



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2024-D-1032]

Risk Evaluation and Mitigation Strategy Logic Model: A Framework to Link Program Design With Assessment; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “REMS Logic Model: A Framework to Link Program Design With Assessment.” The guidance describes FDA’s risk evaluation and mitigation strategy (REMS) logic model. The REMS logic model is a framework that FDA recommends, which provides applicants with a systematic, structured approach to the design, implementation, and evaluation of a REMS. The aim of applying the REMS logic model is to develop clear goals, objectives, and strategies that align with the intended outcomes and to help applicants of new drug applications (NDAs), biologics license applications (BLAs), and abbreviated new drug applications (ANDAs) incorporate REMS assessment planning into the design of a REMS. The principles in this guidance apply to designing a REMS, developing a REMS assessment, and modifying a REMS.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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-2024-D-1032 for "REMS Logic Model: A Framework to Link Program Design With Assessment." 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 the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillendale 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. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Gita Toyserkani, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 1106, Silver Spring, MD, 20993-0002, 301-796-1783, or James Myers, 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

FDA is announcing the availability of a draft guidance for industry entitled “REMS Logic Model: A Framework to Link Program Design With Assessment.” Section 505-1 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355-1) establishes FDA’s REMS authority. A REMS is a required risk management strategy that can include one or more elements to ensure that the benefits of a drug outweigh its risks (see section 505-1(a) of the FD&C Act). A REMS can include a Medication Guide, a patient package insert, a communication plan, and certain packaging and safe disposal technologies for a drug that poses a serious risk of abuse or overdose. FDA also may require certain elements to assure safe use as part of the REMS for drugs or biological products (see section 505-1(f) of the FD&C Act).

A REMS, like other public health programs, involves a set of activities or interventions to achieve an intended outcome. Program evaluation is a systematic method of collecting, analyzing, and using data to examine the effectiveness and efficiency of those programs and to inform continuous program improvement. Several theories, frameworks, and logic models have been used to guide both program design and evaluation. In particular, logic models describe in detail how a program or intervention operationally works to achieve benefits and captures the

logical flow and linkages that exist within the program or intervention and its proximal and distal outcomes. Leveraging this type of systematic approach is a critical aspect to the success and effectiveness of programs.

In 2013, FDA received feedback from the Office of the Inspector General (available at <https://oig.hhs.gov/oei/reports/OEI-04-11-00510.asp>) on the overall effectiveness of REMS. To address the feedback, FDA convened a public meeting on REMS standardization (78 FR 30313, May 22, 2013) (meeting materials available at <https://www.fda.gov/industry/prescription-drug-user-fee-amendments/background-materials-rems-standardization-and-evaluation-public-meeting>). FDA sought stakeholder input on using a commonly cited framework for program planning and evaluation. FDA also encouraged applicants to consider using healthcare program assessment frameworks to assess REMS (see the draft guidance for industry entitled “REMS Assessment: Planning and Reporting” (available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/rems-assessment-planning-and-reporting>)). FDA continued to explore and research the application of theories, frameworks, and models to develop a systematic approach to REMS design, implementation, and evaluation. Existing healthcare program evaluation frameworks, together with stakeholder feedback and FDA’s research, informed the development of FDA’s REMS logic model.

This draft guidance describes FDA’s REMS logic model, which uses common logic model principles adapted for use in a REMS and makes explicit the scientific evidence, assumptions, and underlying logic that support the program and the various processes behind it. The REMS logic model provides applicants¹ with a recommended systematic, structured approach to design, implement, and evaluate a REMS. The REMS logic model delineates the relationship between the goal, objectives, strategies, and intended outcomes. The logic model

¹ For the purposes of the “REMS Logic Model: A Framework to Link Program Design With Assessment” guidance, the term *applicant* refers to sponsors of investigational new drug applications and applicants of NDAs, BLAs, and ANDAs.

includes the three phases of a REMS life cycle: design, implement, and evaluate. Each phase is further separated into two or more steps. Application of the REMS logic model begins with the design phase (situation context, program goal). The next phase is the implement phase (inputs, activities, outputs). The last phase is the evaluate phase (outcome, impact). The REMS logic model, although described in sequential steps, is an iterative process that involves moving back and forth or toggling between steps and phases to address uncertainties, validating assumptions, incorporating new information, and refining the program.

This draft guidance is being issued to fulfill the performance goals (available at <https://www.fda.gov/industry/prescription-drug-user-fee-amendments/pdufa-vii-fiscal-years-2023-2027>) under the sixth reauthorization of the Prescription Drug User Fee Act (PDUFA VII). This REMS logic model guidance is the first in a series of planned guidances for industry and FDA staff to optimize REMS design and improve the way a REMS is assessed.

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 "REMS Logic Model: A Framework to Link Program Design With Assessment." 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. 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 for the submission of investigational new drug applications have been approved under OMB control number 0910-0014. The collections of information in 21 CFR part 314 for the submission of new drug applications and abbreviated new drug applications have been approved

under OMB control number 0910-0001. The collections of information in 21 CFR part 601 for the submission of biologics license applications have been approved under OMB control number 0910-0338. The collections of information in 21 CFR part 208 pertaining to Medication Guides for prescription drug and biological products have been approved under OMB control number 0910-0393. The collections of information in 21 CFR 201.56 and 201.57 for the content and format requirements for labeling of drugs and biologics have been approved under OMB control number 0910-0572. The collections of information in 21 CFR part 316 regarding orphan drug product development are approved under OMB control number 0910-0167. The collections of information pertaining to Prescription Drug User Fee Program have been approved under OMB control number 0910-0297.

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 2, 2024.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2024-09928 Filed: 5/6/2024 8:45 am; Publication Date: 5/7/2024]