investigation by a State agency of complaints relating to compounded drug products distributed outside such State; or (2) if the drug product is compounded in a State that has not entered into such an MOU, the licensed pharmacist, pharmacy, or physician does not distribute, or cause to be distributed, compounded drug products out of the State in which they are compounded in quantities that exceed 5 percent of the total prescription orders dispensed or distributed by such pharmacy or physician (statutory 5 percent limit) (see section 503A(b)(3)(B)(i) and (ii) of the FD&C Act).

In the **Federal Register** of October 27, 2020 (85 FR 68074), FDA announced the availability of the final standard MOU describing the responsibilities of a State Board of Pharmacy or other appropriate State agency that chooses to sign the final standard MOU in investigating and responding to complaints related to drug products compounded in such State and distributed outside such State and in addressing the interstate distribution of inordinate amounts of compounded human drug products.

In the October 27, 2020, **Federal Register** notice, FDA stated that it was providing a 365-day period for States to decide whether to sign the final standard MOU before FDA intended to begin enforcing the statutory 5 percent limit in States that do not sign the final standard MOU. Based on comments from stakeholders, it was FDA's understanding that this timeframe corresponds to a full legislative cycle for most States and would, therefore, afford sufficient time for States to modify their laws and regulations, if necessary in order to enter into the final standard MOU.

Following publication of October 27, 2020, **Federal Register** notice, FDA received requests to extend the period before FDA intends to begin enforcing the statutory 5 percent limit in States that do not sign. The requesters asserted that the time period of 365 days was insufficient to allow State governments to thoroughly evaluate the final standard MOU and modify their laws and regulations, if necessary in order to sign, because many State governments were focused on addressing concerns raised by the Coronavirus Disease 2019 (COVID–19) pandemic.

FDA has considered the requests and other relevant factors and is extending the period before FDA intends to begin enforcing the statutory 5 percent limit in States that do not sign the final standard MOU until October 27, 2022. FDA believes that an additional 1 year will allow sufficient time for States to consider the final standard MOU and modify their laws and regulations, if necessary. FDA's understanding is that emergency pandemic response activities have now begun to ease, permitting States more time to take up other issues. Accordingly, we believe a 1-year extension addresses the need that some States have expressed for additional time, without adding significant delay to FDA's implementation of the important public health protections afforded by section 503A(b)(3)(B) of the FD&C Act.

States may sign the final standard MOU at any time, including after the period is scheduled to end on October 27, 2022.

Dated: August 4, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

[FR Doc. 2021–16937 Filed 8–6–21; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–D–3931]

Nonmetastatic Castration-Resistant Prostate Cancer: Considerations for Metastasis-Free Survival Endpoint in Clinical Trials; 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 ''Nonmetastatic Castration-Resistant Prostate Cancer: Considerations for Metastasis-Free Survival Endpoint in Clinical Trials.'' Recent approvals of several drug products for patients with nonmetastatic castration-resistant prostate cancer have been supported by randomized clinical trials demonstrating improvements in metastasis-free survival. This guidance intends to inform potential future applicants regarding the Agency's expectations for collection, analysis, and reporting of data pertaining to metastasis-free survival. This guidance finalizes the draft guidance of the same title issued on November 14, 2018.

DATES: The announcement of the guidance is published in the **Federal Register** on August 9, 2021.

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–2018–D–3931 for ''Nonmetastatic Castration-Resistant Prostate Cancer: Considerations for Metastasis-Free Survival Endpoint in Clinical Trials.'' 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; or the Office of Communication, Outreach, and Development, Center for Biologics Evaluation and Research, 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: Julia Beaver, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 2100, Silver Spring, MD 20993–0002, 240–402–0489; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm 7268, Silver Spring, MD 20993–0002, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a final guidance for industry entitled ''Nonmetastatic Castration-Resistant Prostate Cancer: Considerations for Metastasis-Free Survival Endpoint in Clinical Trials.'' Nonmetastatic castration-resistant prostate cancer (nmCRPC) is defined by rising prostate-specific antigen (PSA) despite castrate levels of testosterone and no radiographic evidence of distant metastatic disease. Despite earlier detection of localized prostate cancer and advances in surgical and radiation techniques, many patients will continue to have rising PSA after local therapy (*e.g.,* surgery, radiation) for recurrent disease and subsequent androgen deprivation therapy. Patients with nmCRPC can have a prolonged disease course following the detection of a rising PSA until documentation of distant metastases or death. Such a prolonged assessment period (in which patients may receive multiple therapies) with low death rates may make the use of overall survival impractical as a primary endpoint to support approval of products in this disease setting.

These issues were discussed at an Oncologic Drugs Advisory Committee meeting in 2011, during which the committee acknowledged that endpoints that can be measured earlier in the course of disease, such as metastasis-free survival, defined as the time from randomization to distant radiographic disease or death, would be useful in assessing the treatment effect of products in patients with nmCRPC. Additionally, the Oncologic Drugs Advisory Committee noted that the transition from nmCRPC to radiographically detectable metastatic disease (*e.g.,* bone disease or visceral disease) is a clinically relevant event that can be associated with morbidity and the need for additional medical interventions. Conversely, local progression events may be treated with local therapies, may never progress to distant disease, and may not lead to systemic morbidity. Thus, a large treatment effect on metastasis-free survival with an acceptable safety profile could demonstrate clinical benefit and support product approval.

This guidance finalizes the draft guidance of the same title issued on November 14, 2018, (83 FR 56857). Changes from the draft to the final include clarifying edits and expanding upon certain recommendations in the draft guidance.

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 ''Nonmetastatic Castration-Resistant Prostate Cancer: Considerations for Metastasis-Free Survival Endpoint in Clinical Trials.'' 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 parts 50 and 56 (Protection of Human Subjects and Institutional Review Boards) have been approved under OMB control number 0910–0130.

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,* or *https://www.regulations.gov.*

Dated: August 2, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

[FR Doc. 2021–16929 Filed 8–6–21; 8:45 am]

BILLING CODE 4164–01–P