Proposed Rule Snapshot

U.S. FOOD & DRUG ADMINISTRATION

Medication Guide: Patient Medication Information (PMI), Proposed Rule

What does the proposed rule require?

The proposed rule requires applicants to prepare a new type of FDA-approved Medication Guide for (1) prescription drug products[1] used, dispensed, or administered in an outpatient setting and (2) blood and blood components transfused in an outpatient setting. FDA refers to the new Medication Guide as Patient Medication Information (PMI). PMI would be stored in an online central repository managed by FDA and would be freely accessible to the public.

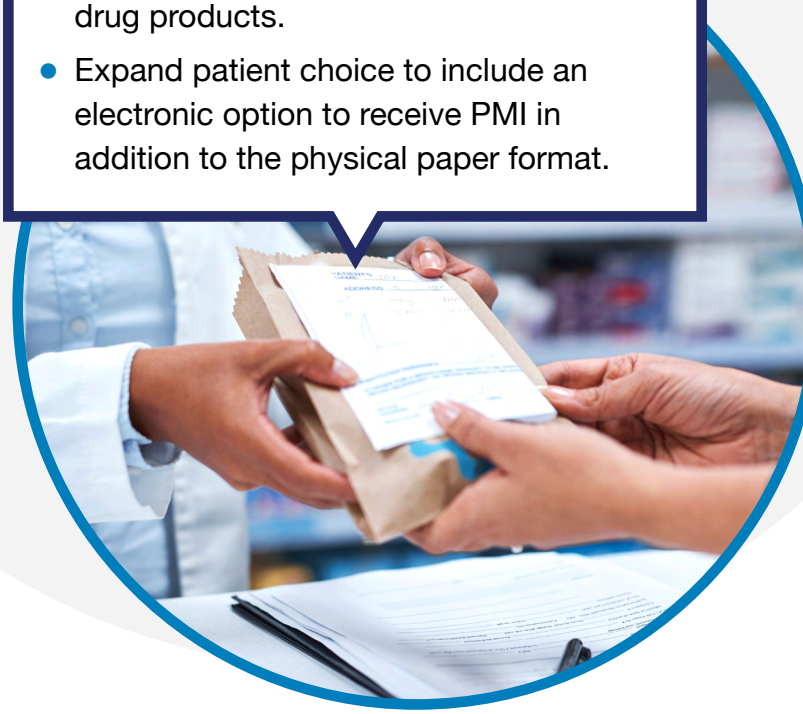
Why is FDA issuing the proposed rule?

FDA recognizes the importance of providing written information to patients about their prescription drug products. Evidence suggests that such information can help patients use their prescription drug products safely and effectively, which may reduce preventable adverse drug reactions and improve health outcomes. Communications that do not provide clarity regarding prescription medications may lead to patient nonadherence, which may, in turn, be responsible for increased hospitalizations, treatment failures, and even increased death rates in the United States.

What are the benefits of the proposed PMI?

Once finalized, PMI would offer the following benefits:

- Improve public health by providing patients with clear, concise, accessible, and useful patient information.
- Highlight the essential information for patients to use their prescription drug products safely and effectively in a patient-friendly manner.
- Consist of a single-page document with standard content and formatting to make it easier for patients to access important information on prescription drug products.
- Expand patient choice to include an electronic option to receive PMI in addition to the physical paper format.



[1] For the purposes of this proposed rule, a prescription drug product also includes a biological product licensed under the Public Health Service Act.

A Proposed Rule Snapshot is a communication tool and is not a substitute for the proposed rule. To learn more about Patient Medication Information (PMI), read the proposed rule. To read other Snapshots, visit the Guidance Snapshot Pilot page.

What are the proposed changes to the current Code of Federal Regulations?

FDA is proposing to revise the part heading and all subparts of current part 208 under Title 21 of the Code of Federal Regulations (CFR). The proposed part heading would be revised from "Medication Guides for Prescription Drug Products" to "Medication Guides: Patient Medication Information" and would be the successor regulation to current part 208. During the implementation of the rule, should the proposed rule become final, current Medication Guides would continue to be available as a potential element of Risk Evaluation and Mitigation Strategies (REMS) under section 505-1(e) of the U.S. Food, Drug, and Cosmetic Act (FD&C Act) until FDA has approved PMI for the prescription drug product. Once PMI is approved for those products, PMI would replace the former Medication Guide as a potential element of REMS.

Consistent with the proposed part 208, FDA is proposing to add 21 CFR § 606.123 to part 606, subpart G, to require establishments that collect blood and blood components intended for transfusion to create and distribute PMI.

Did FDA distribute the PMI proposed rule for public comment?

Yes. FDA notified the public of the proposed rule through the *Federal Register (88 FR 35694)* and requested comments through Regulations.gov (docket ID FDA-2019-N-5959). The public comment period began on May 31, 2023, and ended on November 27, 2023. FDA received over 57,000 comments. FDA is reviewing these comments.

What are the costs associated with implementing the proposed PMI?

The proposed rule would impose costs on the drug development industry. The majority of the cost would stem from developing PMIs. The proposed rule would also impose costs on FDA, primarily from reviewing PMI submissions, developing PMI templates for a small subset of drugs, and establishing and maintaining the online PMI database. FDA estimates the following:

- The total present value of net costs over 10 years would range from $105.0 to $312.5 million with a primary estimate of $192.8 million, using a 3% discount rate, and from $89.0 to $263.6 million with a primary estimate of $162.6 million, using a 7% discount rate.
- Annualizing the costs over 10 years, FDA estimates the cost would range from $12.3 to $36.6 million per year at a 3% discount rate, with a primary estimate of $22.6 million per year, and from $12.7 to $37.5 million per year using a discount rate of 7%, with a primary estimate of $23.2 million.

FDA estimates that the annual costs would be constant beginning in year 5. Dispensers may face additional costs to distribute PMI, which FDA cannot estimate at this time.

Are there exceptions to the proposed rule?

The proposed rule would allow for waivers from one or more of the proposed requirements for PMI if FDA determines that any requirement is inapplicable, unnecessary, impracticable, or contrary to patients' best interests for a particular prescription drug product. For example, waivers may be requested for the format and content of PMI and submitting and distributing PMI. Waivers could be initiated by FDA or requested by a person or entity that is covered by the final rule. Such requests would be evaluated on a case-by-case basis.

With few anticipated exceptions, FDA proposes to exclude manufacturers of preventive vaccines that do not have a Medication Guide from the requirement to create and distribute PMI. The Centers for Disease Control and Prevention manages a comprehensive preventive vaccine program that includes providing information on preventive vaccines to patients. FDA determined that the current system for developing and providing vaccine information statements to patients meets the goal of PMI for these products

What is the implementation schedule for the proposed PMI?

If the proposed rule is finalized, FDA is proposing a 5-year implementation schedule for PMI. The proposed rule would require a staggered implementation schedule for applicants to submit PMI to FDA for New Drug Applications (NDAs), Biologics License Applications (BLAs), and efficacy supplements. FDA proposes that the final rule based on this proposed rule become effective 6 months after the date of publication in the *Federal Register*. Please see the table on the next page for the proposed implementation schedule.

NDAs, BLAs, and efficacy supplements	Time by which PMI must be submitted to FDA
Applications submitted on or after the effective date of the final rule[2]	Time of submission (part of application)
Applications pending at the time of the effective date of the final rule	No later than 1 year after the date of approval of the pending application
Applications approved on or before the effective date and that have a Medication Guide required under part 208 or a PPI required under § 310.501 or § 310.515	No later than 1 year after the effective date of the final rule
Applications approved from January 1, 2013, up to and including the effective date of the final rule that do not have a Medication Guide required under part 208 or a PPI required under § 310.501 or § 310.515	No later than 2 years after the effective date of the final rule
Applications approved from January 1, 2008, up to and including December 31, 2012, that do not have a Medication Guide required under part 208 or a PPI required under § 310.501 or § 310.515	No later than 3 years after the effective date of the final rule
Applications approved from January 1, 2003, up to and including December 31, 2007, that do not have a Medication Guide required under part 208 or a PPI required under § 310.501 or § 310.515	No later than 4 years after the effective date of the final rule
Applications approved on or before December 31, 2002, that do not have a Medication Guide required under part 208 or a PPI required under § 310.501 or § 310.515	No later than 5 years after the effective date of the final rule

[2] Final rule refers to a final rule that may publish based on this proposed rule.

Note: Biologics License Application (BLA), New Drug Application (NDA), Patient Medication Information (PMI), Patient Package Insert (PPI)

When finalized, the proposed rule would also require applicants of new and approved abbreviated new drug applications (ANDAs) that refer to a listed drug, for which FDA has approved PMI, to have PMI that is the same as that of the reference listed drug (RLD) except for certain differences in labeling permitted under the law. FDA would create a PMI template for approved ANDAs if (1) the ANDA references a listed drug whose approval has been withdrawn and (2) no PMI was approved for the RLD before the approval of the RLD was withdrawn.

Would PMI replace any other patient information?

PMI would replace FDA-approved Medication Guides and PPIs (see table on the next page). Once FDA-approved PMI are available for all prescription drug products that currently have Medication Guides, FDA would withdraw the current regulations requiring Medication Guides for certain prescription drug products. During the proposed 5-year implementation schedule of the final rule, the current regulations governing Medication Guides would remain in place but would no longer be applicable to a prescription drug product once that prescription drug product has FDA-approved PMI.

FDA would also withdraw the current regulations requiring PPIs for oral contraceptives and estrogen-containing products after all such prescription drug products have FDA-approved PMI.

FDA would not accept any voluntarily submitted PPIs for other products once the rule is finalized.

PMI is not intended to replace the FDA-approved Prescribing Information, FDA-approved Instructions for Use, or patient counseling.

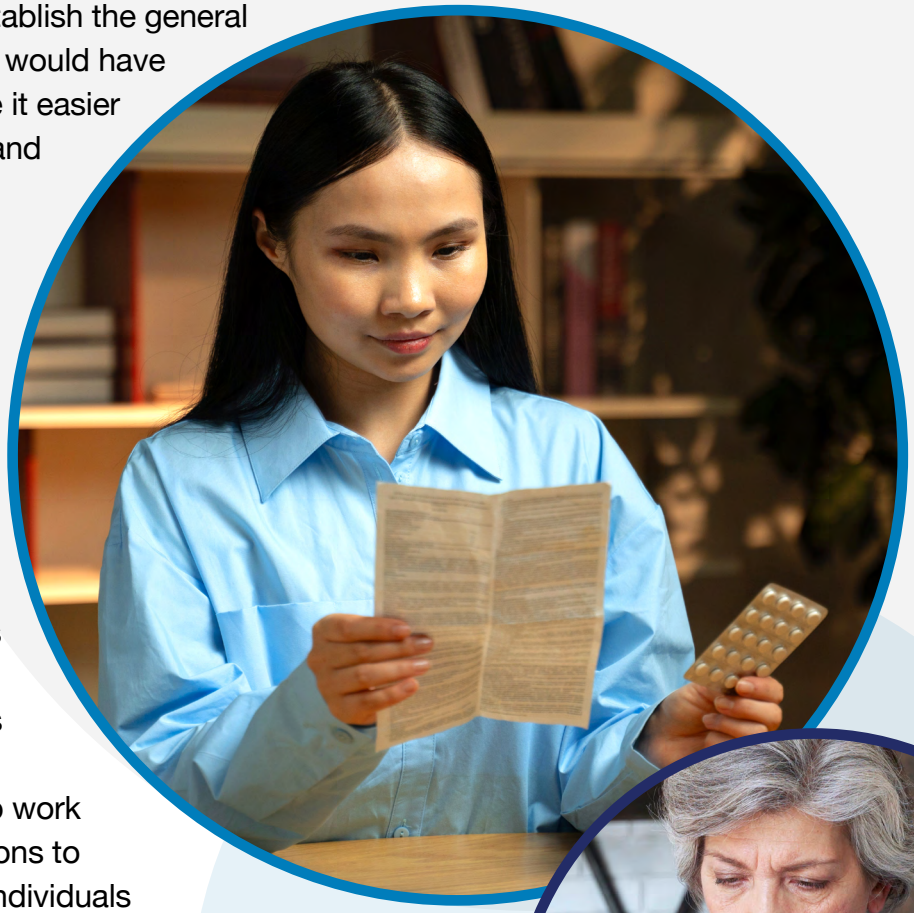
PATIENT PACKAGE INSERTS (PPIs)				
FDA requires PPIs for oral contraceptives and estrogen-containing products	Created by applicant[3]	Approved by FDA	Distribution required	Content defined in CFR: 21 CFR 310.501 and 310.515
Affected by Proposed Rule	PMI would replace PPIs but only after all drugs with PPIs have PMI (exceptions in § 208.10(d)). FDA would withdraw the current regulations in §§ 310.501 and 310.515 for NDAs, BLAs, and ANDAs that have FDA-approved PPIs. However, §§ 310.501 and 310.515 would remain in effect during implementation.			
MEDICATION GUIDES				
FDA requires Medication Guides for: 1. Products where patient labeling could help prevent serious adverse effects 2. Products that have serious risks that could affect patients' decision to use 3. Products where patient adherence to directions for use is crucial to effectiveness	Created by applicant	Approved by FDA	Distribution required	Content defined in CFR: 21 CFR 208.20
Affected by Proposed Rule	PMI would replace PPIs but only after all drugs with PPIs have PMI (exceptions in § 208.10(d)). FDA would withdraw the current regulations in §§ 310.501 and 310.515 for NDAs, BLAs, and ANDAs that have FDA-approved PPIs. However, §§ 310.501 and 310.515 would remain in effect during implementation.			
INSTRUCTIONS FOR USE DOCUMENTS				
FDA requires Instructions for Use documents for drug products with complicated or detailed patient-use instructions.	Created by applicant	Approved by FDA	Generally provided when the drug is dispensed to patient	Content is not defined in CFR See guidance for industry *Instructions for Use—Patient Labeling for Human Prescription Drug and Biological Products—Content and Format* (July 2022)
Not Affected by Proposed Rule				

[3] Defined in 21 CFR 314.3, an applicant is any person who submits an NDA (including a 505(b)(2) application) or ANDA or an amendment or supplement to an NDA or ANDA under this part to obtain FDA approval of a new drug and any person who owns an approved NDA (including a 505(b)(2) application) or ANDA.

Note: Abbreviated New Drug Application (ANDA); Biologics License Application (BLA); Code of Federal Regulations (CFR); U.S. Food, Drug, and Cosmetic Act (FD&C Act); U.S. Food and Drug Administration (FDA); New Drug Application (NDA); Patient Medication Information (PMI); Patient Package Inserts (PPIs)

What format and content would the PMI have?

Proposed rule § 208.30 would establish the general format requirements for PMI. PMI would have a uniform format that would make it easier for patients to read, understand, and use PMI. The proposed PMI must be made available in hardcopy but can be made available in a digital format upon a patient's request. PMI must be easily read and understood by the general population, including by individuals with low literacy and comprehension levels. PMI would highlight essential information that the patient needs to know about the prescription drug product and basic directions on how to use the product. FDA strongly encourages applicants to work with retailers and other organizations to ensure that PMI is accessible to individuals with limited English proficiency.



PMI would be a one-page document with the following headings:

- Drug Name
- Important Safety Information
- Common Side Effects
- Directions for Use

The proposed rule also defines the size and color of the text to maximize readability. PMI must be scientifically accurate and based on and consistent with the Prescribing Information for the prescription drug product required under 21 CFR 201.56, 201.57, 201.80, and 606.122 and under section 505 of the FD&C Act (21 U.S.C. 355). The document must not be promotional in tone and, to avoid any misinterpretation of the content within, must not include icons or pictograms.

On the next page is an example of a proposed PMI for a fictitious drug, Rheutopia.

Example of a Proposed PMI

PMI would need to comply with the content and format requirements set forth in the regulation. There are different approaches that may meet the requirements. The PMI example shown here is for a fictitious drug and is one possible approach that would meet the requirements set forth in the proposed rule. If FDA were to issue the final rule, the requirements for PMI may remain the same as in the proposed rule (shown here) or may differ. Therefore, if FDA were to issue the final rule, applicants would need to comply with the requirements in the PMI final rule.

PATIENT MEDICATION INFORMATION
RHEUTOPIA (roo-toh-pee-ah) (arixalate injection, for subcutaneous use)

RHEUTOPIA Is:

- Used to treat rheumatoid arthritis in adults. RHEUTOPIA reduces painful and swollen joints, slows joint damage, and improves mobility and the ability to do physical activities.
- Used to treat polyarticular juvenile idiopathic arthritis in children at least 4 years old who did not have good results from other medicines. RHEUTOPIA reduces pain, improves mobility, and decreases the number of painful joints.
- Used to treat ankylosing spondylitis. RHEUTOPIA reduces back pain, swelling, and improves mobility.
- Used to treat plaque psoriasis in adults who may benefit from taking medicine or receiving phototherapy (using ultraviolet light). RHEUTOPIA improves or clears up areas of skin with psoriasis.

Important Safety Information

Warnings:

- RHEUTOPIA can cause serious infections. Do not use RHEUTOPIA if you have an active infection.
- Do not use RHEUTOPIA if you are allergic to arixalate or any of the ingredients in RHEUTOPIA.

Serious side effects:

RHEUTOPIA can affect the immune system and lower your ability to fight infection. People taking RHEUTOPIA have gotten serious infections including tuberculosis (TB) and infections caused by viruses, fungi, or bacteria. Some people have died from these infections.

Stop using RHEUTOPIA and call your health care provider right away if you develop:

- Fever, cough, flu-like symptoms, or a skin infection (red, warm, painful skin or open sores).
- Numbness, tingling, weakness, vision problems, or dizziness
- Chills, swollen lymph nodes, night sweats, fever, or weight loss
- Bruising, bleeding, and pale skin
- Shortness of breath, swelling of ankles or feet, or sudden weight gain
- Chest discomfort or pain, shortness of breath, joint pain, or a rash on your cheeks or arms

Tell your health care provider before taking:

- If you have an infection, are being treated for an infection, or think you have an infection (such as cold, flu, or skin infection)
- If you have TB or have been near someone who has TB
- If you have any nervous system or heart problems
- If you have recently been vaccinated or are scheduled to receive a vaccination (including a flu shot)
- If you have lived in or traveled to other countries
- If you are taking the medicine Kineret (anakinra)

Common Side Effects

The most common side effects in adults and children include:

- Headache
- Runny nose
- Redness, rash, swelling, itching, or bruising where the injection (shot) was given

These are not all of the possible side effects of RHEUTOPIA. Call your health care provider if you have side effects that worsen or do not go away. You may also report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Directions for Use

- Use RHEUTOPIA exactly as prescribed. Your health care provider will tell you how often to use RHEUTOPIA.
- RHEUTOPIA is injected directly under the skin (subcutaneous). Do not use RHEUTOPIA until your health care provider has shown you how to give a shot.
- Store RHEUTOPIA in the refrigerator. Do not shake or freeze.
- If you forget to take a dose, take it as soon as you remember. Take your next dose at your regularly scheduled time.

Manufactured by: Drug Company Name, City, State Zip Code

The content of this Patient Medication Information has been approved by the U.S. Food and Drug Administration Revised: Month/Year

What is the evidence for the proposed rule?

FDA has long known that written prescription drug product information is an important part of patient counseling. There is evidence that such information may help patients use prescription drug products safely and effectively and may potentially reduce preventable adverse drug reactions and improve health outcomes. For instance, written prescription drug information reinforces verbal instructions or warnings given by health care providers, may improve patient understanding and recall of instructions, and provides patients with supplemental information about the prescription drug product after visits with health care providers. Studies show that patients prefer a simplified one-page format for written patient information and are more likely to read information that is short and concise. Studies also show that patients understand more information when it is contained in a shorter document and are better able to understand information when it is presented in a simplified one-page format.

Based on the National Adult Literacy Survey, nearly half of the U.S. adult population is functioning at or below an eighth-grade reading level. Other studies have also found that the average American adult reads at an eighth-grade or ninth-grade reading level. The Keystone Action Plan advocates that prescription drug product information intended for patients be written at a sixth-grade through eighth-grade reading level.

In determining specific headings and information to be included in PMI, FDA researched scientific literature, conducted studies examining several PMI prototypes, held public workshops and hearings, and obtained stakeholder input on what information patients need in order to use their prescription drug products safely and effectively.

What is the history of the proposed rule?

Over the course of a decade, FDA gathered and analyzed data from its stakeholders on the significance of PMI and the content of an improved PMI. Stakeholders emphasized the importance of providing clear, concise, and accessible information to patients as this may help them to use their prescription drug products safely and effectively. The table on the next page describes these data gathering activities/events and key findings.

Activity Table

FDA 2009 Public Workshop **Sept. 24-25, 2009**	The workshop explored the following questions through the evaluation of four PMI prototypes: • What content is critical for patients to receive and in what order and format? • How can access be improved? • How should this information be distributed to patients? • What parameters are appropriate with regard to evaluating the usefulness of the materials? Attendees suggested that user testing of written prescription drug product information during the development stage should be mandatory to ensure that the final product is consumer friendly. They described these key attributes and goals of the written information: • Patients should be able to understand what the prescription drug product is used for and how to use it appropriately. • Patients should be able to find, understand, and retain information about the prescription drug product's contraindications and side effects. • Patients should know where they can locate additional information about the prescription drug product that is not included in the written prescription drug product information.
Brookings Institution Workshops and Distribution Studies **July 21 and October 12, 2010 February 23, 2011 July 1, 2014**	**July 21, 2010** Experts from academia, medical professional groups, stakeholders from the private sector (applicants, consumer organizations, and publishers of CMI), and FDA met to discuss improving written patient prescription drug product information. ***Key findings:*** Stakeholders developed the overarching principles for effectively communicating prescription drug product information to patients, as well as FDA's proposed strategy for evaluating the PMI prototypes.
	October 12, 2010 Discussed strategies for making PMI easily accessible and how to most effectively distribute PMI to patients. ***Key findings:*** Began creating models for effective distribution of PMI within current and future healthcare delivery systems. Discussed potential strategies for monitoring and ensuring the effectiveness of PMI.

Activity Table

	February 23, 2011 Summarized the first two workshops and further discussed how to design pilot studies to test the distribution of PMI. Key findings: Determined the goals and objectives of demonstration pilots designed to evaluate feasibility of different methods to distribute the PMI prototype and to assess patient and provider preferences for the PMI prototype that was distributed to patients.
	July 1, 2014 Discussed lessons learned from health literacy researchers engaged in PMI projects and the role of stakeholders in moving the PMI initiative forward. ***Key findings:*** Participants emphasized that enough information now exists to create effective PMI that would provide more value than currently available written prescription drug product information.
FDA 2010 Part 15 Public Hearing **Sept. 27-28, 2010**	FDA hosted a part 15 public hearing to solicit input on a new framework for the development and distribution of PMI to be provided to patients who are prescribed drug products. The hearing solicited input on the processes and procedures for standardizing PMI using a quality system approach for monitoring the development and distribution of PMI. ***Key findings:*** Presentations and comments from the attendees offered support for the following principles: • PMI should be available at pharmacies and should use the existing distribution capabilities of the pharmacy. • FDA should have an active role in the development and approval of PMI and should design content and format guidelines. • Plain language should be used to increase comprehension. • PMI should be consumer tested. • A range of distribution methods should be used for PMI. • Attendees disagreed on whether the length of PMI should be limited to one page.
FDA's Research on PMI Prototypes	FDA conducted the study Experimental Study of Patient Information Prototypes. FDA announced the study in the Federal Register (75 FR 23775, May 4, 2010) and sought public comment through Regulations.gov (Docket No. FDA-2010-N-0184). The study's intent was to use different PMI prototypes to test whether consumers were able to comprehend serious warnings, directions for use, drug indications and uses, contraindications, and side effects in the material presented. ***Key findings:*** Results suggest that the content and format may be important predictors of recall of factual information about prescription drug products.

When would a patient receive PMI?

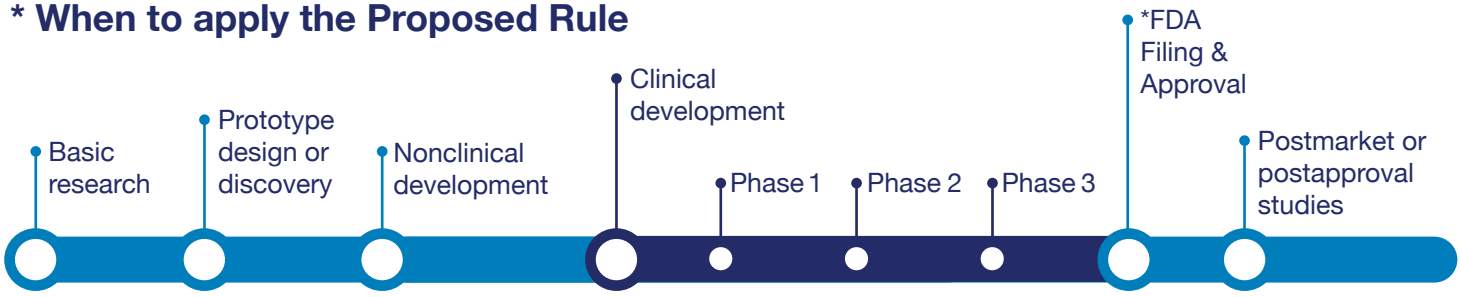
Authorized dispensers would be required to provide PMI to patients each time a prescription drug product for which an FDA-approved PMI exists is used, dispensed, or administered on an outpatient basis. An authorized dispenser is an individual(s) or entity who is licensed, registered, or otherwise permitted by the jurisdiction in which the individual(s) or entity practices to provide prescription drug products in the course of professional practice. In most instances, the authorized dispenser would be a pharmacist.

However, an authorized dispenser may also include physicians, nurses, or other licensed health care providers legally permitted under State law to provide prescription drug products or blood and blood components to patients.

The default method of distribution for PMI is in paper form, although this proposed rule would allow for electronic distribution instead of paper distribution upon a patient's request and would accommodate future technological advances in the methods used to provide PMI.

Drug Development Timeline

*** When to apply the Proposed Rule**



Proposed Rule Recap Podcast

Hear highlights straight from FDA staff

Speaker: Christopher Diamant, Regulatory Counsel, Office of Medical Policy, Center for Drug Evaluation and Research

Click here to listen

Click here to read transcript

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