Resource Guide for Teaching Faculty

Introduction:

Biological products (also called biologics), including biosimilar products (also called biosimilars) and interchangeable biosimilar products (also called interchangeable biosimilars), are a fast-growing market that comprises a broad range of treatment options for patients. The Food and Drug Administration (FDA) is seeking to educate students in health care professional degree programs to improve understanding of biosimilars and interchangeable biosimilars and their corresponding regulatory approval pathway in the United States. As these students transition into professional practice, they play a key role in educating patients about biosimilars and interchangeable biosimilars. They can facilitate the shared decision making needed in patient-centered health care by understanding these important treatment options.

Goal of the Toolkit:

This toolkit provides teaching faculty with a variety of educational resources designed to communicate concepts related to biosimilars and interchangeable biosimilars in teaching modules and curricula, and to increase knowledge and real-world application of the concepts among students in relevant health care professional degree programs (e.g., medicine, nursing, physician assistants, pharmacy).

Objectives of the Toolkit:

The objectives of FDA's biosimilar educational toolkit are:

1. Provide definitions related to biologics, including reference products, biosimilars, and interchangeable biosimilars.
2. Explain the different regulatory approval pathways for reference products and biosimilars.
3. Explain the required data and information needed to support biosimilar and interchangeable biosimilar approval.
4. Explain considerations for prescribing and dispensing biosimilars and interchangeable biosimilars.

Purpose of the Toolkit:

FDA has developed a curriculum toolkit that contains multiple types of resources to assist teaching faculty who would like to incorporate topics related to biosimilars and interchangeable biosimilars into the training they provide students. The materials are modular in nature, allowing teaching faculty to integrate topics about biosimilars into class lectures, online learning platforms, class discussions, and at-home assignments, as appropriate. The materials in this toolkit focus on two different groups of health care degree students and their expected learning needs:

Level 1: Materials at level 1 provide a high-level overview of foundational biosimilar topics and describe how biosimilars fit into the broader category of therapeutic biological products (biologic therapies). The materials also provide a description on the availability of biosimilars and interchangeable biosimilars in the U.S. health care market, the role of providers in prescribing, and information on interchangeability. Students at level 1 may be those beginning their medical training or those with limited exposure to biological products who only need a basic understanding of the concepts.

Level 2: Materials at level 2 provide an in-depth look at scientific and regulatory topics related to biosimilars and their practical applications. Materials at this level describe the relationship between biosimilars and reference products, discuss different approval pathways for biologics, examine variation inherent in all biologics, and provide information related to prescribing biosimilars. Students at level 2 may be those nearing the completion of their didactic training and/or preparing to enter clinical practice where they may encounter patients being prescribed biologics as part of their treatment plans.

Description of Resource Types:

The materials included in the toolkit were designed to meet a variety of teaching needs. Table 1 outlines the materials available by level and type. The materials complement each other so faculty and instructors can select the resources that best fit the knowledge needs and learning styles of their students. The presentation decks serve as the core for the other educational materials, whether for use in a class lecture (e.g., the deck and explanatory videos) or assigned to students in a classroom discussion forum (e.g., information sheet, case study, discussion questions). Table 2 provides details on the topics covered by each resource for its respective level, and Table 3 provides details on resources applicable to both levels.

Table 1: Resources available by level and type

Resource Type	Level 1 Foundational Concepts	Level 2 Regulatory and Scientific Concepts
Presentation Decks	√	√
Case Studies	√	√
Information Sheets	√	√
Explanatory Videos	√	√
Discussion Questions	√	√
Exercises	√	√
Additional FDA Resources	√	√

Presentation Decks: Each deck contains an introductory slide that outlines the covered concepts, animated videos, content slides with text and visuals to illustrate concepts, a key takeaway slide for the most important concepts that students are expected to remember, and a resource slide with links to general information on biologics, including biosimilars. Knowledge assessment questions aligned to the deck sections are provided at the end of each slide deck in a multiple-choice format to assess understanding of biosimilar topics. Additional discussion questions are also available (see the linked question document in Table 2 below).

Case Studies: Case studies explore the topics of biosimilars and biologics in a narrative form and follow the experience of various health care providers as they learn about, interact with, prescribe, and dispense biosimilars and interchangeable biosimilars. One case study introduces basic concepts related to biosimilars and interchangeable biosimilars, while other case studies explore situations of practitioners who prescribe biosimilars in their daily work and who may encounter questions on interchangeability and/or substitution. The case studies provide a summary of the topics covered and a list of questions for students to consider as they read. While the answers to the questions are woven throughout the narrative of each case study, the questions serve as a basis for discussing topics on biosimilarity. The case studies also include a list of potential discussion topics from the shared patient-provider decision-making perspective.

Information Sheets: Information sheets include a more detailed look at the topics included in the presentation decks. Each information sheet is 1-3 pages in length and allows faculty and instructors to target the specific information on which they would like students to focus.

Explanatory Videos: Short animated videos serve as quick and visual learning tools. Foundational topics are covered in level 1 and more detailed visual descriptions of complex concepts are covered in level 2. Most videos range in length from 2 minutes up to 6:30 minutes.

Discussion Questions: Knowledge assessment questions for levels 1 and 2 serve as additional resources to aid in teaching, as well as encourage students to consider and discuss the topics covered in the materials. The questions may require modification based on the specific health specialty or topic area of the class. While the knowledge assessment questions at both levels explore similar topics, level 2 questions require a deeper level of understanding. Level 2 questions also explore interchangeability in more detail and its connection to providers who may prescribe biosimilars or fill prescriptions. Knowledge assessment questions are at the end of the level 1 and level 2 slide decks in a multiple-choice format to facilitate understanding of biosimilar topics.

Table 2: Resources available with details

Level 1 - Foundational Concepts	Level 2 - Regulatory and Scientific Concepts
Presentation Deck (PowerPoint & PDF)	
What is a Biological Product? - What is a Biological Product? - What is a Biosimilar? - What is an Interchangeable Biosimilar Product? **Approved Biosimilars and the US Health Care Market** - The Promise of Biosimilars - Biosimilars and Interchangeable Biosimilar Product Availability **Inherent Variation in Biologics** - Biologics Contain Inherent Variation - Role of Clinical Studies **Differences Between Generics and Biosimilars** - Biosimilars Are Not Generics - Comparing and Contrasting Generics and Biosimilars **Biological Product Approval Pathway** - Biological Product Development - Analytical Studies Form the Foundation of the Biosimilar Application Pathway **Practical Considerations for Using Biosimilars and Interchangeable Biosimilars** - Biologics Naming Convention - Prescribing Biosimilars and Interchangeable Biosimilars - The Purple Book **Adoption of Biosimilars** - Adoption of Biosimilars and Interchangeable Biosimilars - Adoption of Biosimilars - Formulary Coverage and Reimbursement for Biosimilars **Resources** **Key Takeaways** **Knowledge Check** - Multiple choice questions	**Biological Product Complexity** - Biological Product Complexity - Biosimilar Inherent Variation - Consistency in Manufacturing and Analytical Assessments **Biological Product Approval Pathways** - Different Approval Pathways for Reference Products and Biosimilar Products - Biosimilar Manufacturers Must Demonstrate Biosimilarity to the Reference Product - Clinical Studies to Address Residual Uncertainty - Clinical Studies to Demonstrate Similar Exposure, Efficacy, and Safety **Comparative Analytical Assessment** - Comparative Analytical Assessment: The Foundation of the 351(k) Pathway - Identification and Measurement of Product Quality Attributes - Characterizing Quality Attributes of the Reference and Biosimilar Product - Evaluation of Biosimilarity Using a Totality-of-the-Evidence Approach **Comparative Analytical Assessment and Product Quality** - Analytical Studies are the Foundation of the 351(k) Pathway - Identification of Product Quality Attributes - Critical Quality Attributes Example: Insulin Products - Illustrative Critical Quality Attribute: Post-Translational Modifications - Illustrative Quality Attribute: Post-Translational Modifications - Commonly Encountered Post-Translational Modifications - Clinically Inactive Components in Demonstration of Biosimilarity **Insulins/Interchangeability** - Biosimilar and Interchangeable Products in Primary Care and Community Practice: Insulins - Adoption of Biosimilars **Biosimilar Naming** - Biosimilar Naming Conventions **Practical Considerations for Using Biosimilars and Interchangeable Biosimilars** - Biosimilars Are as Safe and Effective as the Reference Product - Immune Response to Biologics - Biosimilars and Interchangeable Biosimilar Labeling **Resources** - Health Care Provider Materials - Addressing Patient Questions - FDA Biosimilar Materials in Spanish - Resources **Key Takeaways** **Knowledge Check** - Multiple choice questions
Information Sheets (PDF)	
• Biological Products, Biosimilar Products, and Interchangeable Biosimilar Products • Generics and Biosimilars • Manufacturing and Variation • Biosimilar Regulatory Approval Pathway • Navigating the Purple Book Database of Licensed Biological Products • Biosimilar and Interchangeable Biosimilar Insulin Products	• Variation in Biological Products • Comparative Clinical Studies • Prescribing Biosimilar and Interchangeable Biosimilar Products • Comparative Analytical Assessment and Product Quality • Biosimilar Product Quality Attributes • Labeling for Biosimilar and Interchangeable Biosimilar Products

Level 1 - Foundational Concepts	Level 2 - Regulatory and Scientific Concepts
Explanatory Videos	
• Biosimilars: Manufacturing and Inherent Variation (3:32 minutes) • Biosimilars: Approval Process (2:46 minutes) • Biosimilars: The Purple Book (5:30 minutes)	• Biosimilars: Critical Quality Attributes (3:11 minutes) • Biosimilars: Interchangeability (2:02 minutes) • A Walk-Through of FDA's Purple Book: Database of Biological Products (11:03 minutes) • Biosimilars: Totality of the Evidence in Biosimilar Development (6:30 minutes) • Biosimilars: Comparative Analytical Assessment (4:38 minutes)
Case Studies (PDF)	
What is a Biosimilar? An R.N. in primary care has started hearing a new term, biosimilars, from patients and in his reading. He explores the connections between reference products and biosimilars. **Topics covered:** • Terms related to biologics • Potential benefits of biosimilars in US health care • Biosimilars and generic drugs • Variation in biologics • Naming of biologics and biosimilars • Biosimilar resources **Biosimilar and Interchangeable Biosimilar Insulin Products** A physician in training is working in a community health clinic, where he learns biosimilar insulin products are available in primary care and other everyday clinical settings. **Topics covered:** • Variation in biological products • Terms related to biological products • Approval pathways • Comparative studies to assess safety and efficacy • Purple Book and naming • Biosimilar labeling • Addressing patient questions	**Biosimilars in Patient Care** A prescriber considers a newly available biosimilar for a patient in the United States. She explores available information on the biosimilar as well as applied practice from peers in her medical field. **Topics covered:** • Variation in biologics • Terms related to biologics • Approval pathways • Comparative studies to assess safety and efficacy • Purple Book and naming • Biosimilar labeling • Addressing patient questions **Interchangeable Biosimilars** A pharmacist considers switching a patient's regular biologic for an interchangeable biosimilar because the patient's new insurance carrier will not cover the reference product. She explores information on the biosimilar medication. **Topics covered:** • Naming of biologics and biosimilars • Interchangeable biosimilars • Pharmacy-level substitution and state laws • Shared decision making and addressing patient questions **Comparative Analytical Assessment – Data Supporting Biosimilarity** A pharmacist in-training gains knowledge about the evaluation of biosimilar products during her clinical rotation. **Topics covered:** • Post-translational modifications • Quality attributes • Comparative assessment of product quality attributes
Discussion Questions Include (PDF)	
• What are biologics? • Why can't a biologic be copied exactly? • What is a reference product and how is it related to a biosimilar? • How is the relationship between generic and brand-name drugs different than the relationship between biosimilars and reference products? • What is the purpose of a biological product's core name and the four-letter suffix? • What benefits might biosimilars bring to patients and the health system? • Can biosimilars and interchangeable biosimilars be substituted for reference products by pharmacists? • Where can medical providers find information on FDA-approved biologics? • What are the benefits of biosimilar products to patients?	• Why does the biosimilar approval process differ from the reference product's approval process? • How can we know that a biologic is safe and effective with its inherent variation? • What is the role of comparative clinical studies in the biosimilarity assessment? • What are interchangeable biosimilars? • Can pharmacists switch or substitute a biosimilar for its reference product? • How and why might a biosimilar label differ from the reference product label? • What questions might a patient have about biosimilars and how can providers respond to those questions?

Exercises: The included exercises (Table 3) provide suggested resources and ideas relevant to a wide range of students. They serve as a starting point for faculty to develop more comprehensive activities targeted to their teaching needs and to enhance information retention by students using real-world examples.

Additional FDA Resources: Resources in Table 3 include FDA's biosimilars website with content available to industry, health care providers, and patients. Links to level 1 and 2 materials are also provided below.

Table 3: Additional resources for levels 1 and 2

Resources Applicable for Levels 1 and 2		
Exercises		
Biosimilar Topic	Activity Outline	Resource
Navigating Purple Book	1. Visit https://purplebooksearch.fda.gov/. 2. Enter the name of a biologic (i.e., reference, biosimilar, or interchangeable biosimilar) in the Search section. 3. Explore the information. For example, if you searched for a reference product, the Results page will provide you with a list of approved products, including the corresponding biosimilar and interchangeable biosimilars, if any. 4. Note the Proprietary name for each biologic listed as well as the non-proprietary name (i.e., core name with a unique 4-letter suffix). 5. Explore the dosing information, route of administration, license type, etc. by clicking on each biologic listed.	Purple Book
Understanding Biosimilar Labeling	1. Visit https://purplebooksearch.fda.gov/. 2. Enter the name of a biologic (i.e., reference, biosimilar, or interchangeable biosimilar) in the Search section. 3. Find the reference product in the Results page. Click "Product Label" to explore the information. Find the corresponding biosimilar in the Results page, if any, and click on "Product Label" to explore the information. 4. Click the "Approval Date(s) and History, Letters, Labels, Reviews." 5. Compare and contrast the labeling and prescribing information provided for the reference product and its respective biosimilar(s) in the "Label (PDF)" section. 6. Click on the "Letter," "Review," and "Supplement" sections, if applicable for the reference product and biosimilar(s), for additional information.	Purple Book
Understanding how Pharmacy and Therapeutic (P&T) committees consider a biosimilar for inclusion in the formulary	1. Visit https://purplebooksearch.fda.gov/. 2. Enter the name of a biologic (i.e., reference, biosimilar, or interchangeable product) in the Search section. 3. Read labels and reviews/approval packages 4. Discuss the strategic considerations made by P&T committees. Evaluations include: a. Consideration of the scientific review of a specific product • Physiochemical and functional studies demonstrating "biosimilarity" to the reference product • Clinical studies demonstrating "no clinically meaningful difference" to the reference product • Extrapolation data, if applicable • Additional switching studies, if applicable, for interchangeable biosimilars. b. Discuss what the Financial assessment* may include and how P&T committees use it in their evaluation. c. Discuss what the Operational assessment* may include and how P&T committees use it in their evaluations. **Note: While financial assessment and operational assessment are important considerations for P&T committees, these topics are beyond FDA's purview.*	Review of specific product: FDA links: • Review section on Purple Book • Product-specific FDA Advisory Committee • Reviews at Drugs@FDA Scholarly resource: Johnson ST, Gosser RA, Kier KL, et. al., Formulary management challenges and opportunities: 2020 and beyond - an opinion paper of the drug information practice and research network of the American College of Clinical Pharmacy. J Am Coll Clin Pharm. 2021;4:81–91. https://doi.org/10.1002/jac5.1332
Additional FDA Resources (PDF)		
Resource list of additional FDA resources: • Biosimilar materials • Provider materials • Patient materials • Purple Book • Drugs@FDA (Drug Information) • Search page for FDA guidances • Advisory committee materials for Biosimilars • Biosimilar approval process information		