Format and Content of a REMS Document

Guidance for Industry

DRAFT GUIDANCE

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For questions regarding this draft document, contact (CDER) Gita Toyserkani at 301-796-1783, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

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Revision 1

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Format and Content of a REMS Document Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. 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. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance provides updated recommendations for the format and content of a risk evaluation and mitigation strategy (REMS) document for a prescription drug product, including a biological drug product.[2] A REMS document, which is part of a REMS that is required by FDA, establishes the goals and requirements of the REMS.

This guidance provides recommendations to applicants on drafting proposed REMS documents and converting an already-approved REMS document to a new, standardized format that is clearer, more informative, and supports submission of a REMS document in Structured Product Labeling (SPL) format. FDA does not expect applicants of an approved product subject to a REMS to submit a proposed REMS modification solely to convert their REMS document to the new format. Changing the REMS document to the new format should be done in conjunction with other REMS modifications.

This guidance provides an overview of the types of information that should be included in a REMS document. Additional and more detailed information is provided in the template appended to this guidance, which is also available on FDA's Web site.[3] This guidance and the appended template are intended to help ensure that REMS documents are clear, understandable to stakeholders, and to the extent possible, consistent in content and format.

[1] This guidance has been prepared by the Office of Medication Error Prevention and Risk Management, Office of Surveillance and Epidemiology in the Center for Drug Evaluation and Research (CDER) in cooperation with other Offices within CDER and the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

[2] For purposes of this guidance, unless otherwise specified, references to *drugs* and *drug products* include drugs submitted for approval or approved under sections 505(b) or 505(j) of the Federal Food, Drug and, Cosmetic Act (FD&C Act) and biological products licensed under section 351 of the Public Health Service Act, other than biological products that also meet the definition of a device in section 201(h) of the FD&C Act (21 U.S.C. 321(h)). These applications are termed *covered applications* and refer to new drug applications (NDAs), abbreviated new drug applications (ANDAs) and biologics license applications (BLAs).

[3] See Appendix for the *REMS Document Template* and https://www.fda.gov/AboutFDA/Transparency/Basics/ucm325201.htm.

This guidance revises the 2009 draft guidance for industry *Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications* to: (1) provide updated recommendations on the format and content of a REMS document[4] and (2) remove information related to REMS assessments and proposed REMS modifications that are being addressed in separate guidance documents.[5] This guidance does not provide detailed information on the format and content of other documents that are part of a REMS submission, such as the REMS materials[6] or the REMS supporting document.[7] Furthermore, the guidance does not include information on how to design, implement, or evaluate a REMS, and does not address submissions that are unique to shared system REMS.[8]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

A. FDA's REMS Authority

Section 505-1 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) 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.

If FDA determines that a REMS is necessary,[9] the Agency may require one or more REMS elements, which could include a Medication Guide,[10] a patient package insert,[11] and/or a

[4] When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA Drugs guidance Website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[5] See guidance for industry *Risk Evaluation and Mitigation Strategies: Modifications and Revisions*, available at http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm441226.pdf.

[6] All proposed materials that are included as part of the REMS (e.g., communication and educational materials, enrollment forms, prescriber and patient agreements) are also approved and are appended to the REMS document. This guidance refers to these materials as *REMS materials.*

[7] For purposes of this guidance, the *REMS supporting document* expands on information in the REMS document and provides additional information about the REMS, such as the rationale for, and supporting information about, the design, implementation, and assessment of the REMS.

[8] See Section 505-1(i)(1)(B) of the FD&C Act. Unless a waiver has been granted, a drug that is the subject of an abbreviated new drug application and the listed drug shall use a single shared system for the elements to assure safe use.

[9] See draft guidance for industry *FDA's Application of Statutory Factors in Determining When a REMS Is Necessary*, available at http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm521504.pdf.

[10] See Section 505-1(e)(2) of the FD&C Act.

communication plan.[12] FDA may also require elements to assure safe use (ETASU) as part of a REMS.[13] ETASU may be required if the drug has been shown to be effective, but is associated with a specific serious risk and can be approved only if, or would be withdrawn unless, such elements are required as part of a strategy to mitigate a specific serious risk(s) listed in the labeling of the drug. ETASU may be required for drug products initially approved without ETASU when other elements are not sufficient to mitigate a serious risk.

Specifically, ETASU may include one or any combination of the following requirements[14]:

- Health care providers who prescribe the drug have particular training or experience, or are specially certified
- Pharmacies, practitioners, or health care settings that dispense the drug are specially certified
- The drug be dispensed to patients only in certain health care settings, such as hospitals
- The drug be dispensed to patients with evidence or other documentation of safe use conditions, such as laboratory test results
- Each patient using the drug be subject to monitoring
- Each patient using the drug be enrolled in a registry

If a REMS includes certain ETASU, the REMS may also include an implementation system to enable the applicant to monitor, evaluate, and improve the implementation of the elements (e.g., development of a REMS specific Web site or call center to facilitate enrollment; establishment of electronic databases of certified health care settings).[15]

All REMS should include one or more overall goals, and if the REMS has ETASU, the REMS must include one or more goals to mitigate a specific serious risk listed in the labeling of the drug and for which the ETASU are required.[16]

Finally, REMS generally must include a timetable for submission of assessments of the REMS.[17] The timetable for submission of assessments of the REMS must include an assessment by the dates that are 18 months and 3 years after the REMS is initially approved, and an assessment in the 7th year after the REMS is approved, or at another frequency specified in the REMS.[18]

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[11] Id.

[12] See Section 505-1(e)(3) of the FD&C Act.

[13] See Section 505-1(f) of the FD&C Act.

[14] See Section 505-1(f)(3) of the FD&C Act.

[15] See Section 505-1(f)(4) of the FD&C Act.

[16] See Section 505-1(f)(3) of the FD& C Act.

[17] New Drug Applications (NDAs) and Biologics License Applications (BLAs) must include a timetable for submission of assessments. ANDAs are not subject to the requirement for a timetable for submission of assessments (Section 505-1(i)), but FDA can require any application holder, including ANDA applicants, to submit REMS assessments under Section 505-1(g)(2)(C).

[18] See Section 505-1(d); see also 505-1(g)(2) of the FD&C Act.

B. FDA's Considerations for Changing the Format of the REMS Document

Since the publication of the 2009 draft guidance for industry *Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications*, FDA has received public feedback on improving the REMS document.[19,20] FDA is revising its recommendations on the format and content of the REMS document in response to the public's feedback and to provide assistance with drafting a clearer, more informative, and standardized document. Additionally, the new format would support submission of REMS documents in SPL format.[21,22]

The new format for the REMS document, as described in this guidance, contains substantially the same content as described in the original guidance; however, the information is reorganized. In the old format, the REMS requirements[23] were organized by the statutory *elements*. In the new format, requirements are organized by who is responsible for implementing the requirement, when the requirement is to be implemented, what action is required, and with what REMS material(s). The new format also makes greater use of tables and bulleted lists to better present and organize the information.

III. FORMAT AND CONTENT OF A REMS DOCUMENT

A REMS document establishes the goals and requirements of the REMS as they relate to the required REMS elements. This information is described in more detail in the sections below.

To facilitate the applicant's implementation of the recommended format, FDA has developed a template to use in conjunction with this guidance. The template is appended to this guidance and is also available on FDA's Web site, at https://www.fda.gov/AboutFDA/Transparency/Basics/ucm325201.htm.

As described here, the template contains specific sections and provides standardized language to describe common REMS requirements. The standardized language was developed by FDA after review and comparison of existing approved REMS documents, consideration of stakeholder feedback on REMS documents, and FDA's experience in reviewing REMS and implementing its REMS authorities. It is the Agency's view that where REMS requirements are the same across REMS, the language used to describe the requirements should be consistent. FDA recommends that applicants use the standardized language whenever possible to help ensure consistency and

[19] See http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm.

[20] See http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm350852.htm.

[21] Structured product labeling (SPL) is a document markup standard approved by Health Level Seven (HL7) and adopted by FDA as a mechanism for exchanging product and facility information.

[22] See additional information on REMS SPL, available at https://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm517343.htm

[23] For the purpose of this guidance, REMS *requirements* are the mandatory activities or other obligations of the application holder, health care providers, patients, and other stakeholders under the REMS.

facilitate efficient review of the REMS document. If alternative language is proposed, FDA recommends that applicants provide an explanation for their proposed language.

A. Administrative Information

The Administrative Information section should include relevant administrative information such as the application number(s), application holder's name, the date that the REMS was initially approved, and the date of the most recent revision or modification of the REMS.[5]

B. REMS Goals

The REMS Goals section should describe the overall, safety-related health outcome(s) that the REMS is designed to achieve. Because risk mitigation goals cannot always be measured directly, it is important to also include one or more intermediate measurable objectives that, if achieved, indicate that the REMS is meeting its goals. For example, a REMS for a drug that causes renal toxicity may include a goal to mitigate the risk of renal failure, and the measurable objectives could be that patients undergo periodic testing of serum creatinine and that appropriate management steps are undertaken based on the test results.

C. REMS Requirements

The REMS Requirements section should establish the requirements of the REMS for both the REMS participant(s) and the applicant(s). REMS participants are stakeholders who participate in the REMS based on their role in clinical assessment, prescribing, dispensing, administering, or monitoring, as well as the distribution process. They can include health care providers who prescribe, patients who receive the drug, health care settings, practitioners, pharmacies that dispense, and wholesalers/distributors that distribute.

The REMS Requirements section should be divided into the following subsections:

1. REMS Participant Requirements

The REMS Participant Requirements are the activities that REMS participants must undertake in REMS with ETASU. Applicants are responsible for ensuring compliance with these requirements, and addressing any noncompliance. For example, if a REMS includes a requirement for prescribers of a drug to complete training, the applicant is required to ensure that prescribers comply with the requirement to complete the training.

If there are no requirements for REMS participants to carry out, the REMS Participant Requirements section should ***not*** be included in a REMS document.

In the REMS document, REMS Participant Requirements should be presented as a series of tables. There should be a separate table for each type of participant and each table should be formatted as follows:

[REMS Participant]

[Timing]	[Requirement] using [REMS material] [Requirement]
[Timing]	[Requirement] [Requirement]

The table describes the participant *who* is responsible for complying with the requirement(s), *what* requirement(s) each participant needs to carry out, *when* the participant should perform each requirement(s), and *with what* REMS material. These items are described in further detail, below.

[**REMS Participant**]: REMS participants are stakeholders who participate in the REMS and are described based on their role in clinical assessment, prescribing, dispensing, administering, or monitoring as well as the distribution process. **Error! Bookmark not defined.** For example, REMS participants can include health care providers who prescribe; patients who receive the drug; health care settings, practitioners, and pharmacies that dispense; and wholesalers/distributors.

[Timing]: The timing of the requirement refers to *when* the participant must carry out the requirement, and generally is associated with either a clinical activity (e.g., before a patient initiates treatment, during treatment, or after treatment discontinuation), or an administrative activity (such as prescriber certification[24]).

[Requirement]: Participant requirements generally include clinical or administrative activities that the participant must comply with as part of the REMS. An example of a clinical requirement is "Monitor the patient for injection site reactions." An example of an administrative requirement is "Enroll the patient in the REMS."[25] In addition, some administrative requirements refer to "documentation of safe use conditions,"[26] which are activities that help ensure that health care providers or patients meet specified criteria before the drug is dispensed. For example, documentation of safe use conditions can include verifying that the prescriber is certified or that a required lab test was completed.

[REMS Material]: Materials, such as enrollment forms and educational materials, refer to the specific documents that participants need to use to comply with a requirement.

[24] Certification requires that health care providers, pharmacies, or health care settings meet certain REMS requirements to be able to prescribe, dispense, or order a drug. Once the health care provider, pharmacy, or setting has met these requirements, they are referred to as "certified." For health care providers who prescribe the drug, the process for obtaining this certification is referred to as "prescriber certification," and for health care providers, pharmacies, and settings that dispense the drug, this process is referred to as "dispenser certification."

[25] For purposes of this guidance, REMS enrollment is the process by which participants provide basic identifying and demographic information to the REMS program, allowing the applicant to track and communicate with REMS participants.

[26] See Section 505-1(f)(3)(D) of the FD&C Act.

They should be included as a hyperlink within the requirement text that directs readers to the material and they are appended to the REMS document.[27]

2. REMS Applicant Requirements

The REMS Applicant Requirements in the REMS are generally the requirements for applicants to (1) develop and provide REMS training; (2) develop and disseminate REMS communications; (3) support REMS operations; and to (4) ensure participants' compliance with the REMS. A REMS may include some or all of these types of requirements.

Requirements related to training can include the requirement for the applicant to develop REMS training materials and provide to health care providers, and develop a knowledge assessment for health care providers to complete as part of the training. The REMS training requirements should include information about how the training is being provided (e.g., website, mailing, in-person) and whether the training is being provided by a continuing education (CE) provider.

Requirements related to communication can include requirements for the applicant to develop materials about the REMS and/or the risks and safe use of the drug, and to disseminate the materials to health care professionals and professional organizations or societies. The following information should be included: the intended recipients, the type of materials to be disseminated, how the materials will be disseminated, and the timing of the dissemination(s).

Requirements related to operations can include requirements for the applicant to develop, establish, and implement systems and infrastructure (e.g., databases, websites, call centers) to support the REMS requirements that enable access to and participation in the REMS.

Requirements related to compliance with the REMS can include requirements for the applicant to monitor and evaluate REMS participants' compliance with the REMS to ensure the REMS requirements are being met. These requirements include ensuring (e.g., through audits) that all REMS processes and procedures to support the REMS requirements are in place, functioning, and are being complied with.

D. REMS Assessment Timetable

The REMS Assessment Timetable section of the REMS document should describe the timetable for submission of assessments of the REMS by the applicant. REMS are generally required to include a timetable for submission of assessments, and applicants are required to submit assessments of the REMS at the specified intervals.[28]

[27] A comprehensive list of all REMS materials is also included at the end of the REMS document (See Section III.E *REMS Materials* of this guidance)

[28] See Section 505-1(d) of the FD&C Act.

E. REMS Materials

The REMS Materials section should provide a comprehensive list of all the materials that are required for the REMS (e.g., enrollment forms, educational materials, counseling tools, and Patient-Provider Agreements). The list should be organized by the REMS participant(s) to which the materials apply and the type of REMS material. The materials themselves should be appended to the REMS document.

IV. PROCEDURES

A. Proposed REMS Submissions

Proposed REMS submissions should include two parts: the REMS (REMS document and REMS materials) and the REMS supporting document.

- REMS document and REMS materials

  The REMS document should use the format and content described in section III (*Format and Content of a REMS Document*). With the exception of the Medication Guide, the REMS materials should be appended to the REMS document. Foreign-language versions of REMS materials are not considered part of the approved REMS, and are not reviewed by FDA.[29]

- REMS supporting document

  The REMS supporting document should expand on information in the REMS document, and provide additional information about the REMS, such as the rationale for and supporting information about the design, implementation, and assessment of the REMS (e.g., why a REMS is necessary based on application of the statutory factors,[30] how the REMS would ensure that the benefits of the drug outweigh the risks, implementation processes, compliance and enforcement policies and procedures, definitions, knowledge assessment scoring criteria, and the REMS assessment plan).

Proposed REMS modifications to convert an already-approved REMS document to the new format should be submitted in accordance with the procedures outlined in the guidance for industry, *Risk Evaluation and Mitigation Strategies: Modifications and Revisions.*[31] FDA does not expect application holders of approved REMS to submit a proposed REMS modification solely to convert their REMS document to the new format. Changing the REMS document to the new format should be done in conjunction with other REMS modifications.

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[29] Consistent with CDER's approach to foreign-language labeling, when applicants distribute foreign-language versions of a currently approved REMS, applicants are responsible for ensuring that such materials are complete and accurate. See 21 CFR 201.15(c).

[30] See draft guidance for industry *FDA's Application of Statutory Factors in Determining When a REMS Is Necessary*, available at http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm521504.pdf.

[31] See guidance for industry *Risk Evaluation and Mitigation Strategies: Modifications and Revisions*, available at http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm441226.pdf.

B. Submission Type

A proposed REMS can be included in the initial submission of an original or supplemental application,[32] or submitted as an amendment to an existing original or supplemental application. All supplemental applications[33] that include a new proposed REMS should be submitted as prior-approval supplements. A proposed REMS submitted after product approval and not associated with an existing supplemental application should be submitted as a new supplemental application.[34]

C. Submission Identification

The first page of a proposed REMS submission should prominently identify the submission as **PROPOSED REMS** in bold capital letters at the top of the page. This wording on the first page of the submission should be combined with any other applicable content identification, for example:

When the proposed REMS is submitted as part of an original application:

NDA/BLA/ANDA [assigned #]
NEW ORIGINAL APPLICATION FOR <name of drug>
PROPOSED REMS

When the original proposed REMS is submitted as an amendment to an existing original or supplemental application:

PROPOSED REMS for NDA ######, ANDA ######, BLA ######

PROPOSED REMS for NDA ######/S-000, ANDA ######/S-000, BLA ###### - AMENDMENT

When the original proposed REMS is submitted postapproval as a new supplemental application:

NEW SUPPLEMENT FOR NDA ######/S-000, ANDA #####/S-000, BLA ######
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS

When the original proposed REMS is submitted postapproval with a new supplemental application:

[32] New drug application (NDA), abbreviated new drug application (ANDA) or biologics license application (BLA).

[33] See 21 CFR 314.70 and 601.12.

[34] For instructions on submission of REMS modifications, see the guidance *Risk Evaluation and Mitigation Strategies: Modifications and Revisions* available at: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm441226.pdf

NEW SUPPLEMENT FOR NDA ######/S-000, BLA ######
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS

On the first page of subsequent submissions related to an already-submitted proposed REMS, prominently identify the submission by including this wording in bold capital letters at the top of the letter:

PROPOSED REMS for NDA ######, ANDA #####, BLA ###### -AMENDMENT

D. Posting REMS Documents on the FDA Web site

All approved REMS documents and their appended REMS materials are posted on FDA's Web site. REMS supporting documents are not made available on FDA's Web site.

APPENDIX: REMS DOCUMENT TEMPLATE

Risk Evaluation and Mitigation Strategy (REMS) Document

[Drug/Class Name (Generic Name)] REMS Program

The REMS document template has five sections: I) Administrative Information II) REMS Goals III) REMS Requirements IV) REMS Assessment Timetable V) REMS Materials. Depending on the REMS requirements, the REMS document will include sections and text, as applicable.

Template Key
Red Text = Instructions
Black Text = Standardized text
Blue text with hyperlink = Name of REMS Material(s)
[Bracketed (blue or black) text] = Information that needs to be entered

I. Administrative Information

Application Number(s): NDA/BLA [application number(s)] Use this only for single-applicant REMS.
Application Holder: [applicant name] Use this only for single-applicant REMS
Initial [Shared System] REMS Approval: [MM/YYYY]
Most Recent REMS Update: [MM/YYYY] Enter the date of the most recent REMS Revision or approved Modification. If there are no updates since the initial approval, delete the text.

II. REMS Goal(s)

This section describes the overall, safety-related health outcome that the REMS is designed to achieve (e.g., mitigate the risk of a particular serious adverse event) and the intermediate, measurable objectives. In many cases, it is not possible to measure a risk mitigation goal directly; therefore, it is important to include one or more intermediate, measurable objectives that, if achieved, indicate that the program is meeting its goal(s).

[Overall REMS goal]

1. [REMS objective]
2. [Other REMS objectives, as needed]

III. REMS Requirements

This section describes the REMS requirements for the applicant, including requirements that the applicant must undertake directly and requirements that the applicant must ensure that REMS participants undertake. REMS participants can include prescribers, dispensers, health care settings, patients (or their guardians), and wholesalers/distributors.

The REMS Requirements section is divided into two subsections. These subsections are labeled A and B in the template.

A. REMS Participant Requirements describes the requirements that REMS Participants must undertake.

B. REMS Applicant Requirements describes requirements for applicants to develop training, communications, systems and processes to support REMS operations and compliance.

Standardized text for the most commonly used REMS requirements is included in each subsection in black text. Retain the subsections that apply to your REMS, and delete the subsections that do not apply.

With-in each subsection, select the REMS requirements that apply to your REMS and delete the REMS requirements that do not apply.

Some REMS requirements have multiple versions to describe the different ways the requirement can be carried out (e.g., with or without using a REMS material). The different versions of the requirement appear in black text, separated by the word "OR" in red text. Select the appropriate version from among the choices provided and delete the version(s) that does not apply to your REMS.

Whenever possible, use the standardized text provided in the template. If you modify from the template text, you should provide a justification for doing so to facilitate FDA review.

----------Start Subsection A----------

REMS Participant Requirements
This subsection describes the requirements that each REMS participant needs to undertake and that the applicant must ensure REMS participants comply with.

The information in this subsection is organized by REMS participant. There is a separate table for each participant that includes the following information:

[REMS Participant]	
[Timing Category]	1. [REMS Requirement] 2. [REMS Requirement] using [REMS Material]

[REMS Participant] = who (which participant) needs to complete the REMS Requirement(s)

[REMS Requirement] = what the REMS participant is required to do

[Timing Category] = when the participant must carry out the requirement

[REMS Material] = with what REMS material the participants need to carry out a requirement. Names of REMS materials are included as a hyperlink within the requirement text.

When listing the REMS materials, do not include the name of the REMS program in the name of the material. For example, use "Prescriber Enrollment Form" instead of "Drug X REMS Prescriber Enrollment Form."

If there are no requirements that a particular REMS participant has to carry out to comply with the REMS, delete the table for that participant.

If there are no requirements that REMS participants have to carry out to comply with the REMS, delete subsection A. For example, if the REMS only includes requirements that the applicant has to carry out, such as developing and disseminating REMS communications to health care providers, delete subsection A.

[Applicant] must ensure that [List the participants who have requirements under this REMS e.g., **health care providers / pharmacies / health care settings / patients / wholesalers-distributors] comply with the following requirements:**

1. Health Care Providers who prescribe [drug / class name] must:

To become certified to prescribe Include this timing category if there are requirements that the health care provider must complete to be able to prescribe	1. Be able to [clinical activity to be performed]. Include this requirement if the prescriber has to have the ability to carry out a particular activity, such as administer a particular treatment, diagnose a particular disease, or recognize a particular adverse event. 2. Review the drug's Prescribing Information. Note that the Prescribing Information is not appended to the REMS. 3. Review the following: [List the Prescriber Educational Material(s)]. Include this requirement if the health care provider is required to review certain educational materials that are provided as part of the REMS. 4. Take training provided by [entity providing the training, e.g. the REMS Program, a CE provider]. Include this requirement if instructor-led training is provided. 5. Successfully complete the [Knowledge Assessment] and submit it to the REMS Program. 6. Enroll in the REMS by completing the [Enrollment Form] and submitting it to the REMS Program.
Before treatment initiation (first dose) Include this timing category if there are requirements that the health care provider must complete with a patient, before the patient initiates treatment	7. Counsel the patient on [topic(s)]. Include this requirement if the health care provider is required to counsel the patient. The provider may be required to cover a particular topic, use a particular REMS material (e.g., counseling tool, Medication Guide), or both. **OR** Counsel the patient using [REMS Material]. **OR** Counsel the patient on [topic(s)] using [REMS Material]. **OR** Counsel the patient on [topic(s)] using [REMS Material]. Provide a copy of the material to the patient. 8. Provide the patient with the [REMS Material(s)]. Include this requirement if there are materials that must be provided to a patient (e.g., Patient Brochure, Medication Guide). Materials that are provided to the patient as part of

1. Health Care Providers who prescribe [drug/class name] must:

another requirement (e.g. see requirements #7, #10, and #11) do not need to be repeated here.

9. Assess the patient's [condition(s) or health status(es)].
   Include this requirement if there is monitoring and/or a particular lab test that must take place (e.g., pregnancy test that needs to take place before each prescription). Repeat this requirement, as needed, to address multiple health conditions and/or lab tests.
   OR
   Assess the patient's [condition(s) or health status(es)]. Document and submit [the results] to the REMS Program using [REMS Material(s)].
   OR
   Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring].
   OR
   Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. Document and submit [the results] to the REMS Program using [REMS Material(s)].
10. Complete the [Patient Form]. Provide a completed copy of the form to the patient.
    OR
    Complete the [Patient Form]. Retain a completed copy in the patient's record.
    OR
    Complete the [Patient Form]. Provide a completed copy of the form to the patient and retain a copy in the patient's record.
    Include this requirement if there is an Patient Form that needs to be completed (e.g., a Patient-Provider Agreement Form), but that is not required to be submitted to the REMS Program (If the patient's information is required to be submitted to the REMS Program, use requirement #11).
11. Enroll the patient by completing and submitting the [applicable enrollment forms] [List all Enrollment Forms] to the REMS Program.
    OR
    Enroll the patient by completing and submitting the [applicable enrollment forms] [List all Enrollment Forms] to the REMS Program. Provide a completed copy of the form to the patient.
    OR
    Enroll the patient by completing and submitting the [applicable enrollment forms] [List all Enrollment Forms] to the REMS Program. Retain a completed copy in the patient's record.
    Include this requirement if the Enrollment Form is required to be submitted to the REMS Program (If the patient's information is not required to be submitted to the REMS Program, use requirement #10). List the applicable

1. Health Care Providers who prescribe [drug/class name] must:	
	Enrollment Forms if there are different Enrollment Forms for different patient populations (e.g., females of reproductive potential). 12. Prescribe no more than a [# of days] days' supply. 13. Not prescribe refills.
During treatment; before each [dose/infusion/prescription] Include this time category if there are requirements that the health care provider must complete with the patient, before each dose, infusion, or prescription	14. Counsel the patient on [topic(s)]. Include this requirement if the health care provider is required to counsel the patient. The provider may be required to cover a particular topic, use a particular REMS material (e.g. a counseling tool, a Medication Guide), or both. **OR** Counsel the patient using [REMS Material]. **OR** Counsel the patient on [topic(s)] using [REMS Material]. **OR** Counsel the patient on [topic(s)] using [REMS Material]. Provide a copy of the material to the patient. 15. Provide the patient with the [REMS Material]. Include this requirement if there are materials that must be provided to a patient (e.g. Patient Brochure, Medication Guide). Materials that are provided to the patient as part of another requirement (e.g. see requirements #7, #10, and #11) do not need to be repeated here. 16. Assess the patient's [condition(s) or health status(es)]. Include this requirement if there is monitoring and/or a particular lab test that must take place (e.g., pregnancy test that needs to take place before each prescription). Repeat this requirement, as needed, to address multiple health conditions and/or lab tests. **OR** Assess the patient's [condition(s) or health status(es)]. Document and submit [the results] to the REMS Program using [REMS Material(s)]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. Document and submit [the results] to the REMS Program using [REMS Material(s)]. 17. Order the prescription using the [Prescription Order Form]. Include this requirement only when there is a separate Prescription Order Form that is not part of another REMS form, such as a Patient Enrollment Form, that the prescriber must use. 18. Prescribe no more than a [# of days] days' supply. 19. Not prescribe refills.

1. Health Care Providers who prescribe [drug/class name] must:	
During treatment; [at specified interval] Include this time category if there are requirements that the health care provider must complete with the patient at specified intervals (i.e. not linked to the time/a visit that a prescription is written)	20. Counsel the patient on [topic(s)]. Include this requirement if the health care provider is required to counsel the patient. The provider may be required to cover a particular topic, use a particular REMS material (e.g. a counseling tool, a Medication Guide), or both. **OR** Counsel the patient using [REMS Material]. **OR** Counsel the patient on [topic(s)] using [REMS Material]. **OR** Counsel the patient on [topic(s)] using [REMS Material]. Provide a copy of the material to the patient. 21. Provide the patient with the [REMS Material]. Include this requirement if there are materials that must be provided to a patient (e.g. Patient REMS Program Brochure, Medication Guide). Materials that are provided to the patient as part of another requirement (e.g. see requirements #7, #10, and #11) do not need to be repeated here. 22. Assess the patient's [condition(s) or health status(es)]. Include this requirement if there is monitoring and/or a particular lab test that must take place (e.g., pregnancy test that needs to take place before each prescription). Repeat this requirement, as needed, to address multiple health conditions and/or lab tests. **OR** Assess the patient's [condition(s) or health status(es)]. Document and submit [the results] to the REMS Program using [REMS Material(s)]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. Document and submit [the results] to the REMS Program using [REMS Material(s)].

1. Health Care Providers who prescribe [drug/class name] must:	
After treatment discontinuation; [At specified interval] Include this time category if there are requirements that the health care provider must complete after the patient has discontinued treatment	23. Assess the patient's [condition(s) or health status(es)]. Include this requirement if there is monitoring and/or a particular lab test that must take place (e.g., pregnancy test that needs to take place). Repeat this requirement, as needed, to address multiple health conditions and/or lab tests. **OR** Assess the patient's [condition(s) or health status(es)]. Document and submit [the results] to the REMS Program using [REMS Material(s)]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. Document and submit [the results] to the REMS Program using [REMS Material(s)]
To maintain certification to prescribe, [specified interval, e.g., every 2 years] Include this time category if there are requirements that the health care provider must complete to be able to continue prescribing	24. Review the drug's Prescribing Information. Note that the Prescribing Information is not appended to the REMS. 25. Review the following: [List the Educational Material(s)]. 26. Successfully complete the [Knowledge Assessment] and submit it to the REMS Program. 27. Re-Enroll in the REMS by completing the [Re-Enrollment Form] and submitting it to the REMS Program.
At all times Include this time category if there are requirements that the health care provider must complete on an ongoing basis, as part of complying with the REMS program	28. Report [adverse event(s) of interest] to [the Manufacturer/the REMS Program/MedWatch]. **OR** Report [adverse event(s) of interest] to the REMS Program using [REMS Form]. 29. Report [treatment discontinuation or transfer of care] to [the Manufacturer/the REMS Program]. Use this requirement if a patient is no longer under the prescriber's care or has discontinued treatment. 30. Maintain records of [REMS activity]. Include this requirement if there are records of certain REMS activities (e.g. records documenting staff's completion of REMS training) that must be maintained, but are not submitted to the REMS program. These records may be requested at any time by the applicant or as part of a REMS audit 31. Comply with audits carried out by [Entity to conduct audit, e.g., applicant, FDA, or third party acting on behalf of the applicant or FDA] to ensure that all processes and procedures are in place and are being followed. Include this requirement if the REMS participant has to agree to be audited.

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2. Patients who are prescribed [drug/class name]:

If a particular REMS requirement applies only to a subset of patients (e.g. patients who can get pregnant), use the following format for the requirement:

For [subset to which the requirement applies]: [Requirement]

Example: For patients who can get pregnant: Counsel the patient on pregnancy prevention

If there are different requirements for different patient populations (e.g. pediatric), repeat this table for each population, and modify the header accordingly.

Before treatment initiation Include this time category if there are requirements that the patient must complete to be able to initiate treatment	1. Review the [List the Patient Material(s)]. 2. Complete [Patient Form] with the prescriber. Include this requirement if the patient form is not submitted to the REMS Program. If the form is submitted to the REMS Program, use requirement #3. 3. Enroll in the REMS Program by completing the [Enrollment Form] with the prescriber. Enrollment information will be provided to the REMS Program. Include this requirement if the form must be submitted to the REMS Program. Otherwise, use requirement #2. 4. Get [description of lab test]. **OR** Be monitored for [description of monitoring] Include this requirement if the patient is required to have a lab test completed or to be monitored. 5. Receive counseling from the prescriber on [topic(s)]. **OR** Receive counseling from the prescriber using [REMS Material]. **OR** Receive counseling from the prescriber on [topic(s)] using [REMS Material]. 6. Complete [Patient Questionnaire] Include this requirement if there are questions that patients need to answer (e.g. monthly questionnaire to assess a patient's understanding of the drug's risks and safe use conditions).

2. Patients who are prescribed [drug/class name]:

During treatment; before each [dose/infusion/prescription] Include this time category if there are requirements that the patient must complete prior to receiving subsequent prescriptions	7. Receive counseling from the prescriber on [topic(s)]. **OR** Receive counseling from the prescriber using [REMS Material]. **OR** Receive counseling from the prescriber on [topic(s)] using [REMS Material]. 8. Get [description of lab test]. **OR** Be monitored for [description of monitoring]. Include this requirement if the patient is required to have a lab test completed or to be monitored. 9. Complete [Patient Questionnaire]. Include this requirement if there are questions that patients need to answer (e.g. monthly questionnaire to assess a patient's understanding of the drug's risks and safe use conditions).
During treatment Include this time category if there are requirements that the patient must adhere to during treatment (i.e. not linked to the time a prescription is written)	10. Adhere to the safe use conditions, including [safe use condition(s), e.g. use of contraception]. **OR** Adhere to the safe use conditions described in the [Patient Educational Material]. **OR** Adhere to the safe use conditions, including [safe use condition(s), e.g. use of contraception] described in the [Patient Educational Material]. 11. Get [description of lab test]. **OR** Be monitored for [description of monitoring]. Include this requirement if the patient is required to have a lab test completed or to be monitored.
During treatment after administration Include this time category if there are requirements that the patient must complete at after administration during treatment (i.e. not linked to the time a prescription is written)	12. Get [description of lab test]. **OR** Be monitored for [description of monitoring]. Include this requirement if the patient is required to have a lab test completed or to be monitored
During treatment; [At specified interval] Include this time category if there are requirements that the patient must complete at specified intervals during treatment (i.e. not linked to the time a prescription is written)	13. Get [description of lab test]. **OR** Be monitored for [description of monitoring]. Include this requirement if the patient is required to have a lab test completed or to be monitored.

2. Patients who are prescribed [drug/class name]:	
After treatment discontinuation; [At specified interval] Include this time category if there are requirements that the patient must complete after they have discontinued treatment	14. Get [description of lab test]. **OR** Be monitored for [description of monitoring]. Include this requirement if the patient is required to have a lab test completed or to be monitored.
At all times Include this time category if there are requirements that the patient must complete on an ongoing basis, while under the REMS program	15. Inform the prescriber if [conditions under which prescriber should be contacted]. 16. Have the [item] with you. Include this requirement if the patient is required to have on hand or carry with them a specific item or intervention (e.g., wallet card, bracelet, emergency treatment).

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3.[Health care settings/prescribers/pharmacies] that dispense [drug/class name] must:	
If there are different requirements for different types of pharmacies and/or health care settings (e.g., inpatient pharmacies vs. outpatient pharmacy) repeat this table for each type of pharmacy and/or health care setting.	
To become certified to dispense Include this time category if there are requirements that the dispenser must complete to be able to dispense	1. Be able to [clinical activity to be performed]. Include this requirement if the dispenser has to have the ability to carry out a particular activity, such as administer a particular treatment. 2. Have [personnel with specific training/experience and/or specific equipment] on-site. Include this requirement if the health care setting needs to have personnel with particular training or particular medical equipment on-site. 3. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the [health care setting/pharmacy]. Include this requirement if the health care setting must designate an authorized representative to act on the healthcare setting's behalf. 4. Have the authorized representative review the [List the Educational Material(s)]. Include this requirement if the authorized representative is required to review certain educational materials that are provided as part of the REMS. 5. Have the authorized representative successfully complete the [Knowledge Assessment] and submit it to the REMS Program. 6. Have the authorized representative enroll in the REMS Program by completing the [Enrollment Form] and submitting it to the REMS Program.

3.[Health care settings/prescribers/pharmacies] that dispense [drug/class name] must:

OR

Have the authorized representative enroll in the REMS Program by completing and submitting the applicable enrollment form(s): [List all Enrollment Forms].

Use this version of the requirement if there are different enrollment forms for different types of settings (e.g. inpatient vs. outpatient pharmacy, chain vs. independent pharmacy).

7. Train all relevant staff involved in [activity] on [training topic(s)].

   OR

   Train all relevant staff involved in [activity] using [REMS Material(s)].

   OR

   Train all relevant staff involved in [activity] on [training topic(s)] using [REMS Material(s)].
8. Take training provided by [entity providing the training, e.g. the applicant, a CE provider].

   Include this requirement if instructor-led training is provided
9. Establish processes and procedures to verify [safe use conditions to be met].

   Include this requirement if the dispenser is responsible for setting up their own system to verify that safe use conditions have been met. If requirement #9 is included, also include requirement #12 to verify that safe use conditions have been met before dispensing.

3.[Health care settings/prescribers/pharmacies] that dispense [drug/class name] must:

Before dispensing Include this time category if there are requirements that the dispenser must complete before dispensing	10. Counsel the patient on [topic(s)]. Include this requirement if the health care provider is required to counsel the patient. The provider may be required to cover a particular topic, use a particular REMS material (e.g. a counseling tool, a Medication Guide), or both. **OR** Counsel the patient using [REMS Material]. **OR** Counsel the patient on [topic(s)] using [REMS Material]. **OR** Counsel the patient on [topic(s)] using [REMS Material]. Provide a copy of the material to the patient. 11. Provide the patient with the [REMS Material]. Include this requirement if there are materials that must be provided to a patient (e.g. Patient REMS Program Brochure, Medication Guide). 12. Verify that [safe use conditions to be met] through the processes and procedures established as a requirement of the REMS Program. Include this requirement if the dispenser must verify that safe use conditions have been met before dispensing, and must use systems established through requirement #9. 13. Obtain authorization to dispense each prescription by contacting the REMS Program to verify [safe use condition to be met]. Include this requirement if the dispenser must obtain authorization from the REMS Program to dispense the drug. 14. Dispense no more than a [# of days] days' supply. 15. Not dispense refills.
After dispensing Include this time category if there are requirements that the dispenser must complete after dispensing	16. Assess the patient's [condition(s) or health status(es)]. Include this requirement if there is monitoring and/or a particular lab test that must take place (e.g., pregnancy test that needs to take place before each prescription). Repeat this requirement, as needed, to address multiple health conditions and/or lab tests. **OR** Assess the patient's [condition(s) or health status(es)]. Document and submit [the results] to the REMS Program using [REMS Material(s)]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. Document and submit [the results] to the REMS Program using [REMS Material(s)].

3.[Health care settings/prescribers/pharmacies] that dispense [drug/class name] must:

Before administering *If the drug is administered by a health care provider*: Include this time category if there are requirements that the healthcare provider must complete before the drug is administered	17. Counsel the patient on [topic(s)]. Include this requirement if the health care provider is required to counsel the patient. The provider may be required to cover a particular topic, use a particular REMS material (e.g. a counseling tool, a Medication Guide), or both. **OR** Counsel the patient using [REMS Material]. **OR** Counsel the patient on [topic(s)] using [REMS Material]. **OR** Counsel the patient on [topic(s)] using [REMS Material]. Provide a copy of the material to the patient. 18. Provide the patient with the [REMS Material]. Include this requirement if there are materials that must be provided to a patient (e.g. Patient Brochure, Medication Guide). 19. Assess the patient's [condition(s) or health status(es)]. Include this requirement if there is monitoring and/or a particular lab test that must take place (e.g., pregnancy test that needs to take place before each prescription). Repeat this requirement, as needed, to address multiple health conditions and/or lab tests. **OR** Assess the patient's [condition(s) or health status(es)]. Document and submit [the results] to the REMS Program using [REMS Material(s)]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. Document and submit [the results] to the REMS Program using [REMS Material(s)].
After administering *If the drug is administered by a healthcare provider*: Include this time category if there are requirements that the health care provider must complete after the drug is administered	20. Assess the patient's [condition(s) or health status(es)]. Include this requirement if there is monitoring and/or a particular lab test that must take place (e.g., pregnancy test that needs to take place before each prescription). Repeat this requirement, as needed, to address multiple health conditions and/or lab tests. **OR** Assess the patient's [condition(s) or health status(es)]. Document and submit [the results] to the REMS Program using [REMS Material(s)]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. **OR** Assess the patient's [condition(s) or health status(es)] by [list lab test(s) or monitoring]. Document and submit [the results] to the REMS Program using [REMS Material(s)].

3.[Health care settings/prescribers/pharmacies] that dispense [drug/class name] must:	
To maintain certification to dispense, [specified interval, e.g. every 2 years] Include this time category if there are requirements that the dispenser must complete to be able to continue dispensing	21. Have the authorized representative review the [List the Educational Material(s)]. Include this requirement if the authorized representative is required to review certain educational materials that are provided as part of the REMS Program. 22. Have the authorized representative successfully complete the [Knowledge Assessment] and submit it to the REMS Program. **OR** 23. Have the authorized representative re-enroll in the REMS Program by completing the [Re-Enrollment Form]. **OR** Have the authorized representative re-enroll in the REMS Program by completing the applicable form(s): [List all Re-Enrollment Forms]. Use this version of the requirement if there are different enrollment forms for different types of settings (e.g. inpatient vs. outpatient pharmacy, chain vs. independent pharmacy). 24. Have the new authorized representative enroll in the REMS Program by completing the applicable form [Enrollment Form]. Include this requirement if the pharmacy designates a new authorized representative.
At all times Include this time category if there are requirements that the dispenser must complete on an ongoing basis, while under the REMS program	25. Report [adverse event(s) of interest] to [the Manufacturer/the REMS Program/MedWatch]. **OR** Report [adverse event(s) of interest] to the REMS Program using [REMS Form]. 26. Return unused product to [the manufacturer]. 27. Not distribute, transfer, loan, or sell [drug/class name]. **OR** Not distribute, transfer, loan, or sell [drug/class name], except to certified dispensers. 28. Maintain records of [activity]. Include this requirement if there are records of certain REMS activities (e.g. records documenting staff's completion of REMS training) that must be maintained, but are not submitted to the REMS program. These records may be requested by the applicant or as part of a REMS audit. 29. Comply with audits carried out by [Entity to conduct audit, e.g., applicant or third party acting on behalf of the applicant] to ensure that all processes and procedures are in place and are being followed. Include this requirement if the REMS participant has to agree to be audited.

4. Wholesalers that distribute [drug/class name] must:

To be able to distribute Include this time category if there are requirements that the wholesaler must complete to be able to distribute	1. Establish processes and procedures to ensure that the drug is distributed only to certified [setting(s)]. 2. Train all relevant staff involved in [activity] on [topic(s)].
At all times Include this time category if there are requirements that the wholesaler must complete on an ongoing basis under the REMS program	3. Distribute only to certified [setting(s)]. 4. Maintain records of [activity]. Include this requirement if there are records of certain REMS activities (e.g., records of drug distribution) that must be maintained, but are not submitted to the REMS program. These records may be requested by the applicant or as part of a REMS audit. **Or** Maintain and submit records of [activity]. Include this requirement if there are records of certain REMS activities (e.g., records of drug distribution) that must be maintained and submitted to the REMS program. 5. Comply with audits carried out by [Entity to conduct audit, e.g., applicant or third party acting on behalf of the applicant] to ensure that all processes and procedures are in place and are being followed. Include this requirement if the wholesaler is required to comply with audits of their activities under the REMS.

----------End Subsection A----------

----------**Start Subsection B**----------

REMS Applicant Requirements

This subsection describes requirements for applicants to develop and make available REMS *training*; develop and disseminate REMS *communications materials*; develop systems and processes to support REMS *operations*; and ensure participants' *compliance* with the REMS.

REMS Training

The requirements under this heading relate to the requirement for the applicant to develop REMS training and provide to health care providers. REMS training requirements might also include the requirement for the applicant to develop a knowledge assessment for health care providers.

The REMS training requirements include information about how the training is being provided (e.g., website, mailing, in-person) and whether the training is being provided by a third party (such as a Continuing Education (CE) provider). The REMS training section may also include whether the applicant is required to provide funding for training.

If there are no requirements for the applicant to develop and make available REMS training, delete the requirements under this heading.

[Applicant] must provide training to health care providers who prescribe [drug/drug class].

The training includes the following educational material(s): [Educational Material(s)]. The training must be [describe how training will be provided, e.g. available on a website, delivered by the applicant or accredited CE providers, etc.].

[Applicant] must provide training to health care settings/prescribers/pharmacies who dispense [drug/drug class].
The training includes the following educational material(s): [Educational Material(s)]. The training must be [describe how training will be provided, e.g. available on a website, delivered by the applicant or accredited CE providers, etc.].

REMS Communications
The requirements under this header support the development and dissemination of REMS communication materials to health care providers and professional organizations or societies. If there are no requirements for the applicant to disseminate REMS communications, delete the requirements under this heading.
The table below describes who should receive the REMS communication materials, what materials they should receive, as well as how, when and how often they should receive the materials. The table includes the following information:

Target Audience: The target audience is the particular group of health care providers that are the intended recipients of a REMS communication. For each target audience, include a description of the audience. Include an additional row for each distinct audience.
Communication Materials: The communication materials are intended to disseminate information about the REMS (e.g., REMS Letter for Health Care Providers and for Professional Societies, REMS Fact Sheets, Journal information piece, and REMS Slides).
Dissemination Plan: The dissemination plan describes how the communication materials will be distributed (e.g., via e-mail), the timing (e.g., start, end, how frequency), and whether there is any follow-up required. Include additional distribution plans if a given material is distributed in multiple ways.

To inform health care providers about the REMS Program and the risks and safe use of [drug/class name], [Applicant] must disseminate REMS communication materials according to the table below:

Target Audience	Communication Materials & Dissemination Plans
[Target Audience]	[Communication Material(s)] • [Dissemination Plan 1] • [Dissemination Plan 2]

Target Audience	Communication Materials-& Dissemination Plans
Health care providers who are likely to prescribe [drug/class name]	Include Communication Materials that apply to this REMS and delete those that do not apply. Under each REMS communication, include dissemination methods that apply to this REMS and delete those that do not apply: REMS Letter(s): [Health Care Provider REMS Letter], [Professional Society REMS Letter*] with attachment(s) [REMS material(s)] 1. Mail within [X] calendar days of the [date [Drug] is first commercially distributed/approval of the REMS modification] ([mm/dd/yyyy]) and again[X] months later. 2. eMail within [X] calendar days of the [date [Drug] is first commercially distributed/approval of the REMS modification] ([mm/dd/yyyy]) and again[X] months later. 3. Make available via a link from the [Drug] REMS Program Website. 4. Disseminate through [field-based sales and medical representatives]. 5. Disseminate through professional societies and request the letter or content be provided to their members. 6. Disseminate at Professional Meetings for [duration] from [the [date [Drug] is first commercially distributed/approval of the REMS modification] [(mm/dd/yyyy)]. [Journal Information Piece] 1. Publish every [frequency, e.g. quarterly] for [duration] after the [date [Drug] is first commercially distributed/approval of the REMS modification] [(mm/dd/yyyy)] in the following journals: [Fact Sheet] 1. Disseminate and prominently display at Professional Meetings where [Applicant] has a presence for [duration] from the [date [Drug] is first commercially distributed/ approval of the REMS modification] [(mm/dd/yyyy)]. 2. Disseminate through [field-based sales and medical representatives] during [the initial and/or follow-up] discussion with healthcare providers for [duration] after [[Drug] is first commercially distributed/approval of this REMS modification] [(mm/dd/yyyy)]. [Field-based sales and/or medical representatives] to orally review the risk messages contained in the REMS Factsheet during the visit with the health care provider. [Website] 1. Include all of the currently approved [REMS materials/Prescribing Information/Medication Guide]. 2. Include a prominent REMS-specific link to the [Drug] REMS Program website. The [Drug] REMS Program website must not link back to the promotional product website(s). 3. Continue for [duration] from the [date [Drug] is first commercially distributed/approval of the REMS modification] ([mm/dd/yyyy]).

* Provide a list of the professional societies in your REMS Supporting Document

REMS Operations

The requirements under this header support activities that are described in subsections A and/or *REMS Training Requirements*. Only include these requirements (or the relevant subset) if the REMS document includes subsection A and/or *REMS Training Requirements*.

To support REMS Program operations, [applicant] must:

1. Establish and maintain a REMS Program website, [REMS Website]. The REMS Program website must include the capability to complete [prescriber/pharmacy/HCS setting] certification or enrollment online, [the capabilitly to enroll and manage patients online], and the option to print the PI, Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS Program website. The REMS Program website must not link back to the promotional product website(s).
2. Make the REMS Program website fully operational and all REMS materials available through [medium e.g. website or call center] [by the date [Drug] is first commercially distributed /within [30/60/90] calendar days of REMS modification] [(mm/dd/yyyy)]. Include implementation dates only if applicable for a REMS modification.
3. Establish and maintain a REMS Program call center for REMS participants at [phone number].
4. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the [drug/class name] REMS Program.
5. Ensure [List REMS participants] are able to [REMS activity(ies), e.g. enrollment, dispensing authorization] by [method(s) through which activity may be completed]. Use this requirement to specify the multiple ways that an applicant must provide for a REMS participant to comply with a particular REMS requirement(s); for example, REMS participants must be able to enroll in the REMS by phone, fax, and online. Repeat this requirement as needed (e.g., to address multiple REMS participants, requirements, or activities).
6. Provide [List REMS Material(s)], and the Prescribing Information to REMS participants who (1) attempt to prescribe/dispense/distribute [Drug] and are not yet certified or (2) inquire about how to become certified.
7. Notify [List REMS participants] within [specific, reasonable amount of time] after they become certified in the REMS Program. Use this requirement if the REMS requires certification to prescribe and/or dispense the drug.
8. Provide certified prescribers access to the database of [certified pharmacies and enrolled patients].
9. Provide certified pharmacies access to the database of [certified prescribers and enrolled patients].

REMS Compliance

The requirements under this header support activities that are described in subsections A and/or REMS Program Training Requirements. Only include these requirements (or the relevant subset) if the REMS document includes subsection A and/or REMS Training Requirements.

To ensure REMS participants' compliance with the REMS Program, [applicant] must:

10. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: [drug] distribution and dispensing; certification of prescribers, pharmacies, and health care settings; enrolled patients; and audits of REMS participants. These records must be readily available for FDA inspections.

11. Establish a plan for addressing noncompliance with REMS Program requirements.

12. Monitor [List REMS participant(s) to be monitored] on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if non-compliance is identified, including de-certification.

13. Audit [REMS participant(s) to be audited] no later than [number of days, e.g. 180 days] after they become certified, to ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements.
    OR
    Audit [REMS participant(s) to be audited] at [timing/interval/frequency of audit] to [goal of audit].Include this version of the requirement if the audit targets a specified percentage of the group (e.g., 10% of certified pharmacies). The [timing/interval/frequency] may specify that audits take place at a specified frequency or within a certain number of days after the REMS participant has enrolled in or become certified in the REMS. Repeat this requirement if the audit approach differs among different groups of REMS participants.

14. Take reasonable steps to improve implementation of and compliance with the requirements in the [drug/class name] REMS Program based on monitoring and evaluation of the [drug/class name] REMS Program. Include this requirement for all REMS with a subsection A.

----------End Subsection B----------

IV. REMS Assessment Timetable

This section describes the timetable for the applicant to submit its REMS Assessments. [NDA/BLA Holder(s)] must submit REMS Assessments at [time intervals/frequency, e.g. 18 months, 3 years, and 7 years from the date of the initial REMS approval **OR** 6 months,12 months, and annually thereafter from the date of the initial approval of the REMS]. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. [NDA/BLA Holder(s)] must submit each assessment so that it will be received by the FDA on or before the due date.

This section does not apply to ANDAs, and should not be included in ANDA REMS document.

V. REMS Materials

This section should include a consolidated list of all materials mentioned in the *REMS Requirements Section.* The materials listed in this section are part of the REMS and must be appended to the REMS document.
When listing the REMS materials, do not include the name of the REMS Program in the name of the material. For example, use "Prescriber Enrollment Form" instead of "Drug X REMS Prescriber Enrollment Form."
Delete headings and items from the list of materials that do not apply to your REMS.

The following materials are part of the [drug/class name] REMS and are appended**:**

Enrollment Forms:

Prescriber:

1. [Prescriber Enrollment Form]

Patient:

2. [Patient Enrollment Form]
3. If the REMS includes different enrollment forms for different patient populations, include them as follows:
   [Patient Enrollment Form for [type of patient]]

Pharmacy:

4. [Pharmacy Enrollment Form]
5. If the REMS includes specific enrollment forms for different types of pharmacies, include them as follows:
   [[Type of pharmacy] Pharmacy Enrollment Form]
   For example:
   [Independent Pharmacy Enrollment Form]
   [Inpatient Pharmacy Enrollment Form]

Health Care Setting:

6. [Healthcare Setting Enrollment Form]
7. [Other setting-specific Enrollment Forms, as needed]

Other Enrollment Form(s): Include the names of other enrollment forms here

Training and Educational Materials

Prescriber:

8. [Prescriber Education]
9. [REMS Program Overview]
10. [Knowledge Assessment]

Pharmacy:

11. [Pharmacy Education]
12. [REMS Program Overview]
13. [Knowledge Assessment]

Patient Care Form(s)

14. [Patient Care Form] Include the names of forms used in patient care (other than enrollment forms), such as forms used to support patient monitoring or to document safe use conditions

Communication Materials

15. [Dear Health Care Provider letter]
16. [Professional Society REMS letter]
17. [Journal Information Piece]
18. [Fact Sheet]

Other Materials

19. [REMS Program website]
20. [Administrative forms and materials] Include any administrative forms or materials here, as well as materials that don't fit into the above categories