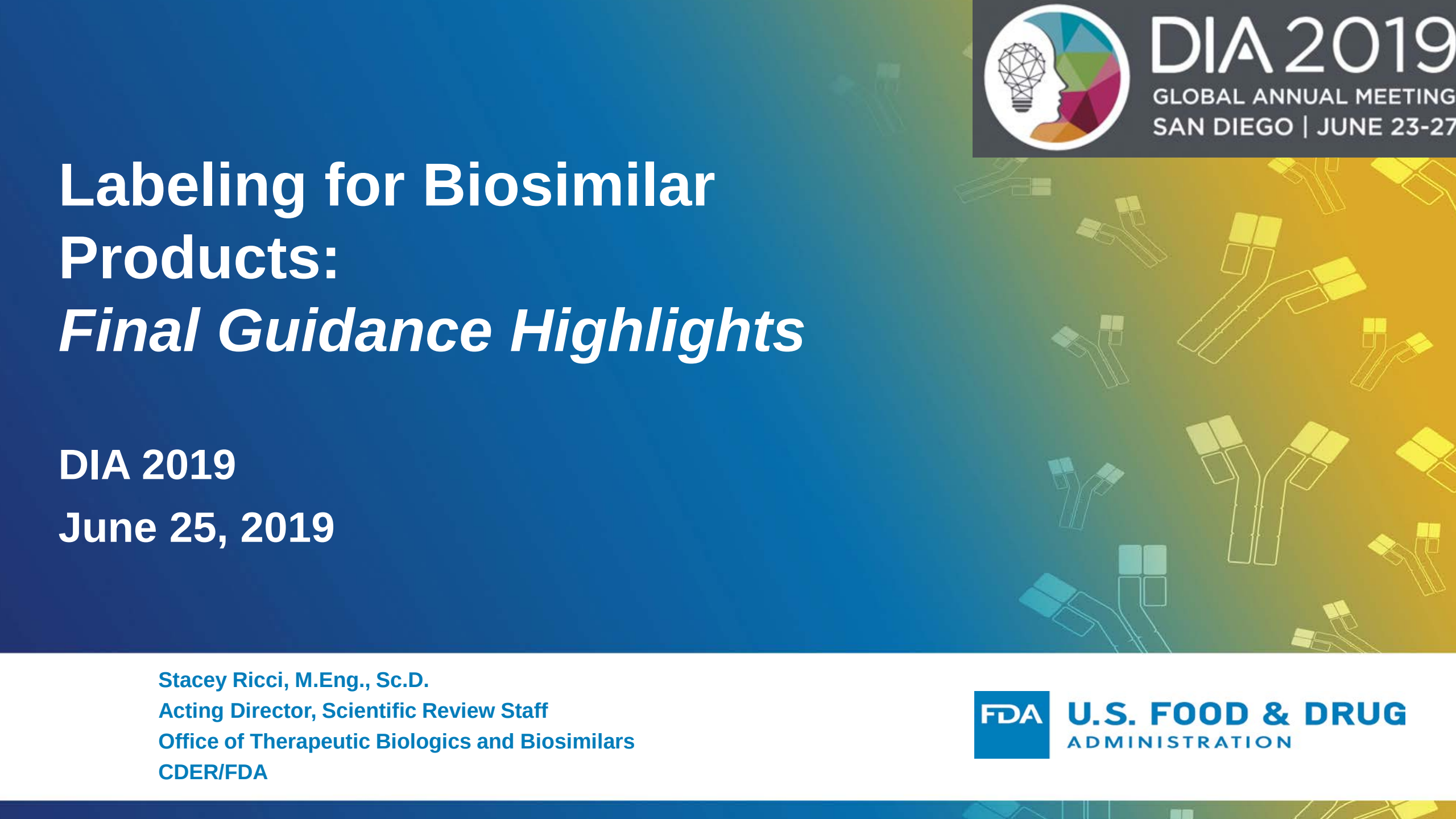

Labeling for Biosimilar Products: *Final Guidance Highlights*

DIA 2019

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Stacey Ricci, M.Eng., Sc.D.
Acting Director, Scientific Review Staff
Office of Therapeutic Biologics and Biosimilars
CDER/FDA

FDA U.S. FOOD & DRUG ADMINISTRATION

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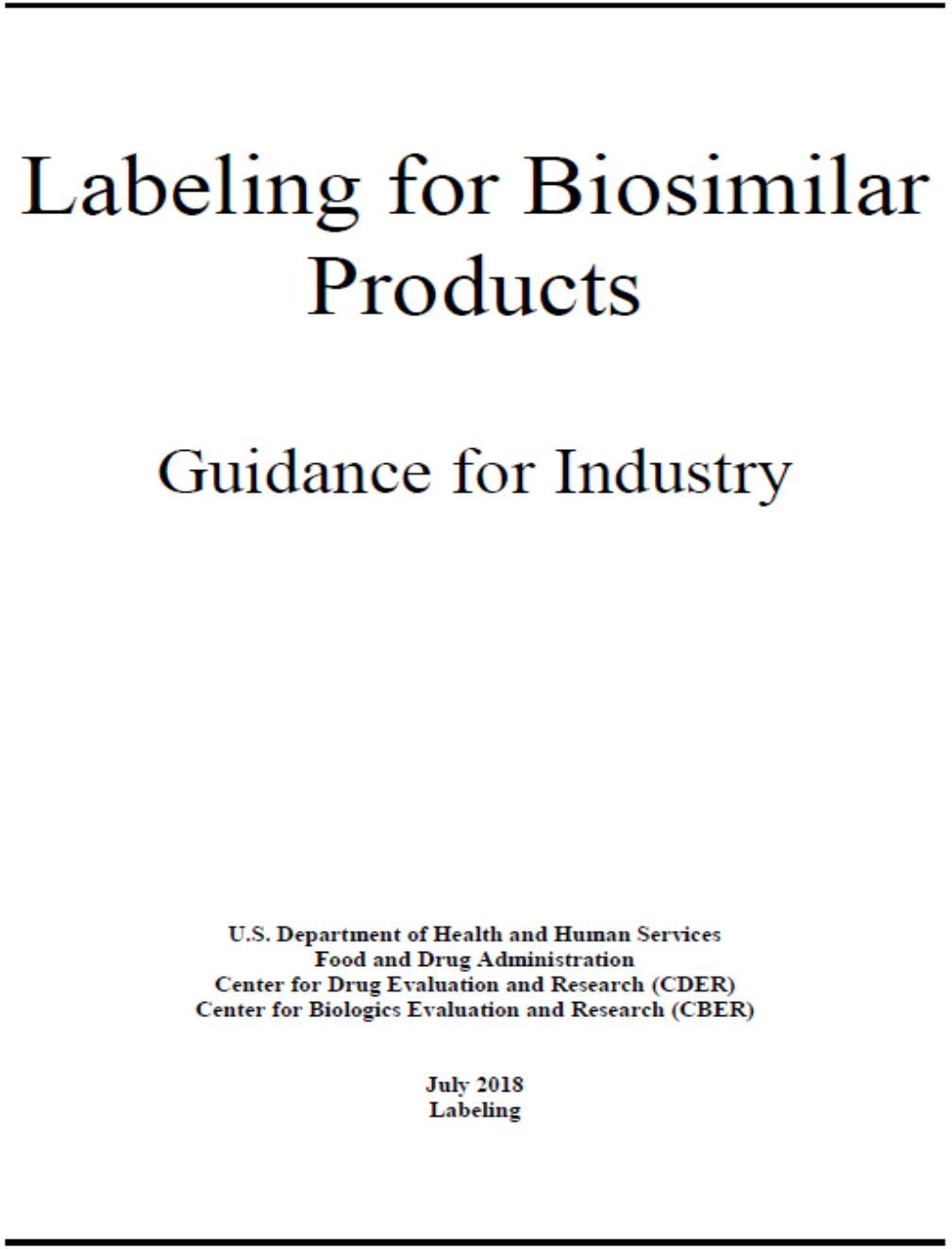

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- Guidance to assist applicants in developing draft labeling for submission in applications for proposed biosimilar products under section 351(k) of the Public Health Service Act (PHS Act)
- Recommendations are for the prescribing information (package insert), and for FDA-approved patient labeling (e.g., Patient Information, Medication Guide, and Instructions for Use)
- Recommendations for interchangeable product labeling will be provided in future guidance

Biosimilarity Study Data

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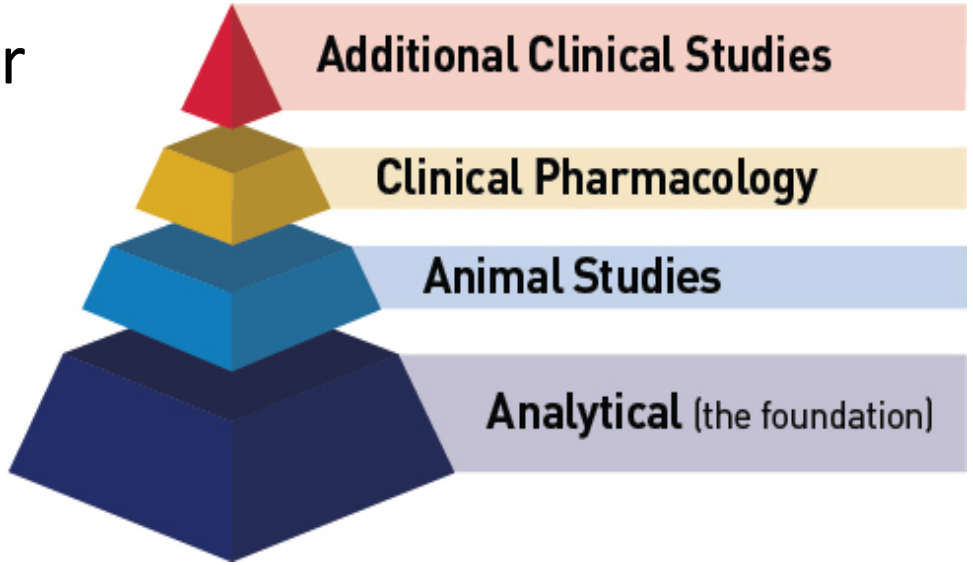
- Comparative analytical data, rather than clinical data, is the foundation of a biosimilar development program
  - A biosimilar product with highly similar structure and function to the reference product is expected to behave like the reference product (i.e., have similar efficacy and safety as the reference product) in clinical use

- The objectives of clinical studies in biosimilar development differs from that in standalone development
  - **Standalone**: De novo safety and efficacy
  - **Biosimilar**: No clinically meaningful differences as part of biosimilarity



General Principles

- Approved prescribing information summarizes the essential scientific information needed by health care practitioners for the safe and effective use of a drug.

- The labeling reflects FDA's finding of safety and effectiveness for the drug under the labeled conditions of use and facilitates prescribing decisions, thereby enabling the safe and effective use of drugs/biological products and reducing the likelihood of medication errors.

Recommendations

- FDA recommends that biosimilar product labeling incorporates relevant data and information from the FDA-approved labeling for the reference product, along with any appropriate modifications specific to the biosimilar product.
- FDA generally does not recommend that clinical data supporting the demonstration of biosimilarity be included in biosimilar product labeling.
  - **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.**
- The Highlights Section contains a "Biosimilarity Statement" describing the biosimilar product's relationship to its reference product.

Recommendations

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- A biosimilar product is not required to have the same labeling as its reference product, so biosimilar product labeling may differ from the 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, and this difference would be reflected in product labeling.
  - Labeling may include information specific to the biosimilar product which could include differences such as preparation, storage, or other information that do not otherwise preclude a demonstration of biosimilarity.
  - Conforming to PLR and/or PLLR because the reference product labeling may not be required to conform to those requirements at the time of licensure of the biosimilar product.

Biosimilarity Statement

- FDA recommends inclusion of a statement, on the line immediately beneath the initial U.S. approval year in Highlights, that the product is biosimilar to the reference product.

NEXSYMEO (replicamab-cznm) is biosimilar* to JUNEXANT (replicamab-hjxf)

- The asterisk is inserted after the word biosimilar indicating a footnote that appears at the end of Highlights and above the Revision Date.

Biosimilarity Statement

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PROPRIETARY NAME safely and effectively. See full prescribing information for PROPRIETARY NAME.

PROPRIETARY NAME (nonproprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY

NEXSYMEO (replicamab-cznm) is biosimilar* to JUNEXANT (replicamab-hjxf).

WARNING: TITLE OF WARNING
See full prescribing information for complete boxed warning.

- **Text (4)**
- **Text (5.x)**

----------RECENT MAJOR CHANGES----------
Section Title, Subsection Title (x.x) M/YYYY
Section Title, Subsection Title (x.x) M/YYYY

----------INDICATIONS AND USAGE----------
PROPRIETARY NAME is a (insert FDA established pharmacologic class text phrase) indicated for … (1)

Limitations of Use
Text (1)

----------DOSAGE AND ADMINISTRATION----------
- Text (2.x)
- Text (2.x)

----------DOSAGE FORMS AND STRENGTHS----------
Dosage form(s): strength(s) (3)

----------CONTRAINDICATIONS----------
- Text (4)
- Text (4)

----------WARNINGS AND PRECAUTIONS----------
- Text (5.x)
- Text (5.x)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence > x%) are text (6.x)

To report SUSPECTED ADVERSE REACTIONS, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Text (7.x)
- Text (7.x)

----------USE IN SPECIFIC POPULATIONS----------

*Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. Biosimilarity of [BIOSIMILAR PRODUCT'S PROPRIETARY NAME] has been demonstrated for the condition(s) of use (e.g., indication(s), dosing regimen(s)), strength(s), dosage form(s), and route(s) of administration described in its Full Prescribing Information.

Revised: M/YYYY

Biosimilarity Statement

NEXSYMEO (replicamab-cznm) is biosimilar* to JUNEXANT (replicamab-hjxf).

*Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. Biosimilarity of NEXSYMEO has been demonstrated for the condition(s) of use (e.g., indication(s), dosing regimen(s)), strength(s), dosage form(s), and route(s) of administration described in its Full Prescribing Information.

Nonproprietary Naming of Biological Products

Updated draft guidance published in March 2019:

- **Newly licensed under 351(a) of the PHS Act (stand-alone BLA):** Nonproprietary name consists of core name and unique suffix
  - **JUNEXANT (replicamab-hjxf)**
- **Newly licensed under 351(k) of the PHS Act (biosimilar and interchangeable products):** Nonproprietary name consists of core name and suffix
  - **NEXSYMEO (replicamab-cznm)**
- **Already licensed under 351 (a) of the PHS Act without a suffix in its nonproprietary name:** Nonproprietary names of already-licensed products without suffixes will not be changed to add a suffix
  - **replicamab**

Approaches to Product Identification

- Biosimilar product name: **NEXSYMEO (replicamab-cznm)**
- Reference product name: **JUNEXANT (replicamab-hjxf)**
- Core name + “products”: **replicamab products**

When to use the biosimilar product name

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- FDA recommends the biosimilar product name be used in labeling text that is specific to the biosimilar product:
  - In sections where the information described is specific to the biosimilar product
    "NEXSYMEO is indicated for the treatment of…"
  - For directive statements and recommendations for preventing, monitoring, managing, or mitigating risks
    "Discontinue NEXSYMEO if a patient develops a serious infection."

When to use the reference product name

- When clinical studies or data derived from studies with the reference product are described in biosimilar product labeling, the reference product's proper name should be used.

- This information would typically be included in sections such as, but not limited to, ADVERSE REACTIONS (Clinical Trials Experience) and CLINICAL STUDIES.

*"Clinical trials with **replicamab-hjxf** in patients with serious infections showed…*

When to use the core name

- The overall risk-benefit profile of the reference product is relevant to the biosimilar product, even if a particular serious adverse reaction or other risk included in the reference product labeling may not have been reported with the biosimilar product at the time of licensure.

- In labeling sections where the risk applies to both the biosimilar product and the reference product, use the core name of the reference product followed by the word "*products*" (i.e., *replicamab products*).

*"**Replicamab products** can cause hepatoxicity and acute hepatic failure."*

Conclusions

- For the Full Prescribing Information, FDA recommends that biosimilar product labeling incorporates relevant data and information from the FDA-approved labeling for the reference product, along with any appropriate modifications specific to the biosimilar product.
- Text based on the reference product labeling does not need to be identical and should reflect currently available information necessary for the safe and effective use of the biosimilar product.
- Health care professionals should review the labeling of the biosimilar product to determine what conditions of use and routes of administration are approved for the biosimilar and to make the appropriate prescribing decision for their patient.

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Thank you for your attention.

For more information, go to www.fda.gov/biosimilars

M. Stacey Ricci, M.Eng., Sc.D.
Acting Director, Scientific Review Staff
Office of Therapeutic Biologics and Biosimilars
Office of New Drugs, CDER
Stacey.Ricci@fda.hhs.gov

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