



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-D-5473]

Promotional Labeling and Advertising Considerations for Prescription Biological Reference Products, Biosimilar Products, and Interchangeable Biosimilar Products: Questions and Answers; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a final guidance for industry entitled “Promotional Labeling and Advertising Considerations for Prescription Biological Reference Products, Biosimilar Products, and Interchangeable Biosimilar Products: Questions and Answers.” The guidance addresses questions that manufacturers, packers, distributors, and their representatives (firms) may have when developing FDA-regulated promotional labeling and advertisements (promotional communications) for prescription reference products, biosimilar products, and interchangeable biosimilar products licensed under the Public Health Service Act (PHS Act). This guidance finalizes the revised draft guidance of the same title issued on April 25, 2024.

DATES: The announcement of the guidance is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to

<https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see “Written/Paper Submissions” and “Instructions”).

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2019-D-5473 for “Promotional Labeling and Advertising Considerations for Prescription Biological Reference Products, Biosimilar Products, and Interchangeable Biosimilar Products: Questions and Answers.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:

<https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one

self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Twyla Mosey, Office of Prescription Drug Promotion, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 3203, Silver Spring, MD 20993-0002, 301-796-1200, CDER-OPDP-RPM@fda.hhs.gov; or Phillip Kurs, Center for Biologics Evaluation and Research, Food and Drug Administration, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled “Promotional Labeling and Advertising Considerations for Prescription Biological Reference Products, Biosimilar Products, and Interchangeable Biosimilar Products: Questions and Answers.” This guidance addresses questions firms may have when developing FDA-regulated promotional communications for prescription reference products licensed under section 351(a) of the PHS Act (42 U.S.C. 262(a)) and prescription biosimilar products, including interchangeable biosimilar products, licensed under section 351(k) of the PHS Act.

Section 351(k) of the PHS Act provides an abbreviated licensure pathway for biological products shown to be biosimilar to or interchangeable with an FDA-licensed reference product. Section 351(i) of the PHS Act defines *biosimilarity* to mean “that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components” and that “there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.” To meet the standard for *interchangeability*, an applicant must provide sufficient information to demonstrate biosimilarity and also to demonstrate that the biological product can be expected to produce the same clinical result as the reference product in any given patient and, if the biological product is administered more than once to an individual, the risk in terms of safety or

diminished efficacy of alternating or switching between the 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 (section 351(k)(4) of the PHS Act). Interchangeable biosimilar products may be substituted for the reference product without the intervention of the prescribing healthcare provider (section 351(i)(3) of the PHS Act). Decisions regarding pharmacy-level substitution are subject to State pharmacy law.

The guidance discusses considerations for presenting data and information about reference products or biosimilar products, including interchangeable biosimilar products, in promotional communications to help ensure that they are accurate, truthful, and non-misleading. The guidance includes information about general requirements for the content of FDA-regulated promotional communications that apply to reference products and biosimilar products and includes more specific considerations for developing these promotional communications for reference products and biosimilar products, such as:

- Identifying reference products and biosimilar products
- Presenting information from the studies conducted to support licensure of the reference product when the information is included in the FDA-approved labeling of both the reference product and the biosimilar product
- Presenting data or information for a biosimilar product related to the safety or effectiveness of the biosimilar product that is not included in the FDA-approved labeling but is consistent with the FDA-approved labeling for that product
- Comparing a biosimilar product and its reference product
- Submitting promotional communications to FDA

The guidance also provides examples to illustrate some of the considerations outlined in the guidance.

This guidance finalizes the revised draft guidance of the same title issued on April 25, 2024 (89 FR 31757) (2024 draft guidance). FDA considered comments received on the 2024 draft guidance as the guidance was finalized.

Changes from the 2024 draft guidance to the final guidance include:

- Clarification that the recommendations in the guidance apply regardless of the medium of communication (e.g., paper, digital)
- Further discussion related to the considerations that firms should take into account when comparing biosimilar products and reference products
- Editorial changes for consistency, readability, and clarity

In conjunction with the enactment of the Biosimilar User Fee Amendments of 2022 (BsUFA III), FDA agreed to work toward publishing a final guidance on promotional labeling and advertising considerations for interchangeable biosimilar products within 18 months after the close of the public comment period on the draft guidance, as described in the document titled “Biosimilar Biological Product Reauthorization Performance Goals and Procedures Fiscal Years 2023 through 2027.”

This guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on “Promotional Labeling and Advertising Considerations for Prescription Biological Reference Products, Biosimilar Products, and Interchangeable Biosimilar Products: Questions and Answers.” It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

FDA considered the applicability of Executive Order 14192, per OMB guidance in M-25-20, and finds this action to be deregulatory in nature.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. The previously approved collections of information

are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521). The collections of information in 21 CFR part 314, Form FDA 2253 (Transmittal of Advertisements and Promotional Labeling for Drugs and Biologics for Human Use), and the guidance for industry entitled “Providing Regulatory Submissions in Electronic and Non-Electronic Format: Promotional Labeling and Advertising Materials for Human Prescription Drugs” have been approved under OMB control number 0910-0001. The collections of information in 21 CFR 601.12 have been approved under OMB control number 0910-0338. The collections of information in 21 CFR 202.1 and in the guidance for industry entitled “Medical Product Communications That Are Consistent With the Food and Drug Administration Required Labeling: Questions and Answers” have been approved under OMB control number 0910-0686. The collections of information in 21 CFR part 11 relating to electronic records and signatures have been approved under OMB control number 0910-0303. The collections of information relating to the submission of biosimilar and interchangeable product applications under section 351(k) of the Public Health Service Act (42 U.S.C. 262(k)) have been approved under OMB control number 0910-0718.

III. Electronic Access

Persons with access to the internet may obtain the guidance at <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>, <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Lowell M. Zeta,

Acting Deputy Commissioner for Policy, Legislation, and International Affairs.