



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-D-4751]

FDA Reauthorization Act Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs; 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 “FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs.” This guidance addresses early planning for pediatric evaluation of certain molecularly targeted oncology drugs, including biological products, for which original new drug applications (NDAs) and biologics license applications (BLAs) are expected to be submitted to FDA, in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act) as amended by the FDA Reauthorization Act of 2017 (FDARA). Early pediatric evaluation of certain molecularly targeted oncology drugs as required by the FD&C Act is expected to accelerate the creation of an informed pediatric development plan and ultimately the development of promising drugs for pediatric patients. This guidance finalizes the draft guidance entitled “FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs” issued on December 13, 2019, and finalizes certain material related to implementation of FDARA that was included in the draft guidance entitled “Pediatric Study Plans for Oncology Drugs: Questions and Answers” issued on January 16, 2020. Accordingly, FDA does not intend to finalize the draft guidance entitled “Pediatric Study Plans for Oncology Drugs: Questions and Answers,” which is now withdrawn.

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-4751 for “FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs.” 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. The guidance may also be obtained by mail by calling CBER at 1-800-835-4709 or 240-402-8010. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Gregory Reaman, Oncology Center of Excellence, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 2202, Silver Spring, MD 20993-0002, 301-796-0785, Gregory.Reaman@fda.hhs.gov; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911, Stephen.Ripley@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled “FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs.” This guidance addresses early planning for pediatric evaluation of certain molecularly targeted oncology drugs (including biological products) for which original NDAs and BLAs are expected to be submitted to FDA, in accordance with the provisions of section 505B of the FD&C Act (21 U.S.C. 355c). Section 505B of the FD&C Act (also referred to as the Pediatric Research Equity Act or PREA) was amended by FDARA.

The amendments to section 505B require pediatric evaluation of certain molecularly targeted oncology drugs, with the goal of helping address the needs of pediatric patients with cancer. FDARA amended section 505B of the FD&C Act to require--for original applications submitted on or after August 18, 2020--pediatric investigations of certain targeted cancer drugs with new active ingredients, based on molecular mechanism of action rather than clinical indication. Specifically, if an original NDA or BLA is submitted on or after August 18, 2020, for a new active ingredient, and the drug or biological product that is the subject of the application is intended for treatment of an adult cancer and directed at a molecular target FDA determines to be substantially relevant to the growth or progression of a pediatric cancer, reports on the molecularly targeted pediatric cancer investigation required under section 505B(a)(3) of the FD&C Act must be submitted with the marketing application, unless the requirement is waived or deferred (sections 505B(a)(1)(B) and (a)(3)(C) of the FD&C Act).

This guidance provides recommendations on regulatory considerations related to the amendments to section 505B of the FD&C Act, including information on molecular targets, factors FDA intends to consider in the determination of whether a molecular target is substantially relevant to the growth or progression of a pediatric cancer, information regarding the molecular target lists, recommendations on the content of the initial pediatric study plan and description of recommended study(ies), additional considerations for rare cancers, information pertaining to oncology drug combination regimens, and considerations regarding planned waivers and deferrals. In addition, the guidance includes information regarding global implications of, and the importance of international collaboration regarding, pediatric oncology studies.

This guidance finalizes the draft guidance entitled “FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs,” issued on December 13, 2019 (see 84 FR 68174). This guidance also finalizes certain recommendations related to implementation of FDARA section 504 that was included in the draft guidance entitled

“Pediatric Study Plans for Oncology Drugs: Transitional Information Until Full Implementation of FDARA Section 504 Questions and Answers,” issued on January 16, 2020 (85 FR 2746). FDA considered comments received on both of these draft guidances as this guidance was finalized. Changes from the draft to the final guidance include the following: describing additional safeguards for children in clinical investigations (see 21 CFR part 50, subpart D), providing information sources that have been used in the development of the molecular target lists, describing information that should be included in a request for a meeting regarding early advice on pediatric development for oncology projects subject to the amended provisions, and providing additional information and clarification regarding planned waivers and deferrals. Recommendations that were finalized in this guidance from the draft guidance entitled “Pediatric Study Plans for Oncology Drugs: Transitional Information Until Full Implementation of FDARA Section 504 Questions and Answers” include the following: clarifying that a supplemental application does not trigger the requirement to submit reports on the molecularly targeted pediatric cancer investigation and describing considerations for initial pediatric study plans for oncology drug combination regimens. In addition, editorial changes were made to improve clarity.

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 “FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs.” 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 parts 50 and 56 have been approved under OMB control number 0910-0130; the collections of information in 21 CFR part 314 have been approved under OMB control number 0910-0001; 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 601 have been approved under OMB control number 0910-0338; the collections of information in FDA’s draft guidance for industry entitled “Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products” have been approved under OMB control number 0910-0429; and the collections of information pertaining to submission of a biologics license application under section 351(k) of the Public Health Service Act and the draft guidance for industry entitled “Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products” have been approved under OMB control number 0910-0719.

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>, or <https://www.regulations.gov>.

Dated: May 18, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.