4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2026-N-3499]

Obesity and Drug Dosing: Clinical Pharmacology Considerations; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; establishment of a public docket; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is establishing a public docket entitled "Obesity and Drug Dosing: Clinical Pharmacology Considerations." The Agency is soliciting input from interested persons on assessing the effect of obesity on drug pharmacokinetics and pharmacodynamics during drug (including biological product) development. These assessments could potentially inform whether obesity impacts the safety and effectiveness of the drug and dosing recommendations for obese patients.

DATES: Submit either electronic or written comments by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: FDA is establishing a docket for public comment on this notice. The docket number is FDA-2026-N-3499. The docket will close on [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Submit either electronic or written comments by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. The https://www.regulations.gov electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Comments received by mail/hand delivery/courier (for

written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

You may submit comments 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-N-3499 for "Obesity and Drug Dosing: Clinical Pharmacology Considerations; Request for Comments." 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.

FOR FURTHER INFORMATION CONTACT:

Martina Sahre, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, 301-796-9659.

SUPPLEMENTARY INFORMATION:

I. Background

Obesity is a critical and increasingly prevalent public health concern in the United States affecting approximately 20% of children[1] and approximately 40% of adults.[2] It is linked to a variety of comorbidities such as diabetes and heart disease. The U.S. Centers for Disease Control and Prevention (CDC) defines obesity as having a body mass index of ≥30 kg/m^2 for adults and a body mass index at or above the 95th percentile (based on age and sex) for children.[1,2] Despite its high prevalence, the effect of obesity on drug pharmacokinetics, pharmacodynamics, effectiveness, and safety is not consistently assessed in clinical trials, except in certain therapeutic areas (e.g., obesity, Type 2 diabetes mellitus, sleep apnea). Furthermore, obesity-related information on these aspects is often absent in drug product labels.

Obesity is reported to affect the pharmacokinetics and pharmacodynamics of drugs in several ways: 1) lipophilic drugs can show increased distribution into fat tissues; 2) absorption can be altered due to changes in gastric transit times and gastrointestinal pH values; 3) metabolism and excretion could be altered due to an impact on drug-metabolizing enzymes, transporters, or changes in renal clearance; and 4) the sensitivity of drug targets could be altered. The impact of body size (usually total body weight) is typically considered as part of population pharmacokinetic analysis. If identified as a significant covariate in population pharmacokinetic analysis, the need for dosing based on body weight, body mass index, or body surface area is routinely assessed. However, limited enrollment of obese patients in clinical trials--particularly

---

[1] U.S. Centers for Disease Control and Prevention (CDC), 2024, Childhood Obesity Facts, CDC, accessed May 8, 2025, https://www.cdc.gov/obesity/childhood-obesity-facts/childhood-obesity-facts.html.
[2] CDC, 2024, Adult Obesity Facts, CDC, accessed May 8, 2025, https://www.cdc.gov/obesity/adult-obesity-facts/index.html.

patients with morbid obesity--limits pharmacokinetic and pharmacodynamic assessments across a full range of body sizes.

II. Request for Information and Comments

FDA invites interested persons to provide detailed information and comments on relevant considerations for evaluating the impact of obesity on drug pharmacokinetics and pharmacodynamics and the need for specific dosage recommendations. Please provide the rationale for your suggestions and include supporting data if available.

FDA is particularly interested in responses to the following overarching questions:

1. Body mass index is often used to identify and classify the degree of obesity. Is the categorization of body mass index sufficient for evaluating the impact of obesity on drug pharmacokinetics or pharmacodynamics and to inform recommendations for use in the obese population? If not, what other pragmatic measures (e.g., anthropometric, biochemical, clinical) can be used in drug development to assess the impact of obesity on drug pharmacokinetics or pharmacodynamics and develop appropriate dosing recommendations for adults and pediatric patients? Please also discuss the applicability of body mass index or other measures in pediatric patients with obesity.
2. What drug-specific characteristics or therapeutic-area/disease-related considerations are important when assessing the impact of obesity on pharmacokinetics or pharmacodynamics?
3. How should the impact of obesity on pharmacokinetics or pharmacodynamics, and potentially safety and effectiveness, be assessed throughout drug development (e.g., standalone phase 1 studies, using model-informed drug development approaches to evaluate data from late phase trials that can also incorporate available data from other phases of drug development)? Please also comment on any specific study design considerations for the different approaches proposed and the timing of such assessments.

III. Electronic Access

Persons with access to the internet may obtain relevant clinical pharmacology guidances at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

Citation Authority: 21 CFR 312, 21 CFR 314, and 21 CFR 601

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2026-08521 Filed: 4/30/2026 8:45 am; Publication Date: 5/1/2026]