# The “Deemed to be a License” Provision of the Biologics Price Competition and Innovation Act of 2009 (BPCI Act)

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# Agenda

- **Overview of the "Transition" Provision of the BPCI Act**
  - Amended statutory definition of "biological product"
  - FDA's interpretation of "transition" provision
- **FDA's Approach to Implementation of "Transition" Provision of the BPCI Act**
  - Proposed Products
  - Approved Products
- **Additional Considerations**

# Overview: Statutory Transition Scheme

- **Background:** The BPCI Act amended the statutory definition of a "biological product" to include **"protein (except any chemically synthesized polypeptide),"** requiring protein products historically regulated as drugs under the FD&C Act (e.g., insulin, human growth hormone) to be regulated as biological products under the PHS Act.
- **Statutory Transition Scheme**:
  - BPCI Act describes requirements for **submission** of an application for a "biological product" during a 10-year transition period ending on March 23, 2020.
  - On March 23, 2020, an **approved** application for a biological product under section 505 of the FD&C Act will be "deemed to be a license" for the biological product under section 351 of the PHS Act.
  - After March 23, 2020, all sponsors seeking approval of a biological product will need to submit a BLA: either a **"stand-alone" 351(a) BLA** or a **351(k) BLA for a biosimilar or interchangeable** product.

# Overview: FDA's Implementation Approach

- **Implementation Approach:** FDA is working to ensure there is a seamless transition of approved NDAs for biological products to deemed BLAs, and that there are minimal impacts on manufacturers and patients.

- **Resources Related to the Transition:** FDA Webpage on the "Deemed to be a License" Provision of the BPCI Act (available at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/deemed-be-license-provision-bpci-act)
  - **Guidances:** Final Guidance on *Interpretation of the "Deemed to be a License" Provision of the BPCI Act* and Draft Guidance on *The "Deemed to be a License" Provision of the BPCI Act: Questions and Answers*
  - **Proposed Rules:** *Definition of the Term "Biological Product"* and *BLAs and Master Files*
  - **Preliminary List** of Approved NDAs for Biological Products That Will Be Deemed to be BLAs on 3/23/20

# “Biological Products” Approved Under FD&C Act

- **Examples of Biological Products Approved Under FD&C Act**:

| | |
|---|---|
| chorionic gonadotropin products | pancrelipase products |
| desirudin products | pegademase products |
| follitropin products, urofollitropin products, and menotropins products | pegvisomant products |
| hyaluronidase products | sacrosidase products |
| imiglucerase products | somatropin products |
| insulin products, insulin mix products, and insulin analog products | taliglucerase alfa products and velaglucerase alfa products |
| mecasermin products | thyrotropin alfa products |

# "Biological Product": Amended Definition

- **BPCI Act Amended the Statutory Definition of a "Biological Product":**

  *". . . a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product … applicable to the prevention, treatment, or cure of a disease or condition of human beings …"*
  *(section 351(i)(1) of the PHS Act).*

- **Interpretation of Statutory Terms**:

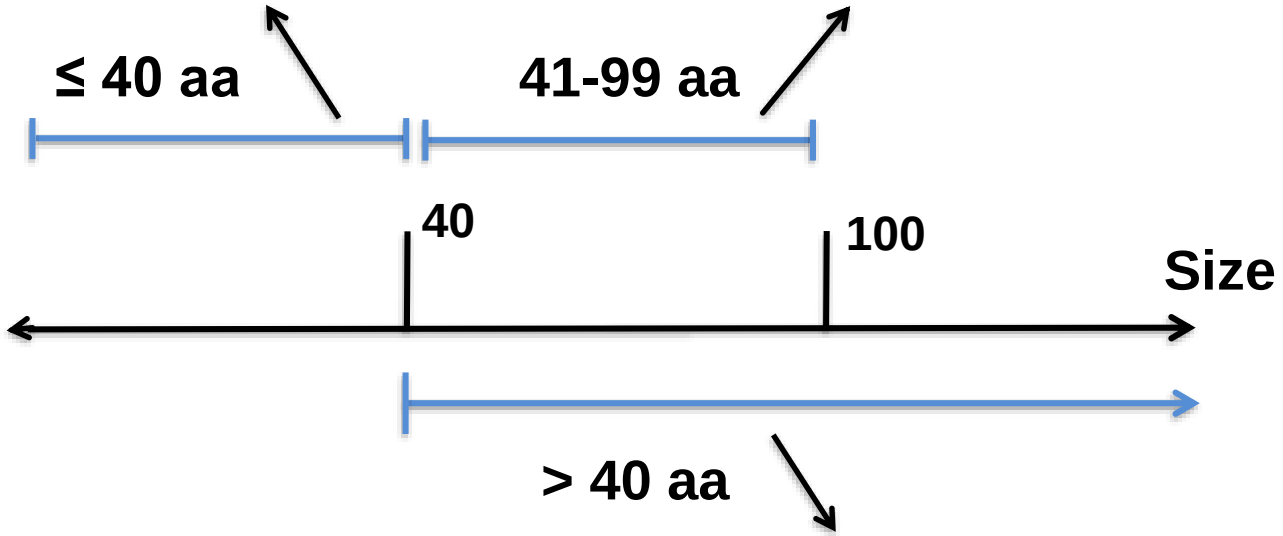
  – As a scientific matter, the terms "protein" and "chemically synthesized polypeptide" are distinguishable from a "peptide," and are used to describe larger chains of amino acids.

  – Based on FDA's scientific expertise and consideration of relevant literature, FDA is proposing to implement this scientific distinction with a bright-line interpretation intended to provide certainty to industry and minimize administrative complexity.

# Interpretation of Key Terms

**Peptide** (regardless of how it is made)

**Chemically Synthesized Polypeptide** (if made entirely by chemical synthesis)




**Protein** (except any chemically synthesized polypeptide)

# Interpretation of Key Terms (cont'd)

- **Protein:** Any alpha amino acid polymer with a specific defined sequence that is greater than 40 amino acids in size.
- **Chemically synthesized polypeptide:** Any alpha amino acid polymer that:
    1. is made entirely by chemical synthesis; and
    2. is greater than 40 amino acids, but less than 100 amino acids in size.
- **Peptide:** Any polymer composed of 40 or fewer amino acids (even if recombinant or naturally sourced).

A peptide or chemically synthesized polypeptide is not a "biological product" and will continue to be regulated as a drug under the FD&C Act, unless it otherwise meets the statutory definition of "biological product" (e.g., peptide vaccine).

# Effect of Amended Statutory Definition

- ***For proposed products***: BPCI Act describes the approval pathways that are available for submission of an application for a "biological product."
  - An application for a "biological product" **must** be submitted under section 351 of the PHS Act, subject to an exception during a transition period ending on March 23, 2020.

- ***For approved products*:** BPCI Act requires that on March 23, 2020, an approved application for a "biological product" under the FD&C Act will be "deemed to be a license" for the product under the PHS Act, and regulated under the PHS Act.

# Proposed Biological Products

- **Statutory transition provision limited to *approved* applications:** FDA will not approve any application for a biological product under section 505 of the FD&C Act after March 23, 2020.

- **Recommendations to sponsors**: FDA guidance provides recommendations to sponsors to facilitate alignment of product development plans with FDA's interpretation of the transition provision of the BPCI Act.
  - Guidance describes considerations for submission of a "stand-alone" 351(a) BLA or a 351(k) BLA for a biosimilar or interchangeable product.
  - Sponsors seeking advice on development programs may request a meeting with FDA in accordance with the PDUFA or BsUFA meeting types, as appropriate.

# Approved NDAs for Biological Products

- **Deemed 351(a) BLAs**: On March 23, 2020, approved NDAs (including 505(b)(2) applications) for biological products will be deemed 351(a) BLAs.
  - Any post-approval requirements or commitments associated with the NDA would transfer to the deemed BLA.
- **Application holder does not need to take any affirmative steps for its NDA to be deemed a BLA:** FDA intends to send a letter to application holders on March 23, 2020, advising that the approved NDA was deemed to be a BLA and no longer exists as an NDA. Letter will provide additional information, including:
  - Application number
  - U.S. License number

# Approved NDAs for Biological Products (cont'd)

- **BLA Requirements**: The holder of a deemed 351(a) BLA will be subject to applicable requirements under the PHS Act and FDA regulations, and also will be subject to requirements under the FD&C Act that apply to BLAs.
  - Certain differences in labeling and CMC-related requirements for NDAs and BLAs.
  - In general, FDA anticipates that the holder of an NDA for a biological product that is deemed to be a BLA will experience minimal disruption due to differences in requirements.

**FDA is committed to working with application holders to minimize any potential burden.**

# Labeling Considerations

- **Deemed BLA Product Labeling:** The holder of a deemed BLA will need to revise product labeling to conform to labeling requirements for biological products regulated under the PHS Act.
  - Most labeling requirements are the same for NDAs and BLAs.
  - There are certain minor differences in requirements for each "package" (e.g., container labels and carton labeling) and the content of prescribing information (see Transition Q&A Draft Guidance for an overview of key labeling changes).
- **FDA Compliance Policy:** To minimize burden, FDA generally does not intend to enforce these BLA-specific labeling requirements for deemed BLAs until **March 23, 2025**.

# Labeling Considerations (cont'd)

- **Deemed BLA Labeling Revisions:** To facilitate implementation, FDA recommends submission of a prior approval supplement with proposed BLA-specific labeling revisions between March 23, 2020, and March 23, 2022.

- **Supplements under review during compliance period:** If the supplement includes proposed revisions to labeling, the BLA-specific labeling requirements will need to addressed before the supplement can be approved.

- **Timing Considerations:** Coordinate BLA-specific revisions to prescribing information with the corresponding revisions to the container labels and carton labeling.

# Supplements to Approved NDAs

- **Administrative Conversion of Pending Supplements**: When FDA deems the approved NDA to be a BLA on 3/23/20, FDA plans to administratively convert any pending supplement to such NDA to a pending supplement to the deemed BLA.
  - ***Review Standards***: Such supplements will be reviewed under applicable BLA standards.
  - ***Goal Date:*** FDA intends to maintain the same goal date, where applicable, for completion of its review of administratively converted supplements.

# On The Horizon



- **<u>Orange Book</u>:** FDA plans to remove NDAs for biological products from the Orange Book on March 23, 2020. Such products will no longer exist as "listed drugs."

- **<u>Purple Book</u>**: Biological products approved in NDAs that are deemed BLAs will be listed in the Purple Book on or shortly after March 23, 2020.

  – A 351(k) BLA can be submitted for a proposed biosimilar or interchangeable to a reference product that is the subject of a deemed BLA upon the transition.

- **<u>Updates to Other FDA Databases</u>**: Other FDA databases will be updated to reflect the transition.

# Thank you for your attention.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