- Look to partner and collaborate with other COP/SOPs, Health Sciences, and others
  - Consortia approach to course delivery
  - Inter-professional Education
  - Can materials be re-purposed
  - Cross-Appointments
- Monitor regulatory actions by FDA, others
- Responsibility Center Management
- Be prepared for some set-backs, but continue moving ahead

Guidance for Industry

Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product

DRAFT GUIDA

This guidance document is being distributed

Comments and suggestions regarding this draft documen
publication in the *Federal Register* of the notice announ
guidance. Submit comments to the Division of Dockets
Drug Administration, 5630 Fishers Lane, rm. 1061, Roc
should be identified with the docket number listed in the
the *Federal Register*.

For questions regarding this draft document contact (CD

U.S. Department of Health and
Food and Drug Admini
Center for Drug Evaluation and
Center for Biologics Evaluation an

February 2012
Biosimilarity

Guidance for Industry

Scientific Considerations in Demonstrating Biosimilarity to a Reference Product

Guidance for Industry

Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Sandra Benton at 301-796-2500 or (CBER) Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-1800.

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Self-Assessment Questions

True or False?

1. ACPE Accreditation Standards specifically require the covering of biosimilars in the PharmD curriculum.
2. Biosimilars can essentially be substituted for brand name biologics without prescriber approval in the US.
3. No one discipline is ideally positioned to cover biosimilars and biologics in the PharmD curriculum.