

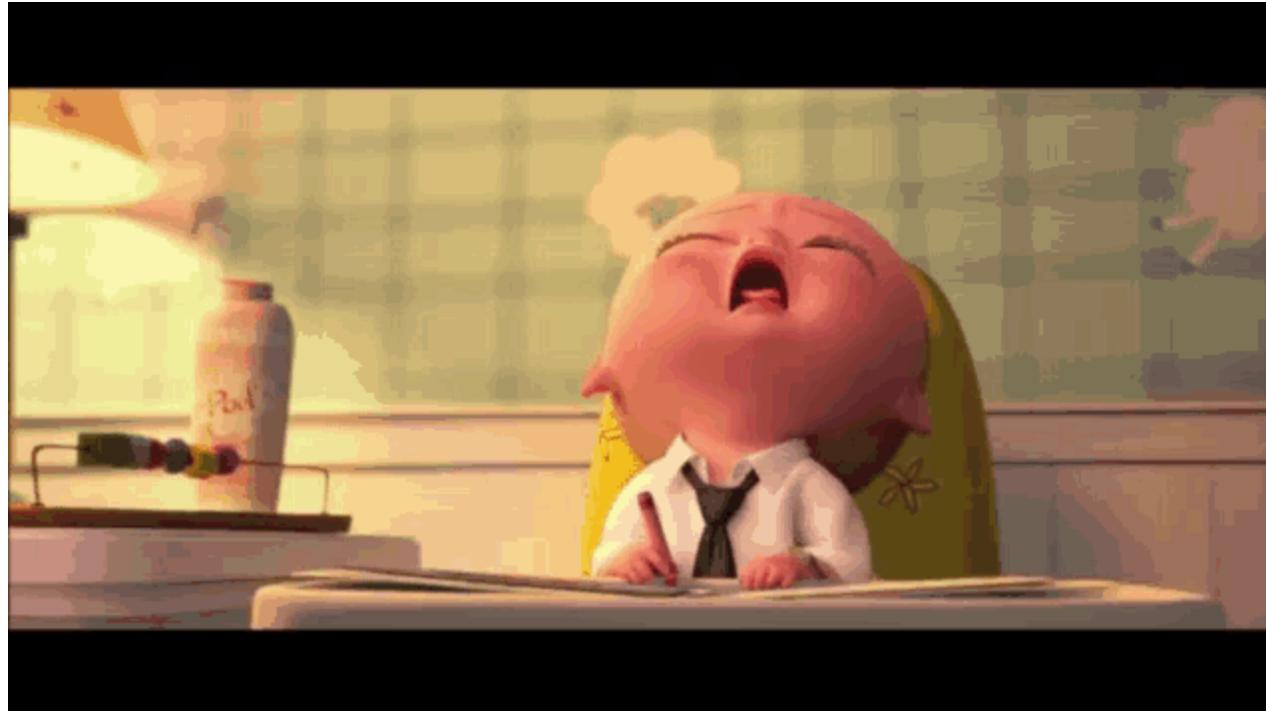
# FDA Biosimilars Overview

*Biosimilars at the Bar*  
GRx-Biosims Conference  
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# Regulatory Landscape





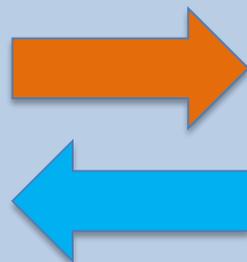
### Reference Product

A reference product is the single biological product, already approved by FDA, against which a proposed biosimilar product is compared



### Biosimilar Product

A biosimilar is a biological product that is highly similar and has no clinically meaningful differences from an existing FDA-approved reference product



### Interchangeable Product

An interchangeable is a biosimilar that can be substituted for the reference product without the intervention of the prescribing health care provider.

# Demonstrating Biosimilarity



- Relationship to reference product
  - Same mechanism(s) of action to the extent known
  - Same route of administration, dosage form, and strength as the reference product
  - Condition(s) of use proposed previously approved for reference product
- Totality of the evidence
- Based upon data from: analytical studies, animal studies, if any; and clinical study or studies
- Nature and scope of clinical studies will depend on the extent of residual uncertainty about biosimilarity after conducting structural and functional characterization and relevant animal studies, if any.

# Demonstrating Interchangeability

1. The proposed interchangeable must be **biosimilar to the reference product**.
2. The application must demonstrate that the proposed interchangeable “can be expected to produce the **same clinical result** as the reference product **in any given patient**.”
3. For products administered more than once to a patient, information sufficient to show that “the ***risk in terms of safety or diminished efficacy of alternating or switching*** between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.”



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# Biosimilar Labeling

- The Full Prescribing Information (PI):
  - summarizes key scientific information that health care providers need to assess a therapeutic product's risk-benefit profile and decide if the product is appropriate for use by their patient
- A biosimilar product is not required to have the same labeling as its reference product
- Biosimilar product labeling may differ from reference product labeling for a variety of reasons.
  - For example, a biosimilar applicant may seek licensure for fewer than all of the indications for which the reference product is approved

# Biosimilar Labeling

- Biosimilar labeling should include:
  - relevant data and information from the FDA-approved labeling for the reference product
    - With any appropriate modifications specific to the biosimilar product.
  - biosimilar product-specific data necessary to inform safe and effective use of the product
  - a “Biosimilarity Statement” in the Highlights section describing the biosimilar product’s relationship to its reference product.
- Biosimilar labeling should not include
  - comparative data supporting the demonstration of biosimilarity
    - Product-specific data supporting a demonstration of biosimilarity, including the comparative clinical data, can be found in FDA’s product reviews at the [Drugs@FDA](#) website.
  - this approach will help avoid potential confusion or misinterpretation of comparative data.

# Transition: Labeling

- Most labeling requirements are the same for BLAs and NDAs
- There are some minor differences, as detailed in guidance
  - Certain labeling requirements for each package (e.g., container labels, and carton labeling)
  - Certain required content of prescribing information
- FDA recommends submission of a prior approval supplement within two years after the transition date



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# Purple Book

- **FDA's Purple Book** provides a list of biological products licensed under the PHS Act, includes:
  - Information about biosimilarity, interchangeability
  - Information about exclusivity
- **An enhanced Purple Book is in development:**
  - Improved interface to provide user-friendly information to the public about approved biologics
  - Enhanced information for patients, prescribers, pharmacists, and other stakeholders

- *Key BAP Action 3: Enhancing the Purple Book to include more information about approved biological products, including information relating to reference product exclusivity determinations.*



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# Interchangeability Considerations



## Demonstrating interchangeability

- Stepwise approach to data generation
- Totality-of-the-evidence approach—no “one-size fits all” assessment

## Switching study design

- Generally necessary only if intended to be administered to an individual more than once
- Endpoints, design and analysis, study population, condition(s) of use, and routes of administration
- Integrated two-part study design may be appropriate
- Option for sponsor to provide justification to FDA for why such data is not needed

# Interchangeability Considerations

- Considerations for the type and extent of “**bridging**” data needed to justify the use of a non-U.S. licensed comparator in switching studies
- Product need not be first licensed as a biosimilar (but can be)
- **Post-marketing data** from a licensed biosimilar product may help when considering what data is necessary.





**“Biobettors”  
and additional  
discussion**