House of Delegates Policy Topic Webinar – Biosimilar Drug Products

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Disclosures

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Learning Objectives

1. Explain the different regulatory types of biological products
2. Describe the differences between biologic products and small molecule drugs.
3. Describe resources available for evaluating biosimilar drug products.
4. Explain barriers to pharmacy when supplying biosimilar drug products.
Which of the following statements is true?

A. All biosimilars are interchangeable with the originator product and with each other like traditional generic drugs
B. The molecular composition of biologic drugs is virtually impossible to fully characterize
C. The manufacturing process for biologics has minimal impact on stability, structure, or immunogenicity of the product
D. A biosimilar is an exact copy of a reference biologic product and is manufactured in an identical manner

Which of the following aspects of a biosimilar product may be different from the reference product?

A. Formulation (e.g., the vehicle)
B. Route of administration
C. Conditions of use (i.e., indications)
D. Strength
According to the U.S. Food and Drug Administration (FDA) draft guidance on biosimilars, which of the following is “fundamental” for demonstrating biosimilarity?

A. Studies evaluating structure and function
B. Human pharmacokinetics and pharmacodynamics studies
C. Clinical safety and effectiveness
D. Postmarketing studies, including pharmacovigilance

State biosimilars legislation typically has addressed all of the following except:

A. Naming of biosimilars
B. Notification of the prescriber and patient
C. Length of recordkeeping
D. Lists of substitutable products
Which of the following statements regarding potential substitution of biosimilars is false?

A. The FDA has created a “Purple Book” to help provide information on interchangeable biosimilar products
B. A number of states have passed legislation addressing the substitution of biosimilar products
C. The ACA created a category of “interchangeable biosimilars” that would be able to be substituted in a manner similar to traditional generic drugs
D. Biologic and biosimilar products are both approved through FDA’s 351(a) pathway

What Is a Biologic (Biopharmaceutical)?

• Technical definition from U.S. Code of Federal Regulations
  • “Any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment or cure of diseases or injuries of man”
• Derived from living sources
  • Various cultures of bacteria or viruses
  • Human or animal sources
• “Therapeutic proteins”

www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfdrf/cfrsearch.cfm?fr=600.3
Differences Between Chemical Drugs and Biologics

<table>
<thead>
<tr>
<th></th>
<th>Chemical Drugs</th>
<th>Biologics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size</strong></td>
<td>Small, low molecular weight</td>
<td>Large, high molecular weight</td>
</tr>
<tr>
<td><strong>Structure</strong></td>
<td>Simple, well-defined</td>
<td>Complex, heterogeneous</td>
</tr>
<tr>
<td><strong>Manufacturing</strong></td>
<td>• Reproducible chemical reactions</td>
<td>• Living cells or organisms</td>
</tr>
<tr>
<td></td>
<td>• Identical copies can be made</td>
<td>• Impossible to ensure identical copies</td>
</tr>
<tr>
<td><strong>Characterization</strong></td>
<td>Completely characterized</td>
<td>Impossible to fully characterize molecular composition</td>
</tr>
<tr>
<td><strong>Stability</strong></td>
<td>Stable</td>
<td>Unstable, sensitive to external conditions</td>
</tr>
<tr>
<td><strong>Immunogenicity</strong></td>
<td>Mostly non-immunogenic</td>
<td>Immunogenic</td>
</tr>
</tbody>
</table>


Relative Size and Complexity of Small Molecule Drugs and Biologics

- **Acetaminophen**: 151 daltons
- **Atorvastatin**: 558 daltons
- **Insulin Glargine**: 6,063 daltons
- **Filgrastim**: 158,880 daltons
- **Rituximab**: 145,000 daltons
- **Coagulation Factor VIII**: 264,400 daltons

DrugBank 4.1. www.drugbank.ca
Manufacturing Process for Biologics

- Cloning into DNA Vector
- Transfer into Host Cell Expression Screening / Selection
- Cell Expansion
- Recovery through Filtration or Centrifugation
- Purification through Chromatography
- Characterization and Stability
- Purified Bulk Drug

Biologics Have Varying Risks of Immunogenicity

- Manufactured in living cells
  - Hamster cells, rabbit cells, bacteria (E. coli), etc.
- The body can detect and attack foreign proteins
- Neutralizing antibodies can be developed by the body
- The more similar a therapeutic protein is to the human protein, the less chance of immunogenicity
- Scientific tools for detecting immunogenicity exist, but they are not precise


Changes in Manufacturing Can Have Real Consequences

- Differences in manufacturing can lead to differences in structure, stability, and impurities as well as excipients
- Changes in the manufacturing of an epoetin alfa resulted in a small change in formulation
  - Decreased protein stability and increased aggregate formation
  - Resulted in cases of pure red cell aplasia
- Excessive host cell protein contamination increased immunogenicity with somatropin
  - Resolved with additional purification


What Is a Biosimilar?

- A biosimilar is a “copy” of a commercially available biologic agent (reference or originator product) that has gone off patent
- A biosimilar is “similar” to the reference product with demonstrated similarity in physicochemical characteristics, efficacy, and safety based on data from analytical studies, animal studies, and clinical study or studies

What Is a Biosimilar?

- Approved via an abbreviated pathway
- Exhibits “highly similar” efficacy and safety compared with reference product
- Interchangeable biosimilar
  - Can switch back and forth between biosimilar and reference with no clinical consequences
  - Appropriate for substitution without consulting the prescriber


Manufacturing Process for Biosimilars

Potential Differences vs Reference

- Primary amino acid sequence
- Modification of amino acids (e.g., glycosylation)
- Higher-order structure
  - Folding
  - Quaternary structure


Biosimilar vs Generic

- A generic is an identical copy of a chemical drug that has gone off patent
- Biosimilars are not generics
  - Biosimilars are not identical to the reference product because of differences in manufacturing processes
- Therefore, an assessment of biosimilarity is much more complex than the assessment of “bioequivalence” for small-molecule generic drugs
Biosimilarity vs Bioequivalence

• **Biosimilarity**¹
  - Unlikely to have “clinically meaningful” differences between biosimilar and reference product
  - Recognizes that the two molecules are, in fact, different, but exert highly similar effects

• **Bioequivalence**²
  - “The absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives become available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study”

• **These terms are not equal**

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General Principles for Demonstrating Biosimilarity

• Biosimilars approved via an abbreviated pathway

• Demonstration of biosimilarity is a comparability exercise and not a therapeutic equivalence study

• The goal of the biosimilarity exercise is to establish that the candidate biosimilar is not significantly different from the reference product and is **unlikely to have any clinically significant differences**
  - Smaller-scale direct comparisons and extrapolation are used

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## Biosimilar vs Reference Product

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Comparison with Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stability</td>
<td>May be different</td>
</tr>
<tr>
<td>Efficacy</td>
<td>Unlikely to have clinically meaningful differences</td>
</tr>
<tr>
<td>Safety</td>
<td>Unlikely to have clinically meaningful differences</td>
</tr>
<tr>
<td>Active ingredient</td>
<td>Not exactly the same</td>
</tr>
<tr>
<td>Manufacturing</td>
<td>Different process</td>
</tr>
<tr>
<td>Immunogenicity</td>
<td>May be different</td>
</tr>
</tbody>
</table>


## FDA Specifications for Biosimilars

<table>
<thead>
<tr>
<th>Biosimilar Product Specification</th>
<th>Comparison with Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formulation</td>
<td>May be different</td>
</tr>
<tr>
<td>Delivery device/container</td>
<td>May be different</td>
</tr>
<tr>
<td>Routes of administration</td>
<td>May obtain licensure for fewer than all routes of administration for which reference product is licensed</td>
</tr>
<tr>
<td>Indications for use</td>
<td>May obtain licensure for fewer than all conditions of use for which reference product is licensed</td>
</tr>
<tr>
<td>Strength</td>
<td>Must be the same</td>
</tr>
</tbody>
</table>

### Projected U.S. Patent Expirations for Major Biologics

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Potential Biosimilar Entry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filgrastim</td>
<td>Neupogen</td>
<td>2014</td>
</tr>
<tr>
<td>Epoetin alfa</td>
<td>Epogen/Procrit</td>
<td>2014</td>
</tr>
<tr>
<td>Insulin glargine</td>
<td>Lantus</td>
<td>2015</td>
</tr>
<tr>
<td>Pegfilgrastim</td>
<td>Neulasta</td>
<td>2015</td>
</tr>
<tr>
<td>Palivizumab</td>
<td>Synagis</td>
<td>2015</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Rituxan</td>
<td>2016</td>
</tr>
<tr>
<td>Cetuximab</td>
<td>Erbitux</td>
<td>2016</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>Humira</td>
<td>2016</td>
</tr>
<tr>
<td>Infliximab</td>
<td>Remicade</td>
<td>2018</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>Herceptin</td>
<td>2019</td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>Avastin</td>
<td>2019</td>
</tr>
<tr>
<td>Darbepoetin alfa</td>
<td>Aranesp</td>
<td>2024</td>
</tr>
<tr>
<td>Etanercept</td>
<td>Enbrel</td>
<td>2028</td>
</tr>
</tbody>
</table>


### Demonstrating Biosimilarity: Things to Keep in Mind

- The clinical efficacy and safety of the biologic molecule has already been demonstrated (i.e., by the innovator)
- The biosimilar sponsor only requires evidence that the candidate biosimilar is not significantly different from the reference product
  - Goal is not to replicate unnecessary clinical trials
  - Smaller-scale direct comparisons and extrapolation
- When a biosimilar is approved, there should not be an expectation that there will be differences in safety and efficacy

FDA. Guidance for industry: scientific considerations in demonstrating biosimilarity to a reference product. April 2015.  
Biosimilar Development Approach

Develop highly similar biologic

Test and confirm biosimilarity

FDA Approval

Postmarketing monitoring

Test and confirm interchangeability

- Analytical methods for structure/function
- Cell lines
- In vitro/vivo models
- Substance pilot and final scale
- Formulation and final drug product
- Human clinical trials
- Consideration of clinically sensitive endpoints
- Clinically sensitive patient population
- Immunogenicity
- Efficacy and safety

- EU Guidance and risk management plans
- FDA consultation of proposed approach
- May be mandatory

Varying Regulatory Types

<table>
<thead>
<tr>
<th></th>
<th>351(a) Originator</th>
<th>351(h) Biosimilar</th>
<th>351(k) Interchangeable Biosimilar</th>
<th>351(a) Non-originator biologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>First-to-market biologic molecule; will likely be the reference product</td>
<td>“Highly similar” to reference product; approved via Biosimilars pathway</td>
<td>A biosimilar that meets additional standards so that it can be substituted for the reference without permission from prescriber</td>
<td>It is “another brand name” of an already approved biologic</td>
</tr>
<tr>
<td>Depth of data submitted to the FDA</td>
<td>“Standard” data package of efficacy and safety</td>
<td>Abbreviated data package for comparability</td>
<td>Abbreviated data package for comparability; more information on switching</td>
<td>“Standard” data package of efficacy and safety</td>
</tr>
<tr>
<td>Compared to originator?</td>
<td>N/A</td>
<td>Yes</td>
<td>Yes</td>
<td>Not necessary (yes or no)</td>
</tr>
<tr>
<td>Implications</td>
<td>Biosimilar pricing; explicit regulatory oversight on comparison with reference; possible pharmacist substitution (for interchangeable biosimilars)</td>
<td>Different pricing structure and substitution issues</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Approval Processes

Demonstrating Biosimilarity: A Stepwise Approach

- Compare proposed biosimilar to reference in terms of:
  1. **Structure**
  2. **Function**
  3. **Animal Toxicity Studies**
  4. **Human Pharmacokinetics (PK) and Pharmacodynamics (PD)**
  5. **Clinical Immunogenicity**
  6. **Clinical Safety and Effectiveness**

- FDA intends to utilize a “totality of the evidence” approach

Biosimilar and Biologic Development

Structure and Function

- Serve as the “foundation” of biosimilar development
- Useful in determining future studies that are necessary
- Structure
  - Amino acid sequence, higher-order structures, glycosylation, pegylation, etc.
  - Analyze lot-to-lot variability
- Function
  - Evaluate pharmacologic activity via *in vitro* or *in vivo* experiments
  - Functional evaluation that compares candidate to reference

Four Assessments of Analytical Characterization

Studies of Structure and Function: Residual Uncertainty

- High
  - Not similar
  - No further development through 351(k)

- Similar
  - Additional information needed: analytical, comparative PK/PD, etc.

- Highly similar
  - High confidence; appropriate for targeted clinical studies

- Highly similar with fingerprint-like similarity
  - Very high confidence; appropriate for more targeted clinical studies

Human Pharmacokinetics and Pharmacodynamics

- “Fundamental” for demonstrating biosimilarity
- Both PK and PD will be necessary
  - PK: patient population considerations
  - PD should study measures that:
    - Are relevant to clinical outcomes
    - Can be quickly assessed with precision
    - Have the sensitivity to detect clinically meaningful difference
- Ideally correlate exposure to clinical outcomes
- Utilize crossover and parallel designs

PK=pharmacokinetics; PD=pharmacodynamics

Clinical Studies

• Clinical immunogenicity
  • Goal is to evaluate potential differences in incidence and severity of immune responses using endpoints such as antibody formation (binding, neutralizing), cytokine levels, etc.
  • FDA recommends a comparative parallel study

• Efficacy and safety: specific clinical trial design will depend on what residual questions remain
  • Clinical studies should be designed to demonstrate neither decreased nor increased activity
  • Use clinically relevant and sensitive endpoints in the right population
  • Biosimilar sponsor to justify comparability delta


Clinical Trial Design: Equivalence

• Establish the equivalence margin (δ) via the 95-95 method
• 95% CI should fall between -δ and +δ for equivalence

• However, non-inferiority studies may be appropriate if it is well-established that the biologic saturates the receptors at the clinical dose

Biosimilar Products: Summary

- A comprehensive comparability exercise is conducted for biosimilar products in preparation for regulatory approval
  - Physiochemical characterization is foundational to the data package
  - Efficacy and safety studies assess equivalence to the reference product
- Insulins present a challenge in the United States because they are approved via the new drug application (NDA) pathway

Biosimilar Development Approach

Postmarket Monitoring: EU Risk Management Plans

- "Comprehensive and proactive application of scientifically based methodologies to identify, assess, communicate, and mitigate risk throughout a drug's life cycle so as to establish and maintain a favorable benefit-risk profile"
- Mandatory for biologics (immune reactions)
- Four steps for a particular risk:

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
<th>Risk Management Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Detection</td>
<td>Identify risk</td>
<td>Pharmacovigilance</td>
</tr>
<tr>
<td>2. Assessment</td>
<td>Understand/monitor risk</td>
<td></td>
</tr>
<tr>
<td>3. Communication</td>
<td>HCP education</td>
<td>Risk minimization</td>
</tr>
<tr>
<td>4. Minimization</td>
<td>Act to reduce risk</td>
<td></td>
</tr>
</tbody>
</table>


FDA Guidance: Postmarketing Monitoring for Safety

- Important to assure safety for all biologics
  - Consider risks seen in reference
  - Are there any new safety concerns?
  - Population-based assessments gives larger N to identify rare safety concerns
  - Might be mandatory for some products
- Biosimilar manufacturers should work with FDA early to discuss approach
- Current pharmacovigilance guidance by FDA

FDA. Guidance for industry. February 2012.
Pharmacovigilance Challenges: Enoxaparin Case Study in the United States

- Commercial claims data analysis of patients receiving prescriptions for enoxaparin
  - No statistical difference between branded vs generic with incidence of HIT (1.2% vs 1.5%, $P<0.0001$)
  - Increasing market share of generic products after loss of exclusivity in 2010 (to about 44% in 2012)

Enoxaparin thrombocytopenia reports by sponsor: FDA AERS Analysis


Pharmacovigilance: Challenges in the United States

- Health care providers need to correctly attribute the safety signal
- How?
  - Traceability and attribution
    - Naming
    - Codes: NDC vs HCPCS
  - Data
    - Prospective registries
    - Administrative claims
    - Electronic health record
    - Linked databases
    - Spontaneous adverse event reporting
Interchangeability

- Safety standards for determining interchangeability
  - Must be a biosimilar
  - Produces same clinical result as the reference in any given patient
  - Risk of safety or diminished efficacy due to alternating or switching between biosimilar and reference is no more than using the reference product with no switching
  - Will be “difficult” in the initial 351(k) application due to the sequential nature of the assessment
  - Appropriate to be “substituted for the reference product without the intervention of the health care provider who prescribed the reference product”

Public Health Service Act, section 351(k)(4).
www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/ucm216146.pdf

Interchangeability Study Design

- FDA interchangeability criteria: switch between reference (R) and biosimilar (B) with no clinical consequences
  - What is switching?
    - R → B
    - B → R
    - R → R
    - B → B
  - Various designs proposed
    - Standard two-sequence, two-period crossover
    - Balaam’s 4 x 2 crossover design

Key Points thus far...

- There is a robust regulatory pathway for the approval of biosimilar agents in the United States
- A biosimilar’s analytical characterization serves as the foundation for further studies
- Interchangeability and pharmacovigilance are important but unresolved issues in the United States

Issues and Considerations: Premise Statements

Biosimilars are not generics
- Different regulatory pathway vs generics
- Different data submitted to FDA to establish efficacy and safety vs originators

Product and data differences create operational and clinical challenges
### Operational Challenges

<table>
<thead>
<tr>
<th>Domain</th>
<th>Elements</th>
<th>Institutional Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Formulary analysis</strong></td>
<td>• Product approval pathway and data package</td>
<td>• Institution's use results in poor clinical outcomes</td>
</tr>
<tr>
<td></td>
<td>• Appropriate indications (on-label and off-label) for use</td>
<td>• Over-burdensome policies</td>
</tr>
<tr>
<td></td>
<td>• Extrapolation considerations</td>
<td>• Poor considerations of transitions of care lead to logistical problems</td>
</tr>
<tr>
<td></td>
<td>• Therapeutic interchange +/- guided use policies</td>
<td>• Off-policy requests (time waste)</td>
</tr>
<tr>
<td></td>
<td>• Transitions of care</td>
<td></td>
</tr>
</tbody>
</table>
Pharmacist Substitution

- State law gives pharmacists the authority to act independently of the prescriber to dispense the lowest-cost, equivalent medicinal product

Framework
- Product criteria
  - Orange book (ANDA generics)
  - Purple book (351(k) biosimilars)
- DAW
- Communication with prescriber/patient
- Record keeping
- Hospital/health system exemption


Biosimilar Legislation by State

Legislation on Biologics and Biosimilar Substitution, 2013-2015

16 states enacted statutes
- 3 states passed but vetoed
- 7 states did not pass
- 4 pending


(c) 2015 NCSL - Updated 9/1/2015
Sample of Enacted Biosimilar Substitution Laws

<table>
<thead>
<tr>
<th>State</th>
<th>DAW</th>
<th>Product’s criteria for substitution/interchange</th>
<th>Prescriber/patient communication</th>
<th>Record Keeping</th>
</tr>
</thead>
<tbody>
<tr>
<td>DE</td>
<td>Yes</td>
<td>FDA designated interchangeable or therapeutic equivalent</td>
<td>Inform patient; inform prescriber in 10 days</td>
<td>Same as generic law</td>
</tr>
<tr>
<td>FL</td>
<td>Yes</td>
<td>FDA determined interchangeable</td>
<td>Inform patient same as generic; EMR notification for institutions</td>
<td>2 years</td>
</tr>
<tr>
<td>VA</td>
<td>Yes</td>
<td>FDA determined interchangeable</td>
<td>Inform patient of cost; inform prescriber within 5 days</td>
<td>2 years</td>
</tr>
<tr>
<td>MA</td>
<td>Yes</td>
<td>FDA determined interchangeable</td>
<td>Inform patient and prescriber (no timeline)</td>
<td>1 year</td>
</tr>
</tbody>
</table>

http://delcode.delaware.gov/title24/c025/sc06/index.shtml
http://www.flsenate.gov/Session/Bill/2013/0365/BillText/ex/PDF
https://leg1.state.va.us/cgi-bin/legp504.exe?131+ful+CHAP0412

Pharmacy Practice Implications

- Generic substitution may not be appropriate for biosimilars, but therapeutic equivalence programs are likely within health systems
- Pharmacists will need to lead evaluation of biosimilars for formulary inclusion
  - Range of indications
  - Therapeutic equivalence
  - Process for therapeutic interchange within health systems
  - Information systems to enable pharmacovigilance
Clinical Issues and the Desired Use of the Biosimilar

“Appropriate” indications

Reference biologic labeled indications

Biosimilar labeled indications

Desired use within institution

P&T determination
Must incorporate patient, disease and endpoint factors with biosimilarity data

Considerations for Formulary Selection of Biosimilars

<table>
<thead>
<tr>
<th>Efficacy/Safety</th>
<th>Manufacturer Considerations</th>
<th>Product Considerations</th>
<th>Hospital and Patient Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Clinical data</td>
<td>• Supply reliability</td>
<td>• Product packaging and labeling</td>
<td></td>
</tr>
<tr>
<td>• Range of indications</td>
<td>• History of drug shortages</td>
<td>• Bedside bar coding</td>
<td></td>
</tr>
<tr>
<td>• Immunogenicity concerns</td>
<td>• Supply chain security</td>
<td>• Compatibility with CSTDs*, robotics</td>
<td></td>
</tr>
<tr>
<td>• Potential for therapeutic interchange</td>
<td>• Anti-counterfeit measures</td>
<td>• Product preparation and administration</td>
<td></td>
</tr>
<tr>
<td>• Number of similar agents on formulary</td>
<td>• Patient assistance programs</td>
<td>• Storage requirements</td>
<td></td>
</tr>
<tr>
<td>• Pharmaco-vigilance requirements</td>
<td>• Reimbursement support</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CSTDs = closed-system transfer devices

Major Challenges for P&T Committees With Biosimilars

• Indication extrapolation by the P&T Committee
• Product naming and impact on ordering, errors, traceability, and pharmacovigilance
• Evaluation of overall economic impact of use of biosimilars
  • Combined inpatient and outpatient impact
  • Challenges of portfolio pricing
  • Impact on patient out-of-pocket expense
• How many “similar” products to carry on the formulary
• How to manage transitions of care
  • Desire to minimize switching
    • Reduced chance for error
    • Avoid potential immunogenicity problems
  • Analogy with generic immunosuppressants in transplant recipients?

Recommendations to Pharmacists for Biosimilars

• Utilize existing formulary system and processes to evaluate for formulary inclusion
• Carefully consider scope of indications for use
• Conduct sophisticated economic analysis, considering costs, reimbursement, and patient impact
• Plan for therapeutic equivalence and guided-use policy and processes
• Consider processes for transitions of care
• Prepare information technology (IT) systems to facilitate effective pharmacovigilance programs
• Meet educational needs of patients and providers
Current Resources for Pharmacists

- FDA’s “purple book”
- Biosimilars Draft Guidance Documents
- State specific legislation or regulation
- Biosimilars Proposed Rule

Conclusion

- Biosimilars present significant opportunities and challenges for pharmacists managing formularies and providing patient care
- A framework for biosimilar introduction is being defined in the United States
- Pharmacists must educate themselves to be prepared to play leadership roles in the safe and appropriate introduction of biosimilars
- Integration of biosimilar agents into clinical practice present many operational and clinical challenges
- Key issues yet to be determined include interchangeability, pharmacovigilance requirements, naming, and traceability
- Pharmacists should take leadership in planning a strategy for successful operational/clinical use of these agents
- Transitions of care and medication reconciliation will be ongoing practice management issues
Which of the following statements is true?

A. All biosimilars are interchangeable with the originator product and with each other like traditional generic drugs
B. The molecular composition of biologic drugs is virtually impossible to fully characterize
C. The manufacturing process for biologics has minimal impact on stability, structure, or immunogenicity of the product
D. A biosimilar is an exact copy of a reference biologic product and is manufactured in an identical manner

Which of the following aspects of a biosimilar product may be different from the reference product?

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B. Route of administration
C. Conditions of use (i.e., indications)
D. Strength
According to the U.S. Food and Drug Administration (FDA) draft guidance on biosimilars, which of the following is “fundamental” for demonstrating biosimilarity?

A. Studies evaluating structure and function
B. Human pharmacokinetics and pharmacodynamics studies
C. Clinical safety and effectiveness
D. Postmarketing studies, including pharmacovigilance

State biosimilars legislation typically has addressed all of the following except:

A. Naming of biosimilars
B. Notification of the prescriber and patient
C. Length of recordkeeping
D. Lists of substitutable products
Which of the following statements regarding potential substitution of biosimilars is false?

A. The FDA has created a “Purple Book” to help provide information on interchangeable biosimilar products
B. A number of states have passed legislation addressing the substitution of biosimilar products
C. The ACA created a category of “interchangeable biosimilars” that would be able to be substituted in a manner similar to traditional generic drugs
D. Biologic and biosimilar products are both approved through FDA’s 351(a) pathway