



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2026-D-8693]

Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosage; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry titled “Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosage.” This guidance assists sponsors in the design and analysis of studies that assess the influence of hepatic impairment on the pharmacokinetics and, where appropriate, the pharmacodynamics of a drug, including therapeutic biological products. When final, this guidance will represent FDA’s current thinking. FDA is also withdrawing the guidance for industry titled “Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling” (May 2003), which formerly provided FDA’s thinking relating to studies to assess the effect of hepatic impairment on the pharmacokinetics or pharmacodynamics of a drug and recommendations to include hepatic impairment information in labeling.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance 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-2026-D-8693 for "Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosage." 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 draft 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 draft guidance document.

FOR FURTHER INFORMATION CONTACT: Martina Sahre, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave, Silver Spring, MD, 20993, 301-796-9659, Martina.Sahre@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry titled “Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosage.” This guidance assists sponsors in the design and analysis of studies that assess the influence of impaired hepatic function, herein referred to as hepatic impairment (HI), on the pharmacokinetics and, where appropriate, the pharmacodynamics of a drug, including therapeutic biological products.

The liver is a major organ involved in the elimination of drugs through metabolism and/or through biliary excretion of unchanged drug or metabolites. Liver disease can change these metabolic and excretory pathways by impacting drug metabolizing enzymes and transporters. In addition, the absorption and distribution of drugs can also be affected by liver disease. In summary, liver disease can lead to changes in a drug’s pharmacokinetics, to a degree necessitating different recommendations for use of the drug (e.g., a different recommended dosage in patients with HI). Patients with HI have often been excluded from clinical trials, even when they are part of the intended target population. Characterizing the impact of HI on pharmacokinetics during early clinical drug development and employing modeling and simulation strategies, where feasible, can facilitate inclusion of patients with HI in clinical trials.

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on “Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosage.” 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 is also withdrawing the guidance for industry titled “Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling” (68 FR 32531, May 30, 2003), which formerly provided FDA’s thinking relating to studies to assess the effect of HI on the pharmacokinetics or pharmacodynamics of a drug and recommendations to include HI information in labeling.

As we develop final guidance on this topic, FDA will consider comments on costs or cost savings the guidance may generate, relevant for Executive Order 14192.

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 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. The collections of information in 21 CFR 201.56 and 201.57 relating to certain prescription product labeling requirements 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/regulatory-information/search-fda-guidance-documents>, or

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

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

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