4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2020-D-1480]

Drug-Drug Interaction Assessment for Therapeutic Proteins; 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 "Drug-Drug Interaction Assessment for Therapeutic Proteins." With the continued market growth and increased clinical use of therapeutic proteins, it is important to understand the nature of and the potential for drug-drug interactions (DDIs) with these products. The purpose of this guidance is to help sponsors of investigational new drug applications (INDs) and applicants of biologics license applications (BLAs) determine the need for DDI studies for a therapeutic protein by providing a systematic, risk-based approach. This guidance finalizes the draft guidance of the same title issued on August 10, 2020.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-1480 for "Drug-Drug Interaction Assessment for Therapeutic Proteins." 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: Elimika Pfuma Fletcher, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51,

Rm. 2162, Silver Spring, MD 20993, 301-796-3473; or Diane Maloney, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-8113.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "Drug-Drug Interaction Assessment for Therapeutic Proteins." With the continued market growth and increased clinical use of therapeutic proteins, it is important to understand the nature of and the potential for DDIs with these products. This guidance supplements the final FDA guidances for industry entitled "In Vitro Drug Interaction Studies--Cytochrome P450 Enzyme- and Transporter-Mediated Drug Interactions" and "Clinical Drug Interaction Studies--Cytochrome P450 Enzyme- and Transporter-Mediated Drug Interactions" (January 2020) by providing recommendations for a systematic, risk-based approach to determining the need for DDI studies for therapeutic proteins. This guidance discusses considerations for assessing DDIs for therapeutic proteins, including situations where determining the DDI potential of a therapeutic protein is warranted. The guidance also discusses various types of DDI assessments, considerations for study design, and recommendations for labeling.

This guidance finalizes the draft guidance entitled "Drug-Drug Interaction Assessment for Therapeutic Proteins" issued on August 10, 2020 (85 FR 48259). FDA considered comments received on the draft guidance as the guidance was finalized. Changes from the draft to the final guidance include: (1) clarifying that FDA review divisions should be consulted related to novel modalities, and that limitations exist in knowledge related to effect of therapeutic proteins on transporters; (2) including more literature references; (3) limiting the text related to antibody-drug conjugates (ADCs) because a draft guidance on clinical pharmacology considerations for ADCs has been published; and (4) including language about potential use of various modeling approaches on a case by case basis. 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 "Drug-Drug Interaction Assessment for Therapeutic Proteins." 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 for the submission of investigational new drug applications in 21 CFR part 312 have been approved under OMB control number 0910-0014. The collections of information for the submission of new drug applications in 21 CFR part 314 have been approved under OMB control number 0910-0001. The collections of information for the submission of biologics license applications in 21 CFR part 601 have been approved under OMB control 0910-0338. The collections of information pertaining to the submission of prescription drug labeling under 21 CFR 201.56 and 201.57 have been approved under OMB control number 0910-0572.

III. Electronic Access

Persons with access to the internet may obtain the draft 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.

Dated: May 31, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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