



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2021-N-0031]

Best Practices for Development and Application of Disease Progression Models; Public Workshop; Establishment of a Public Docket; Request for Comments

AGENCY: Food and Drug Administration, HHS.

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

SUMMARY: One of the goals of the Prescription Drug User Fee Act of 2017 (PDUFA VI), part of the FDA Reauthorization Act of 2017 (FDARA), is advancing model-informed drug development (MIDD). The "Best Practices for Development and Application of Disease Progression Models" workshop fulfills FDA's performance commitment under PDUFA VI to hold a workshop. The Food and Drug Administration (FDA or Agency) is opening a docket to solicit public input on topics areas for an upcoming disease progression modeling workshop. The purpose of this public workshop is to discuss the best practices for developing disease progression models and their application to support drug development decisions; share experiences and case studies that highlight the opportunities and limitations in the development and application of disease progression models including models for natural history of disease and clinical trial simulations; and discuss the knowledge gaps and research needed to advance the development and use of disease progression models.

DATES: To ensure that the Agency considers your input, submit either electronic or written comments by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: FDA is establishing a docket for public comment on this workshop. The docket number is FDA-2021-N-0031. The docket will close on [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Submit either electronic or written

comments on this public workshop by [INSERT DATE 30 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 30 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 30 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-2021-N-0031 for "Best Practices for Development and Application of Disease Progression Models; Public Workshop; Request for Comments." Received comments, those filed in a timely manner (see ADDRESSES), 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: Maryanne Dingman, Office of Clinical Pharmacology, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, 301-796-8777, 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.

SUPPLEMENTARY INFORMATION:

I. Background

Under FDARA, FDA agreed, in accordance with section I of the PDUFA VI Performance Goals, "Ensuring the Effectiveness of the Human Drug Review, part J, Enhancing Regulatory Decision Tools to Support Drug Development and Review," to hold several workshops to identify best practices for MIDD. The workshop entitled "Best Practices for Development and Application of Disease Progression Models," to be held in 2021, fulfills FDA's performance commitment under PDUFA VI. FDA is requesting comments from the public to help identify areas of interest to be discussed during the workshop given the wide range of approaches to data collection, aggregation modeling, model development, verification and validation, and potential applications in drug development and regulatory review. The outcome will help the Agency inform the public on current experience, emerging techniques, and limitations to streamline the drug model development and facilitate the decision-making process.

II. Request for Information and Comments

Interested persons are invited to provide detailed information and comments on areas of interest to discuss during the upcoming "Best Practices for Development and Application of Disease Progression Models " workshop. FDA is interested in responses about best practice considerations including, but not limited to, the following:

1. The development and application of different types of disease progression models (e.g., empirical, semi-mechanistic, and fully mechanistic or systems modeling).
2. Modeling natural history of disease, specifically methodological considerations and challenges in characterizing the natural relationship between pharmacodynamic markers and clinical outcomes.
3. Clinical trial simulations based on disease progression/natural history models to support drug development and regulatory decisions.

Dated: February 16, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

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