



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2020-D-1553]

Premenopausal Women with Breast Cancer: Developing Drugs for Treatment; 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 “Premenopausal Women with Breast Cancer: Developing Drugs for Treatment.” This guidance provides recommendations regarding the inclusion of premenopausal women in breast cancer clinical trials. The guidance is intended to assist stakeholders, including sponsors and institutional review boards, responsible for the development and oversight of clinical trials for breast cancer drugs. This guidance finalizes the draft guidance of the same title issued on October 8, 2020.

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-2020-D-1553 for "Premenopausal Women with Breast Cancer: Developing Drugs for Treatment." 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 (CDER), Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002 or Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, 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: Jennifer Gao, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 2135, Silver Spring, MD 20993, 240-402-4683; or Julia Beaver, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 2100, Silver Spring, MD 20993, 240-402-0489; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled “Premenopausal Women with Breast Cancer: Developing Drugs for Treatment.” This guidance provides recommendations regarding the inclusion of premenopausal women, as defined by serum hormonal levels (including but not limited to follicle-stimulating hormone and estradiol), in breast cancer clinical trials. The issues of fertility and fertility preservation when treating premenopausal women with breast cancer are outside the scope of this guidance.

Historically, premenopausal women have been excluded from some trials that have investigated the efficacy of certain drugs that rely upon manipulation of the hormonal axis for the treatment of hormone receptor (HR) positive breast cancer. In some cases, separate studies have been conducted to confirm the benefit in this patient population. Certain groups of drugs, such as chemotherapy, immunotherapy, and targeted therapy (which act independent of the hormonal axis), have similar efficacy in pre- and postmenopausal women with breast cancer. Based on a review of the literature, FDA believes hormonal drugs administered to premenopausal women with HR-positive breast cancer, with adequate estrogen suppression, are likely to have the same efficacy and safety profile as in postmenopausal women.

The guidance encourages sponsors to discuss their breast cancer drug development plan with CDER and CBER, as applicable, early in development. The guidance recommends that

menopausal status should not be the basis for exclusion from breast cancer clinical trials. The guidance includes recommendations regarding eligibility criteria and study planning and design intended to facilitate the inclusion of premenopausal women in breast cancer clinical trials.

This guidance finalizes the draft guidance entitled “Premenopausal Women with Breast Cancer: Developing Drugs for Treatment” issued on October 8, 2020 (85 FR 63559). FDA considered comments received on the draft guidance as the guidance was finalized. Changes from the draft to the final guidance include additional recommendations on the importance of clinical studies reflecting racial and ethnic diversity and to collect patient experience data throughout the development program. Other changes include updated recommendations on collection of clinical effects as part of the clinical development program or as part of a postmarketing requirement or commitment as applicable.

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 “Premenopausal Women with Breast Cancer: Developing Drugs for Treatment.” 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.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014; the collections of information in 21 CFR part 314 have been approved under OMB control number 0910-0001; and the collections of information in 21 CFR part 601 have been approved under 0910-0338.

III. Electronic Access

Persons with access to the internet may obtain the guidance at either <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>.

Dated: June 15, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

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