

Biosimilars and the PPACA: Clinical Considerations and Educational Needs



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*Christopher J. Topoleski
Director, Federal Regulatory Affairs
American Society of Health-System Pharmacists*



American Society of
Health-System Pharmacists®

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Disclosure Statement

I do not have any conflicts of interest to disclose.

Learning Objectives

- **Define unresolved issues related to biosimilars, the potential impact on pharmacy practice, and proposed solutions.**
- **Identify areas that pharmacists and other clinicians should consider when determining how biosimilars will be used within a health system.**
- **Describe educational needs of clinicians and patients related to the use of biosimilars.**

Key Issues for ASHP Members

- Promote research on safety, efficacy, and interchangeability
- Support legislative and regulatory pathway
- Require post-marketing surveillance
- Advocate for adequate reimbursement
- Promote pharmacist education on appropriate use in hospitals and health-systems
- Encourage pharmacist evaluation and application of formulary system

ASHP Policy 0906: Approval of Follow-on Biological Medications

To encourage the development of safe and effective follow-on biological medications in order to make such medications more affordable and accessible; further,

To encourage research on the safety, effectiveness, and interchangeability of follow-on biological medications; further,

To support legislation and regulation to allow Food and Drug Administration approval of follow-on biological medications; further,

To require postmarketing surveillance for all follow-on biological medications to ensure their continued safety, effectiveness, purity, quality, identity, and strength; further,



ASHP Policy 0906: Approval of Follow-on Biological Medications

(cont'd)

To advocate for adequate reimbursement for biological medications that are deemed interchangeable; further,

To promote education of pharmacists about follow-on biological medications and their appropriate use within hospitals and health systems; further,

To encourage pharmacist evaluation and the application of the formulary system before follow-on biological medications are used in hospitals and health systems.



ASHP Activities

- **Response to Energy and Commerce Subcommittee on Health questions: 2008**
 - ❖ Science and safety
 - ❖ Interchangeability
- **January 2011: Letter to Docket No. FDA-2010-N-0477: Approval Pathway for Biosimilar and Interchangeable Biological Products**
 - ❖ Biosimilarity as pre-requisite to interchangeability
 - ❖ Evaluation of immunogenicity
 - ❖ Impact of current REMS program on biosimilars
- **Comment on FDA guidances issued in February 2012**

Biosimilar Legislative Pathway

- **Amends Section 351 of the PHS Act to allow for the licensure of biosimilar and interchangeable products**
- **Requires a biosimilar applicant to show that there are no clinically meaningful differences in safety, purity, and potency between the biosimilar product and the U.S.-licensed reference product. This requires:**
 - ❖ **Analytical data**
 - ❖ **Animal testing data (including toxicity data)**
 - ❖ **Clinical study data (including immunogenicity and PK or PD)**
- **The requirement for animal or clinical studies may be waived by the Secretary if deemed unnecessary**

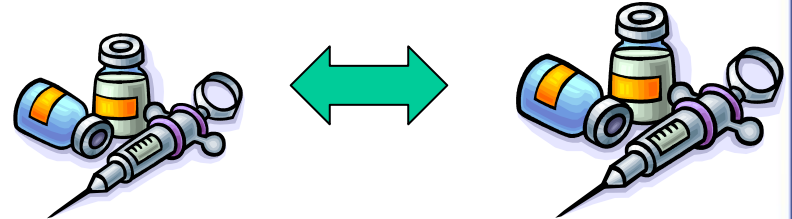
Biosimilar Regulatory Pathway

- Applications for licensure of the biosimilar product will be reviewed by the FDA division that was responsible for the review and approval of the innovator product
- Risk Evaluation and Mitigation Strategies (REMS)
 - ❖ REMS apply equally to biosimilar products as to biological products licensed as innovators.

Draft Guidance on Interchangeability

- An interchangeable product must be shown to be biosimilar to the reference product and meet the other standards described in section 351(k)(4) of the PHS Act
- At this time, it would be difficult as a scientific matter for a prospective biosimilar applicant to establish interchangeability in an original 351(k) application given the statutory standard for interchangeability and the sequential nature of that assessment
- FDA is continuing to consider the type of information sufficient to enable FDA to determine that a biological product is interchangeable with the reference product

Interchangeability



- **Biological product may be considered interchangeable with the reference product if it is biosimilar to the reference product and can be expected to produce the same clinical result in any given patient.**
- **For a product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and reference product is not greater than the use of the reference product by itself.**

Interchangeability Matters

- A biological product that is biosimilar to a reference product but has not been determined to be interchangeable shall be considered as a new active ingredient.
 - ❖ Direct substitution can NOT occur
- A biological product that is interchangeable with a reference product shall not be considered to have a new active ingredient.
 - Substitution can occur as defined under state practice acts

Drugs: Therapeutic Equivalents

- Drug products are considered to be therapeutic equivalents only if they are pharmaceutical equivalents and if they can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling.
 - ❖ FDA classifies as therapeutically equivalent those products that meet the following general criteria: (1) they are approved as safe and effective; (2) **they are pharmaceutical equivalents** ...; (3) they are bioequivalent in that (a) they do not present a known or potential bioequivalence problem, and they meet an acceptable in vitro standard, or (b) if they do present a known or potential problem, they are shown to meet an acceptable bioequivalence standard ...

“Approved Drug Products with Therapeutic Equivalence” (The Orange Book)



Cost Savings from Biosimilars

- Estimates range between 10 to 40 percent cost savings compared to the reference product
- Significantly less than the 90 percent savings realized with generic formulations of small molecule drugs
 - ❖ Why: complexity of approval and manufacturing process
- In 2008, the Congressional Budget Office estimated that biosimilars would save approximately \$25 billion over 10 years
- Actual savings remains to be seen



Why Biosimilars Matter to Health Systems: An Example

- In 2011, 6 of 20 of the highest expenditure cancer treatments for outpatient oncology clinics were biologics
 - ❖ Accounted for 49% of the total costs of these 20 drugs
 - ❖ Excludes supportive therapies, such as ESAs
- The top three expenditures were biologics (bevacizumab, rituximab, transtuzumab)
 - ❖ Cost: \$4,095,222
 - ❖ Projected cost savings with biosimilars: \$409,522 to \$1,638,089 (*estimated at 10 to 40 percent*)
 - ❖ If biosimilars provide the same effectiveness and safety, the cost savings will be substantial!

Health-System Formulary



- **Defines the use of drugs that are medically appropriate and cost-effective for treating the patient population served by the health system**
- **Provides a continually updated list of medications available within a health system**
- **Establishes processes that guide drug use**
- **Formularies are evidence-based and developed through the multidisciplinary P&T Committee process**

Overview of P&T Committee Process

- Grounded in patient care and unbiased reviews of peer reviewed biomedical literature
- Decisions should take clinical, legal, safety, ethical, and quality-of-life factors into consideration
- Active engagement of patient care team including pharmacists
- Evidence-based but recognize economic considerations

Additional Clinical Considerations for P&T Committees

- **Efficacy and safety relative to innovator
for all indications**
- **Equivalence/conversion**
- **Post-marketing
surveillance/pharmacovigilance**
- **Nomenclature/identification**
- **Transitions of care**
- **Therapeutic interchange**

Additional Economic Considerations for P&T Committees

- **Copayments/coinsurance**
- **Institutional costs/relative savings**
- **Relative cost advantages**
- **Contracting considerations**

Health-System Practice and Biosimilars

- **Biosimilars open the door to more treatment options, but at a cost of increased complexity for health systems and pharmacists**
 - ❖ **Current generic substitution scenarios not directly applicable**
 - ❖ **Pharmacy can take lead in evaluation of biosimilars in the formulary process**
 - Therapeutic interchange
 - Risk evaluation in switching between biosimilars and reference product

Therapeutic Interchange

- **Authorized exchange of therapeutic alternatives in accordance with previously established and approved written guidelines, policies, or within a formulary system**
- **Provides for interchange of drugs with different chemical structures that are expected to have similar therapeutic effects and safety profiles when administered to patients in therapeutically equivalent doses**
 - ❖ E.g., Simvastatin versus lovastatin
- **Once established through P&T process, interchange may occur as part of the physicians' overall agreement to formulary process**
- **An opt-out process is defined in policy**

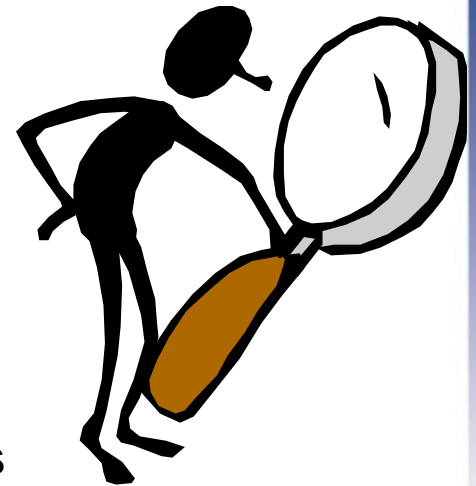
From: ASHP Guidelines on the Pharmacy and Therapeutics Committee and the Formulary System.

www.ashp.org/DocLibrary/BestPractices/FormGdlPTCommFormSyst.pdf



Considerations for Formulary Status

- Take into account the unique patient populations served by the health system
- Decision points will include:
 - ❖ FDA approval package
 - ❖ Post-approval clinical studies
 - ❖ Studied versus unstudied patient populations
 - ❖ Labeled versus extrapolated indications
- Ideally, clinicians will want to see pharmacodynamic or outcomes studies in actual patients



Example Questions

- **What does it mean when a drug is deemed to have no clinically significant difference?**
- **How does the available evidence apply to my unique patient population?**
- **If more than one product is required, how will this affect medication-use processes? What adjustments will be needed?**
- **What changes are required for current purchasing contracts?**

Nomenclature

ASHP comment to FDA in January, 2011:

There should be a mechanism to differentiate biosimilar and interchangeable biological products from the innovator product for the purposes of postmarketing safety surveillance...However, the name of the biosimilar and interchangeable biological product should not be so dissimilar from the innovator product that it causes confusion about the identity of the drug product or creates bias that limits use of the product.

Nomenclature (cont'd)

- **Identical names**

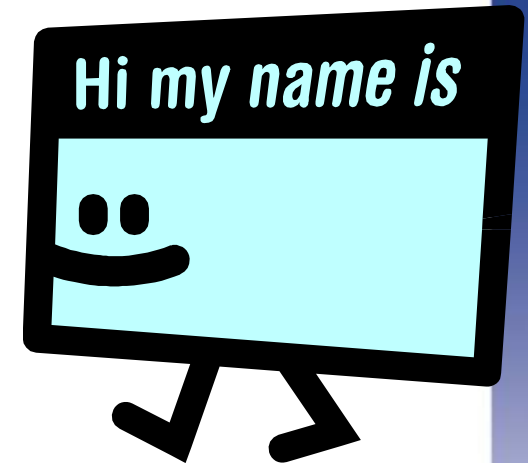
- ❖ Pros: supports utilization and prevents product confusion and medication errors
- ❖ Cons: presents challenges to ADR reporting because of current limitations in technology

- **Related, but unique names**

- ❖ Pros: aids in tracking ADRs, facilitates recalls, avoids unintentional substitution
- ❖ Cons: could delay uptake

- **NDC numbers have also been proposed**

- ❖ Could address some, but not all issues



Biosimilars: Other Considerations and Challenges

• Health-system level

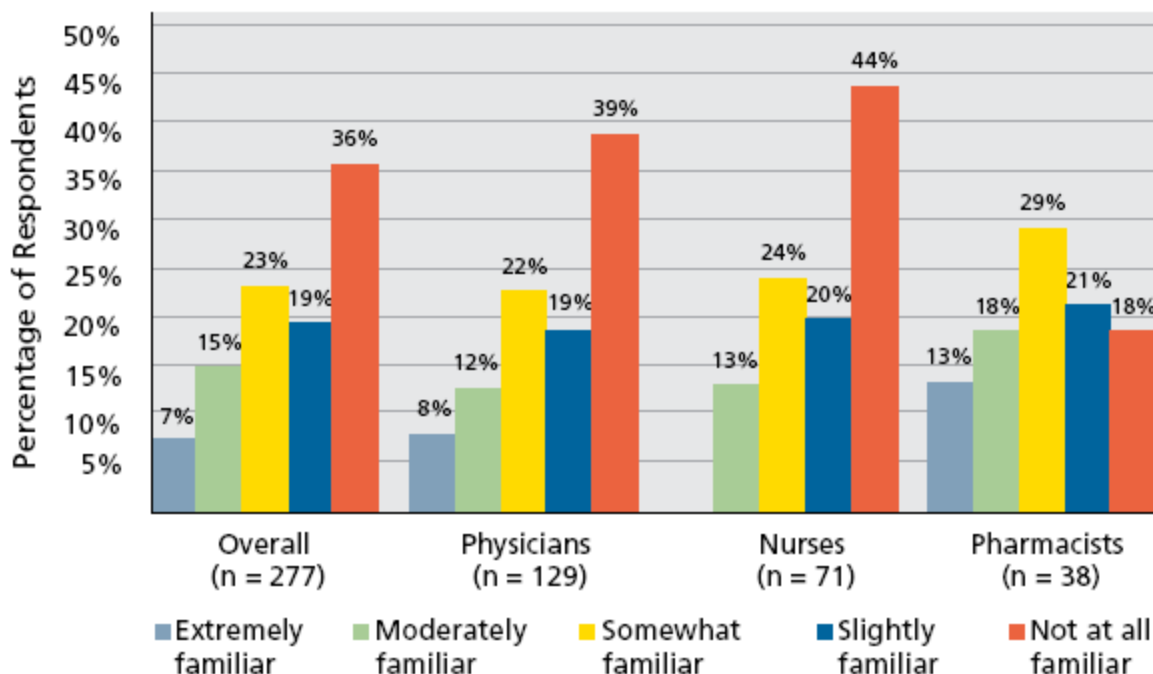
- ❖ Management of patients receiving a different product pre- or post-admission (will also be decided at policy level)
- ❖ Support of pharmacovigilance efforts
- ❖ Labeling and IT systems
- ❖ Patient and provider education

• National/state level

- ❖ Reimbursement
 - Role of payors in labeled and off label uses—TBD
- ❖ State versus federal oversight
 - Once FDA establishes interchangeability, states may guide how substitution occurs (e.g., IL and GA legislation)

Pharmacists and Other Clinicians' Knowledge of Biosimilars

Familiarity with developments for biosimilars



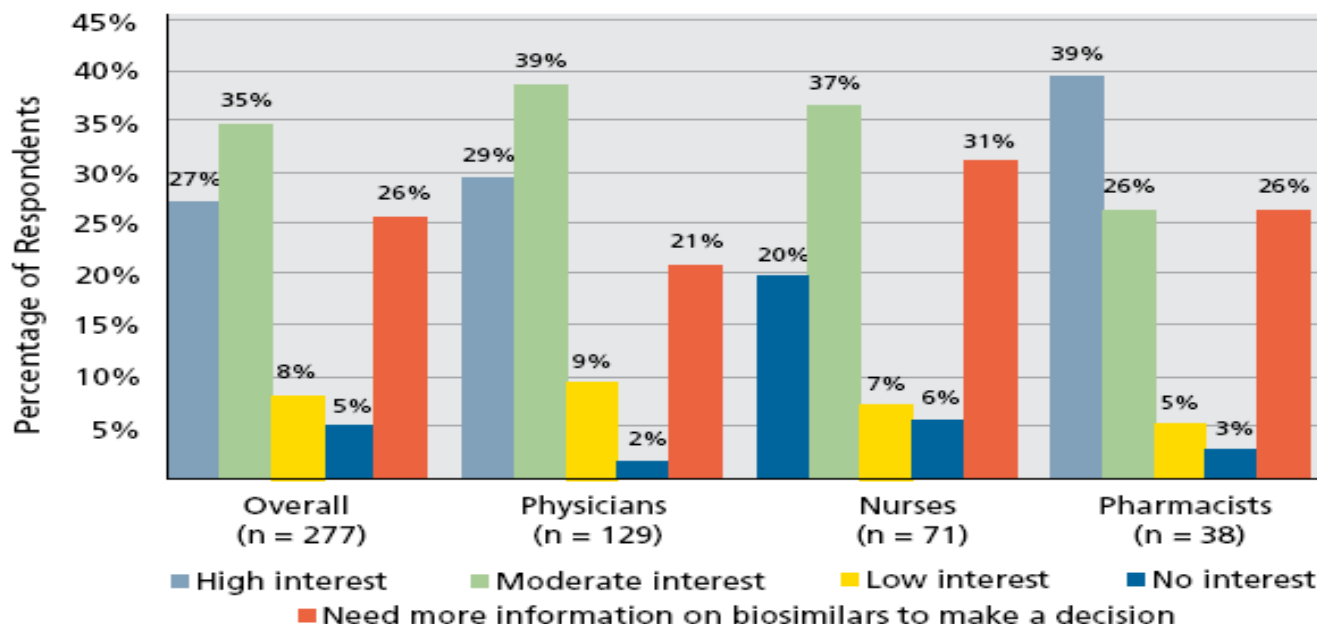
From: National Comprehensive Cancer Network Biosimilars White Paper: Regulatory, Scientific, and Patient Safety Perspectives.

www.nccn.org/JNCCN/supplements/PDF/2011_Vol9_Suppl_4_Biosimilars.pdf



Pharmacists and Other Clinicians' Knowledge of Biosimilars *(cont'd)*

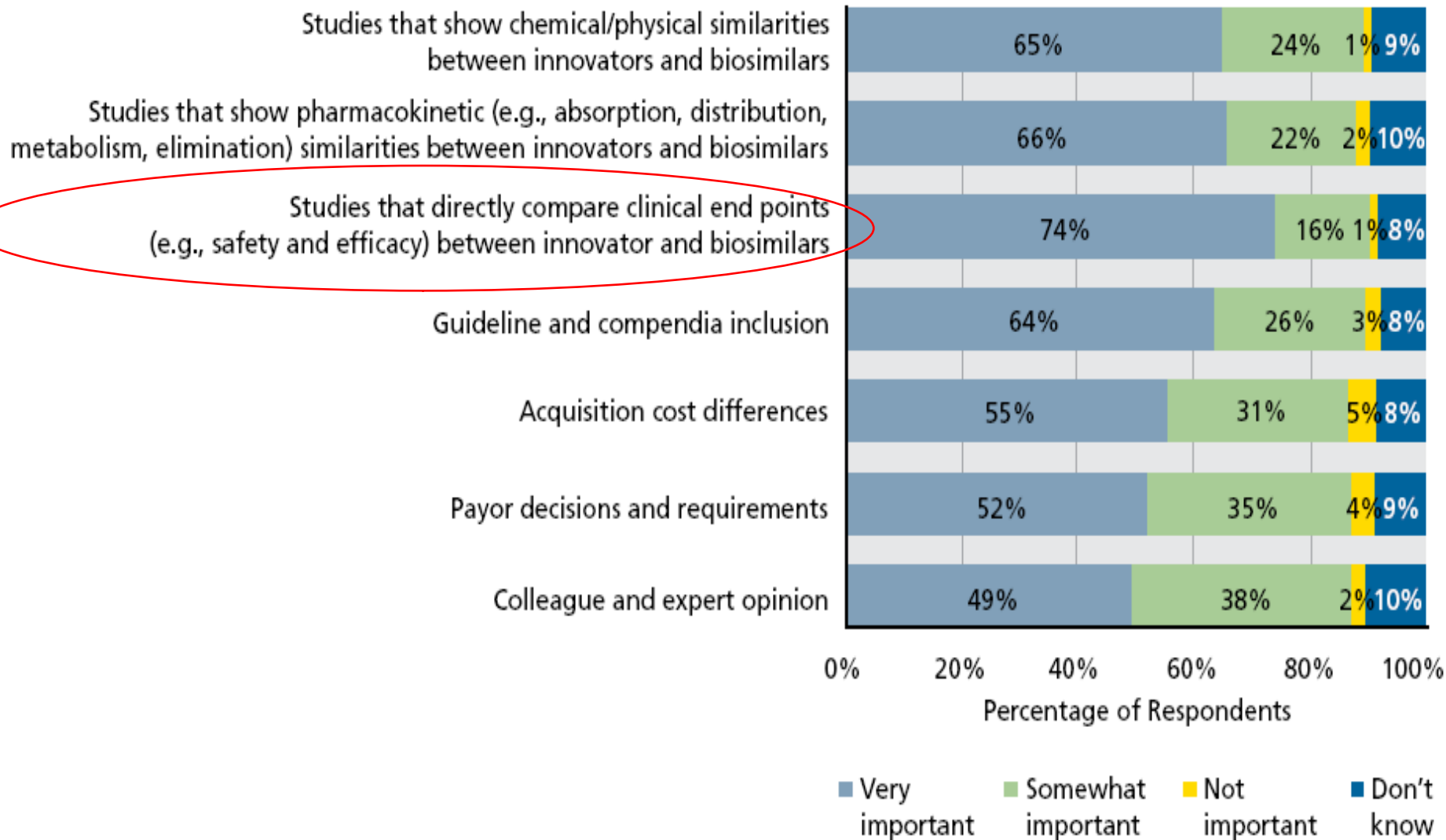
Interest in prescribing, dispensing, or administering biosimilars in your practice setting



From: National Comprehensive Cancer Network Biosimilars White Paper: Regulatory, Scientific, and Patient Safety Perspectives.

www.nccn.org/JNCCN/supplements/PDF/2011_Vol9_Suppl_4_Biosimilars.pdf





From: National Comprehensive Cancer Network Biosimilars White Paper: Regulatory, Scientific, and Patient Safety Perspectives.

www.nccn.org/JNCCN/supplements/PDF/2011_Vol9_Suppl_4_Biosimilars.pdf



Implications for Education



- **Knowledge about biosimilars differs based on discipline**
 - ❖ More knowledge generally increases comfort level
- **There is a substantial need for education**
- **Need will be ongoing as evidence and regulatory process evolves (e.g., published studies, issuance of first designation of interchangeability, etc.)**
- **It will be important to educate patients as well as providers**
- **Pharmacists should take a leadership role in these activities**

Conclusion: Planning for Biosimilars

- **Best choice is to employ formulary review process to adopt biosimilars**
- **Careful balance of efficacy, safety, and costs evidence**
- **Not analogous to generic substitution**
- **Pharmacists should take proactive role in educating health care professionals and patients**

Self-assessment Questions

1. **Cost savings from biosimilars compared to innovator products will likely be _____ percent.**
 - a. **Around 90**
 - b. **Up to 30**
2. **Therapeutic interchange applies to drugs with the same chemical structure that are expected to have similar therapeutic effects and safety profiles.**
 - a. **True**
 - b. **False**
3. **The highest area of interest for clinician education related to biosimilars is:**
 - a. **Clinical endpoint comparisons for innovator and biosimilar products**
 - b. **Pharmacokinetic comparisons**
 - c. **Payor determinations**

Answers: 1. b; 2. b; 3. a

