Overview of the REMS Integration Initiative

December 4th 2017

Center for Drug Evaluation and Research (CDER)
Purpose

• To introduce the new REMS document template, and...

• To discuss work completed under the REMS Integration Initiative
Agenda

1. Introduction & Background  
   (Aaron Sherman)

2. The new REMS document template  
   (Gita Toyserkani and Suzanne Robottom)

3. REMS@FDA website update  
   (Amy Ramanadham)

4. REMS SPL update  
   (Adam Kroetsch)
What is a REMS?

- **Risk Evaluation and Mitigation Strategy**
- A required risk management plan that uses risk minimization strategies beyond professional labeling to ensure that the benefits of the drug outweigh its risks
- Authority given under the FDA Amendments Act (FDAAA) of 2007
  - Section 505-1 of the FD&C Act
- FDA can require a REMS:
  - Before approval if FDA determines a REMS is necessary to ensure the benefits of the drug outweigh the risks
  - After approval if FDA becomes aware of new safety information and determines that a REMS is necessary to ensure the benefits of the drug outweigh the risks
- There are currently 76 approved REMS
Key Components of the REMS Integration Initiative

• Stakeholder outreach to evaluate and improve REMS

• Standardization and integration of REMS into existing healthcare practices, and reducing associated burden

• Implementation of REMS commitments included in the 5th reauthorization of the Prescription Drug User Fee Act (PDUFA)¹
  – Guidance development
  – 4 priority projects to address specific areas of improvement

## Stakeholder Engagement

<table>
<thead>
<tr>
<th>Date</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 8, 2013</td>
<td>PDUFA Stakeholders Meeting</td>
</tr>
<tr>
<td>March – June 2013</td>
<td>15 Stakeholder Listening Sessions — Experience Implementing ETASU REMS</td>
</tr>
<tr>
<td>May 16, 2013</td>
<td>Drug Safety Board Meeting</td>
</tr>
<tr>
<td>May 23, 2013</td>
<td>Trends Emerging in Risk Management (TERM) Meeting</td>
</tr>
<tr>
<td>July 25-26, 2013</td>
<td>Public Meeting: REMS Standardization and Evaluation</td>
</tr>
<tr>
<td>Sept. 25, 2013</td>
<td>Strengthening REMS Through Systematic Analysis, Standardized Design, and Evidence-Based Assessment (Brookings)</td>
</tr>
<tr>
<td>Sept. 2014</td>
<td>Report: Standardizing and Evaluating REMS (<a href="#">link</a>)</td>
</tr>
<tr>
<td>Feb. 6 / May 6, 2015</td>
<td>NCPDP Workgroup Meeting and Annual Conference</td>
</tr>
<tr>
<td>Feb. 9, 2015</td>
<td>HL7 SPL Tech Team Meeting</td>
</tr>
<tr>
<td>May 18, 2015</td>
<td>Incorporating continuing education into single-drug REMS: Exploring the challenges and opportunities (Brookings)</td>
</tr>
<tr>
<td>Oct. 5-6, 2015</td>
<td>Public Meeting: Understanding and Evaluating REMS Impact on the Health Care Delivery System and Patient Access</td>
</tr>
<tr>
<td>Dec. 2015 – May 2016</td>
<td>REMS SPL Pilot with 9 companies to test &amp; refine the REMS data model/terminology</td>
</tr>
</tbody>
</table>
Thank you
Stakeholder Feedback: Key Themes

*Stakeholders told us that:*

- REMS materials and requirements are not communicated clearly and consistently
- Specific activities and requirements are not always clearly outlined
- Stakeholders reported spending excessive time trying to locate, understand, and comply with different REMS requirements
Guidances

• Use of a Drug Master File [DMF] for Shared System REMS Submissions (link)
• Format and Content of a REMS Document (link)
• Providing Regulatory Submissions in Electronic Format – Content of the REMS Document Using Structured Product Labeling (link)
• FDA’s Application of Statutory Factors in Determining When a REMS Is Necessary (link)
• REMS: Modifications and Revisions (link)
# REMS Priority Projects

The following priority projects were selected as part of a PDUFA V commitment and completed under the REMS Integration Initiative.

<table>
<thead>
<tr>
<th>Projects Selected</th>
<th>Deliverable</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Providing Patient <em>Benefit/Risk Information</em> by Improving Tools for Prescriber-to-Patient Counseling</td>
<td>A Framework for Benefit-Risk Counseling to Patients about Drugs with a REMS (<a href="#">link</a>)</td>
</tr>
<tr>
<td>2 <em>Prescriber Education</em>—REMS and Continuing Education (CE) for Health Care Providers</td>
<td>A report on the feasibility of REMS-related CE including a description of potential models for REMS-related CE development and delivery (<a href="#">link</a>)</td>
</tr>
<tr>
<td>3 Standardizing REMS Information for Inclusion into <em>Pharmacy Systems</em> Using Structured Product Labeling (SPL)</td>
<td>A revised SPL implementation guide describing how to make structured REMS information available to patients and healthcare providers.</td>
</tr>
<tr>
<td>4 Providing a Central Source of REMS Information for <em>Practice Settings</em></td>
<td>An enhanced FDA REMS Website (<a href="#">REMS@FDA</a>)</td>
</tr>
</tbody>
</table>
The “4 W’s” of REMS

This is the key organizational principle serving as the foundation for how REMS information is organized in the new REMS document template, in SPL format, and on the REMS@FDA website.

<table>
<thead>
<tr>
<th>“W”</th>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Who”</td>
<td>The participant who must meet the REMS requirement</td>
<td>prescriber, dispenser, health care setting</td>
</tr>
<tr>
<td>“When”</td>
<td>A particular “stage” in the treatment or medication use process around which REMS activities needs to occur</td>
<td>certification, prescribing, dispensing, administration</td>
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<tr>
<td>“What”</td>
<td>a clinical or administrative activity that must be performed as part of the REMS</td>
<td>counseling a patient, completing an enrollment form, lab testing</td>
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<tr>
<td>“With What”</td>
<td>Approved REMS material with which the requirement is carried out</td>
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Overview

• History of the REMS Document

• Development of the New REMS Document Template

• Overview of the New REMS Document Template

• Submitting a REMS Document
HISTORY OF THE REMS DOCUMENT
What does FDA approve?

**REMS Document**

**REMS Materials**
REMS Document

• The ‘face’ of the REMS
  – Introduced with the first approved REMS in 2008

• Purpose of the REMS document
  – Establishes the REMS requirements for applicants
  – Communicates the REMS requirements for stakeholders (e.g., prescribers, pharmacists, healthcare administrators, distributors, patients)

• The only document that captures the requirements for all applicable stakeholders

• A REMS Document ‘Template’ was included in 2009 as part of draft guidance for Industry Format and Content of REMS, REMS Assessments, and Proposed REMS Modifications
APPENDIX A: REMS TEMPLATE

If you are not proposing to include one of the listed elements, include a statement that the element is not necessary.

Application number TRADE NAME (DRUG NAME)

Class of Product as per label
Applicant name
Address
Contact Information

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S):
List the goals and objectives of the REMS.

II. REMS ELEMENTS:

A. Medication Guide or PPI
   If a Medication Guide is included in the proposed REMS, include the following:
   A Medication Guide will be dispensed with each [drug name] prescription. [Describe in detail how you will comply with 21 CFR 208.24]

B. Communication Plan
   If a Communication Plan is included in the proposed REMS, include the following:
   [Applicant] will implement a communication plan to healthcare providers to support implementation of this REMS.

   List elements of communication plan. Include a description of the intended audience, including the types and specialties of healthcare providers to which the materials will be directed. Include a schedule for when and how materials will be distributed. Append the printed material and web show to the REMS Document.

C. Elements To Assure Safe Use
   If one or more Elements to Ensure Safe Use are included in the proposed REMS, include the following:
   List elements to assure safe use of Section 505.1(f)(3)(A.F) included in this REMS. Elements to assure safe use may, to mitigate a specific serious risk listed in the labeling, require that:

   A. Healthcare providers who prescribe [drug name] have particular training or experience, or are specially certified. Append any enrollment forms and relevant attestations/certifications to the REMS;
   B. Pharmacies, practitioners, or healthcare settings that dispense [drug name] are specially certified. Append any enrollment forms and relevant attestations/certifications to the REMS;
   C. [Drug name] may be dispensed to patients only in certain healthcare settings (e.g., hospitals);
   D. [Drug name] may be dispensed to patients with documentation of safe-use conditions;
   E. Each patient using [drug name] is subject to certain monitoring. Append specified procedures to the REMS;
   F. Each patient using [drug name] be enrolled in a registry. Append any enrollment forms and other related materials to the REMS Document.

D. Implementation System
   If an Implementation System is included in the proposed REMS, include the following:
   Describe the implementation system to monitor and evaluate implementation for, and work to improve implementation of, Elements to Ensure Safe Use (D), (C), and (D), listed above.

   E. Timetable for Submission of Assessments
   For products approved under an NDA or BLA, specify the timetable for submission of assessments of the REMS. The timetable for submission of assessments shall be no less frequent than by 18 months, 3 years, and in the 7th year after the REMS is initially approved. You should specify the reporting interval (dates) that each assessment will cover and the planned date of submission to the FDA of the assessment. 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 days before the submission date for that assessment. For example, the reporting interval covered by an assessment that is to be submitted by July 31st should conclude no earlier than June 1st.

   Include the following paragraph in your REMS:
   COMPANY will submit REMS Assessments to the FDA <<Insert schedule of assessments: at a minimum, by 18 months, by 3 years and in the 7th year from the date of initial approval of the REMS (DATE of Approval)>>. 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 days before the submission date for that assessment. COMPANY will submit each assessment so that it will be received by the FDA on or before the due date.
I. Goals

II. REMS Elements
   A. Medication Guide
   B. Communication Plan
   C. Elements to Assure Safe Use
      A. Healthcare providers who prescribe [drug name] have particular training or experience, or are specially certified. Append any enrollment forms and relevant attestations/certifications to the REMS;
      B. Pharmacies, practitioners, or healthcare settings that dispense [drug name] are specially certified. Append any enrollment forms and relevant attestations/certifications to the REMS;
      C. [Drug name] may be dispensed to patients only in certain healthcare settings (e.g., hospitals);
      D. [Drug name] may be dispensed to patients with documentation of safe-use conditions;
      E. Each patient using [drug name] is subject to certain monitoring. Append specified procedures to the REMS; or
      F. Each patient using [drug name] be enrolled in a registry. Append any enrollment forms and other related materials to the REMS Document.

D. Implementation System

E. Timetable for Submission of Assessments
DEVELOPMENT OF THE NEW REMS DOCUMENT TEMPLATE
Lack of Standardization

REMS requirements are described in a variety of ways and lack consistent terminology:

• Similar concepts often have different names
• Different concepts may have the same name
• REMS are often described using regulatory terms like “ETASU”, “Communication Plan” and “Element A-F”, which do not provide useful information about how REMS programs work
Stakeholder Feedback on REMS Requirements

- Requirements are not communicated in a clear and consistent manner
- Unclear who is responsible for implementing each REMS requirement
- Too much time spent trying to understand and comply with REMS
- Difficult to integrate REMS into existing health information systems and health care delivery processes
Purpose of the Revising the REMS Document

• Develop a method to share clear and consistent information about the REMS requirements

• Facilitate integrating REMS into the healthcare system

• Provide a better resource for industry for creating a REMS document

• Provide a foundation for developing best practices and continuous quality improvement
Efforts to Improve how REMS Requirements are Captured

To address stakeholder concerns, we have taken the following steps:

1. Characterized existing REMS by creating an inventory of REMS requirements and various ways they have been communicated across REMS programs

2. Created a new way of communicating REMS requirements called the REMS Participant Section
   - Standardized how REMS requirements are described and minimized unnecessary variations
   - Made REMS requirements more consistent, predictable and easier to understand

3. Received additional feedback from stakeholders through ongoing outreach efforts

4. Refined the new REMS document template
Additional Benefits of the Initiative

Enables information to be repurposed for REMS SPL submissions and REMS@FDA Website:

• REMS SPL
  – Once applicants start using the new REMS document template, creation of “REMS summaries” for the purpose of submitting REMS in SPL will no longer be necessary

• REMS@FDA Website
  – Website REMS Summary uses a similar approach to the new REMS document template. Once applicants start using the new template, the website REMS Summary can be automatically populated using the participant section of the REMS document
Guiding Organizational Principle

Who has to do what, when and with what
# New Template & “4 W’s” of REMS

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OVERVIEW OF THE NEW REMS DOCUMENT TEMPLATE
New REMS Document Template
The Template is 19 Pages?!?!?

Substantially more instruction and standardized text to choose from.
How to Use the Template

- **Red Text** = Instructions
- **Black Text** = Standardized template text
- **Blue text** = Name of REMS Material
- [Bracketed (blue or black) text] = Information that needs to be entered
How to Use the Template

• Formatting is standardized
  – Margins
    • “narrow” setting (0.5” top, bottom, left, and right)
  – Font
    • Headers: **Verdana 14 bold**
    • Text: *Verdana 10*
How to Use the Template

• Retain what requirements apply, delete what requirements do not apply

• Requirements are not changing, how the requirements are organized has changed

• Use the standardized text
  – Covers the most commonly used requirements
  – Some REMS requirements have multiple versions of standardized text to describe the different ways the requirement can be carried out
  – The different versions of a requirement appear in black text, separated by the word “OR” in red text
Sections of the New REMS Document Template

I. Administrative Information
II. REMS Goals
III. REMS Requirements
   – Section A: REMS Participant Requirements
     • Healthcare providers who prescribe must
     • Patients who are prescribed
     • Healthcare settings/prescribers/pharmacies that dispense must
     • Wholesalers that distribute must
   – Section B: REMS Applicant Requirements
     • Training
     • Communication
     • Operations
     • Compliance
IV. REMS Assessment Timetable
V. REMS Materials
Administrative Information

Initial REMS approval: 01/2017
Most recent modification: 12/2017

BLA 123456 Welipax (welimab)
Human Interleukin-111 Receptor Z Antagonist
FarmFa, Inc.
111 Corporate Boulevard, Industry, NJ 12345
Phone: (111) 111-1234

RISK EVALUATION AND MITIGATION STRATEGY (REMS)
I. Goals

Risk Evaluation and Mitigation Strategy (REMS) Document
Welipax (welimab) REMS Program

I. Administrative Information

Application Number: BLA 123456
Applicant: FarmFa, Inc
Initial REMS Approval: 01/2017
Most Recent REMS Update: 12/2017

II. REMS Goal
I. Administrative Information

II. REMS Goals

III. REMS Requirements
   – Section A: REMS Participant Requirements
     • Healthcare providers who prescribe must
     • Patients who are prescribed
     • Healthcare settings/prescribers/pharmacies that dispense must
     • Wholesalers that distribute must
   – Section B: REMS Applicant Requirements
     • Training
     • Communication
     • Operations
     • Compliance

IV. REMS Assessment Timetable

V. REMS Materials
New Template

I. Administrative Information

II. REMS Goals

III. REMS Requirements
   - Section A: REMS Participant Requirements
     - Healthcare providers who prescribe
     - Patients who are dispensed
     - Healthcare settings/prescribers/pharmacies that dispense
     - Wholesalers that distribute
   - Section B: REMS Applicant Requirements
     - Training
     - Communication
     - Operations
     - Compliance

IV. REMS Assessment Timetable

V. REMS Materials
REMS Requirements – Old Template

1. Healthcare providers who prescribe Welipax must be certified
   a. To become certified to prescribe Welipax, prescribers must:
      i. Review the Prescribing Information for Welipax
      ii. Review the Welipax REMS Education Program.
      iii. Enroll in the Welipax REMS Program by completing the Welipax REMS Program Prescriber Enrollment Program.
   b. As a condition of certification, prescribers must:
      i. Enroll each patient in the Welipax REMS Program by performing the following:
         1) Prior to providing the first prescription, counsel the patient that holiday stress has occurred in patients treated with Welipax by informing the patient of the following:
         2) Complete the Welipax REMS Program Patient-Prescriber Agreement Form for each patient. Submit the completed form to the Welipax REMS Program and store a copy in the patient’s records.
         3) Provide the patient with the Welipax REMS Program Patient Wallet Card.
         4) Inform the Welipax REMS Program if an enrolled patient has discontinued therapy or is no longer under your care.
   c. FarmFa must:
      i. Ensure that prescribers who prescribe Welipax are certified in accordance with the requirements described above.
      ii. Provide all the following mechanisms to complete the certification process for the Welipax REMS Program: online.
Rems requirements – New Template

FarmFa must ensure that health care providers, patients, pharmacies, and wholesalers/distributors comply with the following requirements:

<table>
<thead>
<tr>
<th>Who</th>
<th>When</th>
<th>What</th>
<th>With</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health care providers who prescribe Welipax must:</td>
<td>Before treatment initiation (first dose)</td>
<td>To become certified to prescribe</td>
<td></td>
</tr>
</tbody>
</table>

1. Review the drug’s Prescribing Information
2. Review the Prescriber Education Program.
3. Enroll in the REMS by completing the Prescriber Enrollment Form and submitting it to the REMS Program.
4. Counsel the patient that holiday stress occurs with patients treated with Welipax, to be aware of symptoms and steps to take if symptoms occur.
5. Provide the patient with the Patient Wallet Card
6. Enroll the patient by completing and submitting the Patient-Prescriber Agreement Form to the REMS Program. Retain a copy in the patient’s record.
7. Inform FarmFa if a patient is no longer under your care or has discontinued treatment.
Key Points - REMS Participant Requirements

• What to Include
  – Activities required by REMS participants to undertake

• What not to include
  – Activities that REMS participants learn about, understand, or acknowledge but do not agree to undertake
  – Activities that REMS participants do not need to complete in order to be able to use the drug

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

• If there are different requirements for different types of health care settings, repeat this table for each type of health care setting (e.g., inpatient pharmacy vs outpatient pharmacy)

• Dedicated section for patients and wholesalers
I. Administrative Information
II. REMS Goals
III. REMS Requirements
   – Section A: REMS Participant Requirements
     • Healthcare providers who prescribe
     • Patients who are dispensed
     • Healthcare settings/prescribers/pharmacies that dispense
     • Wholesalers that distribute
   – Section B: REMS Applicant Requirements
     • Training
     • Communication
     • Operations
     • Compliance
IV. REMS Assessment Timetable
V. REMS Materials
Applicant Requirements

• **Old template**
  – “[Applicant] must...” appears in a variety of places
    • under each element (i.e., MG, CP, ETASU) as well as, if applicable, the Implementation System

• **New template**
  – All requirements pertaining to the Applicant are organized under “Section B - Applicant Requirements”
    • Training
    • Communication
    • Operations
    • Compliance
Communication Materials

- All materials related to communication are organized into one section
- In tabular format and includes standardized text

To inform healthcare providers about the REMS Program and the risks and safe use of Welipax, FarmFa must disseminate REMS communication materials according to the table below:

<table>
<thead>
<tr>
<th>Target Audience</th>
<th>Communication Materials &amp; Dissemination Plans</th>
</tr>
</thead>
</table>
| All prescribers likely to prescribe Welipax | **REMS Letter:** Healthcare Provider REMS Letter with attachment: Fact Sheet  
1. Mail within 30 calendar days of the date Welipax is first commercially distributed and again 6 months later.  
2. eMail within 30 calendar days of the date Welipax is first commercially distributed and again 6 months later.  
3. Make available via a link from the Welipax REMS Program Website.  
4. Disseminate through professional societies and request the content be provided to their members.  
5. Disseminate at Professional Meetings for 1 year from the date Welipax is first commercially distributed. |
New Template

I. Administrative Information
II. REMS Goals
III. REMS Requirements
   – Section A: REMS Participant Requirements
     • Healthcare providers who prescribe
     • Patients who are dispensed
     • Healthcare settings/prescribers/pharmacies that dispense
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     • Communication
     • Operations
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IV. REMS Assessment Timetable
V. REMS Materials
New Template

I. Administrative Information

II. REMS Goals

III. REMS Requirements
   – Section A: REMS Participant Requirements
     • Healthcare providers who prescribe
     • Patients who are dispensed
     • Healthcare settings/prescribers/pharmacies that dispense
     • Wholesalers that distribute
   – Section B: REMS Applicant Requirements
     • Training
     • Communication
     • Operations
     • Compliance

IV. REMS Assessment Timetable

V. REMS Materials
REMS Materials

• **Old template**
  - Materials are listed under each section they correspond to

• **New template**
  - Hyperlink when they appear in the text of the REMS Document
  - Organized by type of material and target audience
  - Complete list of ALL the REMS materials appear in their own section at the end of the REMS Document

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V. **REMS Materials**

The following materials are part of the Welipax REMS and are appended:

**Enrollment Forms**
- Prescriber
  1. Prescriber Enrollment Form
- Patient
  2. Patient-Prescriber Agreement Form
- Pharmacy
  3. Pharmacy Enrollment Form

**Training and Educational Materials**
- Prescriber
  4. Prescriber Education Program
- Patient
  5. Patient Wallet Card

**Communication Materials**
- 6. Healthcare Provider REMS Letter
- 7. Fact Sheet

**Other Materials**
- 8. REMS Program website
SUBMITTING A REMS DOCUMENT
Submitting a REMS Document

• **If you plan to submit a new REMS....**
  – Expect all REMS submissions in the new format

• **If you have an approved REMS....**
  – Do not expect submission solely to convert to the new format
  – Recommend submitting with other modifications
  – We can assist in converting to the new format

• **Provide feedback!**
  – We encourage you to provide feedback on the new REMS document template and the accompanying draft guidance

The new REMS document template and instructions for use can be found in the draft guidance for industry *Format and Content of a REMS Document*, available at: https://www.fda.gov/AboutFDA/Transparency/Basics/ucm325201.htm.
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4. REMS SPL update
   (Adam Kroetsch)
The Food and Drug Administration Amendments Act of 2007 gave FDA the authority to require a Risk Evaluation and Mitigation Strategy (REMS) from manufacturers to ensure that the benefits of a drug or biological product outweigh its risks.

The table below provides links to currently approved individual and shared system REMS.

Information on historical and released REMS is available in downloadable data files.

<table>
<thead>
<tr>
<th>Name</th>
<th>REMS Approved</th>
<th>Last Updated</th>
<th>MedGuide (MG)*</th>
<th>Comm. Plan (CP)</th>
<th>ETASU</th>
<th>Imp. System (IS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adasuve (loxapine), aerosol, powder</td>
<td>12/21/2012</td>
<td>10/10/2017</td>
<td></td>
<td>ETASU</td>
<td></td>
<td>IS</td>
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<tr>
<td>NDA #022549</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Addyi (flibanserin), tablet</td>
<td>08/18/2015</td>
<td>06/16/2017</td>
<td></td>
<td>ETASU</td>
<td></td>
<td>IS</td>
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<tr>
<td>NDA #022526</td>
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</tr>
<tr>
<td>Adempas (rociguat), tablet, film coated</td>
<td>10/08/2013</td>
<td>01/17/2017</td>
<td>MG</td>
<td>ETASU</td>
<td></td>
<td>IS</td>
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<tr>
<td>NDA #204819</td>
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www.fda.gov/rems
Objectives

• Understand how the website is organized to meet the needs of different users.

• Identify enhancements to the website made based on user feedback.

• Recognize the website’s features, including displaying the “4 W’s”
Brief history of REMS@FDA

• In 2008, launched website to improve transparency.\(^1\)

• In 2015, launched website which is a centralized, standardized, reliable, and user-friendly repository of information about REMS that can:
  – Help participants understand and comply with REMS requirements.
  – Minimize the confusion associated with complying with multiple REMS programs.
  – Provide participants, researchers, and others with access to convenient, up-to-date and comprehensive REMS info

• In 2017, made enhancements to website based on users feedback.

\(^1\)FD&C Act Section 505(r)(2)(B)(v)
The website must meet the needs of a wide range of users

Who uses the website?

- Patients
- Healthcare providers
  - Prescribers
  - Pharmacists
  - Nurses
  - Health system pharmacists
- Distributors
- Drug data vendors
- Academics/researchers
- Industry
- FDA
<table>
<thead>
<tr>
<th>Website Use Case</th>
<th>Key User Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient or healthcare provider wants to learn about a specific REMS.</td>
<td>Does the product I use have a REMS? What do I have to do to comply with the REMS?</td>
</tr>
<tr>
<td>Health system pharmacist wants to implement one or more REMS in their organization.</td>
<td>What do all of the participants have to do in this REMS? How does this REMS compare to other REMS that our organization has implemented in the past? Do we need to set up new systems or processes to implement this REMS?</td>
</tr>
<tr>
<td>Researcher wants to study FDA’s use of REMS</td>
<td>How many REMS are there? What elements do they use, and what do they require of participants? How has that changed over time?</td>
</tr>
<tr>
<td>Drug data vendor wants to incorporate data about REMS into their database.</td>
<td>How can we download and extract all of the information found on the REMS website?</td>
</tr>
</tbody>
</table>
How the site is organized?

Homepage

REMS-specific pages
How the site is organized?

Homepage

Reports & Data Files page
What you can find on REMS@FDA

• A searchable and sortable table of current REMS programs on the homepage.

• On REMS specific-pages:
  – A listing of what participants need to do to quickly orient prescribers, patients and pharmacists (i.e. the four ‘W’s)
  – Links to relevant information: labeling, Drugs@FDA, the application holder’s REMS website, and REMS materials.

• More detailed REMS data in downloadable CSV format on the Reports & Data Files page.

• Uses an adaptive design to view from a mobile device.
User-friendly homepage

Download historic REMS data in CSV format, including report of released REMS

Get email alerts when the site changes

Contact us to provide feedback
User-friendly homepage

Search for REMS using the REMS name, active ingredient or element.
User-friendly homepage

Search example 1, fentanyl products

<table>
<thead>
<tr>
<th>Name</th>
<th>REMS Approved</th>
<th>Last Updated</th>
<th>MedGuide (MG)</th>
<th>Comm. Plan (CP)</th>
<th>ETASU</th>
<th>Imp. System (IS)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Extended-Release and Long-Acting (ER/LA) Opioid Analgesics</strong></td>
<td>07/09/2012</td>
<td>05/26/2017</td>
<td>MG</td>
<td></td>
<td>ETASU</td>
<td></td>
</tr>
<tr>
<td>Shared System REMS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ionsys (fentanyl iontophoretic transdermal system), patch</strong></td>
<td>04/30/2015</td>
<td>03/29/2017</td>
<td>MG</td>
<td></td>
<td>ETASU</td>
<td>IS</td>
</tr>
<tr>
<td>NDA #021338</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Transmucosal Immediate-Release Fentanyl (TIRF) Products</strong></td>
<td>12/28/2011</td>
<td>09/07/2017</td>
<td>MG</td>
<td></td>
<td>ETASU</td>
<td>IS</td>
</tr>
<tr>
<td>Shared System REMS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Showing 1 to 3 of 3 entries (filtered from 75 total entries)
User-friendly homepage

Search for REMS using the REMS name, active ingredient or element.

Search example 2, shared system

<table>
<thead>
<tr>
<th>Name</th>
<th>REMS Approved</th>
<th>Last Updated</th>
<th>MedGuide (MG)</th>
<th>Comm. Plan (CP)</th>
<th>ETASU</th>
<th>Imp. System (IS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloestron</td>
<td>11/22/2016</td>
<td>11/22/2016</td>
<td></td>
<td></td>
<td>ETASU</td>
<td></td>
</tr>
<tr>
<td>Buprenorphine Transmucosal Products for Opioid Dependence (BTOD)</td>
<td>02/22/2013</td>
<td>05/23/2017</td>
<td>MG</td>
<td>ETASU</td>
<td>IS</td>
<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>09/15/2015</td>
<td>09/15/2015</td>
<td></td>
<td></td>
<td>ETASU</td>
<td>IS</td>
</tr>
</tbody>
</table>
User-friendly homepage

Print or download current list of REMS in CSV / Excel format

Sort to find approval date of the REMS

Sort to find the most recently updated REMS

Click for more detailed info on each REMS-specific page
Detailed information on each REMS

- Organized by tabs
- View products in shared system REMS
- Link to prescribing information, medication guides, and Drugs@FDA
Detailed information on each REMS

The REMS goal statement

What is the purpose of the REMS?
The goals of the isotretinoin risk evaluation and mitigation strategy are:
1. To prevent fetal exposure to isotretinoin
2. To inform prescribers, pharmacists, and patients about isotretinoin’s serious risks and safe-use conditions
Detailed information on each REMS

Go to application holder’s REMS website
See overview of REMS for each participant
Detailed information on each REMS

What do participants need to know?

Below is a general overview of the REMS for all REMS participants (e.g., patients, pharmacies, and healthcare providers). See the application holder(s) REMS Website or the approved REMS materials for more information.

Link to REMS material

Find out who has to do what, when and with what

- Health Care Providers who prescribe isotretinoin products must

To become certified to prescribe

- Be able to correctly identify and document females of reproductive potential, females of non-reproductive potential, or males.
- Enroll in the REMS by completing the Prescriber Enrollment Form and submitting it to the REMS Program. [Patient information/Informed Consent for Females of Reproductive Potential]

Before treatment initiation

- For a female of reproductive potential: counsel the patient on contraception or refer to an expert for a method of contraception or interruption or deviation for pregnancy.
- For a female of reproductive potential: assess the patient's pregnancy status by ordering and reviewing two CLIA-certified pregnancy tests and document the results.
Detailed information on each REMS

View the REMS Document

Download individual REMS materials
Detailed information on each REMS

<table>
<thead>
<tr>
<th>Date</th>
<th>Summary of change</th>
</tr>
</thead>
<tbody>
<tr>
<td>06/17/2017</td>
<td>Modified to provide for implementation of a REMS Pharmacy Network and use of an electronic verification system for iPLEDGE Program certified pharmacies to request and receive a Risk Management Authorization (RMA) directly through the prescription claim adjudication process workflow at the point of dispensing an isotretinoin prescription. It also provides for the changes made to the REMS educational materials to streamline and improve clarity.</td>
</tr>
<tr>
<td>07/08/2016</td>
<td>Modified to:</td>
</tr>
<tr>
<td></td>
<td>1. make minor typographical and formatting changes.</td>
</tr>
<tr>
<td></td>
<td>2. add the iPLEDGE Terms of Use, which includes the Privacy Statement</td>
</tr>
<tr>
<td></td>
<td>3. add the following statement in the Interactive Voice Recognition System (IVRS) public protocol for all stakeholders: “I understand and will comply with the iPLEDGE Terms of Use and Non-Compliance Action Policy. The iPLEDGE Terms of Use and the Non-Compliance Action Policy are available at <a href="http://www.ipledgeprogram.com%E2%80%9D">www.ipledgeprogram.com”</a>;</td>
</tr>
</tbody>
</table>

Summarizes the reason for the change
Downloadable REMS Reports & Data Files

Current count of REMS by element
### Downloadable REMS Reports & Data Files

Report of released REMS

<table>
<thead>
<tr>
<th>REMSID</th>
<th>REMS_Name</th>
<th>Application_Number</th>
<th>REMS_Shared_System</th>
<th>Date REMS approved</th>
<th>Date REMS released</th>
</tr>
</thead>
<tbody>
<tr>
<td>369</td>
<td>Bupropion (ANDA 091520)</td>
<td>091520;</td>
<td>No</td>
<td>6/9/2011</td>
<td>8/25/2017</td>
</tr>
<tr>
<td>66</td>
<td>Victoza</td>
<td>022341;</td>
<td>No</td>
<td>1/25/2010</td>
<td>7/26/2017</td>
</tr>
<tr>
<td>370</td>
<td>Bupropion (ANDA 077475)</td>
<td>077475;</td>
<td>No</td>
<td>6/25/2010</td>
<td>6/30/2017</td>
</tr>
<tr>
<td>371</td>
<td>Bupropion (ANDA 079094)</td>
<td>079094;</td>
<td>No</td>
<td>4/27/2010</td>
<td>6/30/2017</td>
</tr>
<tr>
<td>372</td>
<td>Bupropion (ANDA 075914)</td>
<td>075914;</td>
<td>No</td>
<td>5/13/2010</td>
<td>6/30/2017</td>
</tr>
<tr>
<td>65</td>
<td>Vibativ</td>
<td>022110; 022407;</td>
<td>No</td>
<td>9/11/2009</td>
<td>5/24/2017</td>
</tr>
<tr>
<td>39</td>
<td>Nulojix</td>
<td>125288;</td>
<td>No</td>
<td>6/15/2011</td>
<td>5/9/2017</td>
</tr>
<tr>
<td>73</td>
<td>Zyban</td>
<td>020711;</td>
<td>No</td>
<td>2/26/2010</td>
<td>5/4/2017</td>
</tr>
<tr>
<td>19</td>
<td>Forteo</td>
<td>021318;</td>
<td>No</td>
<td>7/22/2009</td>
<td>4/28/2017</td>
</tr>
<tr>
<td>6</td>
<td>Aranesp</td>
<td>103951;</td>
<td>No</td>
<td>2/16/2010</td>
<td>4/13/2017</td>
</tr>
<tr>
<td>16</td>
<td>Epogen / Procrit</td>
<td>103234;</td>
<td>No</td>
<td>2/16/2010</td>
<td>4/13/2017</td>
</tr>
<tr>
<td>320</td>
<td>Symlin</td>
<td>021332;</td>
<td>No</td>
<td>6/27/2014</td>
<td>3/8/2017</td>
</tr>
<tr>
<td>50</td>
<td>Stelara</td>
<td>125261;</td>
<td>No</td>
<td>9/25/2009</td>
<td>2/15/2017</td>
</tr>
<tr>
<td>12</td>
<td>Chantix</td>
<td>021928;</td>
<td>No</td>
<td>10/19/2009</td>
<td>12/16/2016</td>
</tr>
</tbody>
</table>
Downloadable REMS Reports & Data Files

Downloadable REMS data in CSV format

Detailed description of the data contained in downloadable REMS data
Downloadable REMS Reports & Data Files

<table>
<thead>
<tr>
<th>REMSID</th>
<th>REMS_Name</th>
<th>VersionID</th>
<th>Version_Date</th>
<th>Released_Flag</th>
<th>Moved_to_Shared_System_Flag</th>
<th>Medication_Guide_Flag</th>
<th>Communication_Plan_Flag</th>
<th>Elements_to_Assure_Safe_Use_Flag</th>
<th>Implementation_Flag</th>
</tr>
</thead>
<tbody>
<tr>
<td>244</td>
<td>16 Epogen / Procrit</td>
<td>50</td>
<td>2/16/2010</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>245</td>
<td>16 Epogen / Procrit</td>
<td>51</td>
<td>6/24/2011</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>246</td>
<td>16 Epogen / Procrit</td>
<td>52</td>
<td>5/31/2012</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>247</td>
<td>16 Epogen / Procrit</td>
<td>53</td>
<td>3/27/2013</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>248</td>
<td>16 Epogen / Procrit</td>
<td>326</td>
<td>12/31/2013</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>249</td>
<td>16 Epogen / Procrit</td>
<td>976</td>
<td>4/13/2017</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Next steps

- A series of enhancements made the REMS website responds to user feedback.
- The new REMS document template (REMS Participant Requirements Section), organized by the “4 W’s”, will be displayed on REMS-specific pages.
- Plan to use REMS SPL submissions to help maintain the website

www.fda.gov/rems
Agenda

1. Introduction & Background
   *(Aaron Sherman)*

2. The new REMS document template
   *(Gita Toyserkani and Suzanne Robottom)*

3. REMS@FDA website update
   *(Amy Ramanadham)*

4. REMS SPL update
   *(Adam Kroetsch)*
What is SPL?

SPL is a data standard for capturing information about drug products:

- SPL stands for “Structured Product Labeling” but covers product information beyond labeling
- SPL is developed and maintained by a Standards Development Organization called Health Level Seven International (HL7)

Proposal to capture REMS in SPL format was identified by stakeholders (in particular, the National Council for Prescription Drug Programs, NCPDP) and was adopted in 2014 as a “priority project” towards REMS Standardization.
What is SPL not?

REMS SPL is not currently used for the exchange of patient or healthcare provider-specific information

• For example, prescribers cannot use SPL to enroll in a REMS, prescribe drugs, or monitor patients.

• A related effort, the REMS Platform Standards Initiative, is designed to develop standards to exchange this type of information.
REMS SPL starts with the official “REMS Document”

REMS Document

REMS Materials
What REMS SPL Looks Like

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

   1. Be able to [clinical activity to be performed].
   2. Review the drug’s Prescribing Information.
   3. Review the following: [List of Prescriber Educational Material(s)].
   4. Receive training provided by [entity providing the training, e.g. the applicant, a CE provider].
   5. Successfully complete the [Knowledge Assessment Form] and submit it to the REMS Program.
   6. Enroll in the REMS by completing the [Enrollment Form] and submitting it to the REMS Program.

To become certified to prescribe

7. Counsel the patient on [topic]
   OR
   Counsel the patient using [REMS material].
   OR
   Counsel the patient on [topic] using [REMS material].
   8. Provide the patient with the [REMS Material].
   9. Assess the patient’s [condition(s) or health status(es)].
   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 or health status] by [list of lab test(s) or monitoring].
   OR
   Assess the patient’s [condition(s) or health status(es)] by [list of lab test(s) or monitoring]. Document and submit the results to the REMS Program using [REMS Material(s)].

Before treatment initiation (first dose)

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.
11. Enroll the patient by completing and submitting the [Patient Enrollment Form] to the REMS program.
   OR
What REMS SPL Really Looks Like

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

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.</strong></td>
<td>Be able to [clinical activity to be performed].</td>
</tr>
<tr>
<td><strong>2.</strong></td>
<td>Review the drug’s Prescribing Information.</td>
</tr>
<tr>
<td><strong>3.</strong></td>
<td>Review the following: [List of Prescriber Educational Material(s)].</td>
</tr>
<tr>
<td><strong>4.</strong></td>
<td>Receive training provided by [entity providing the training, e.g. the applicant]</td>
</tr>
<tr>
<td><strong>5.</strong></td>
<td>Successfully complete the [Knowledge Assessment Form] and submit it to the REMS</td>
</tr>
<tr>
<td><strong>6.</strong></td>
<td>Enroll in the REMS by completing the [Enrollment Form] and submitting it to the</td>
</tr>
</tbody>
</table>

Before treatment initiation (first dose)
Why SPL?

1. Presents information about REMS in a consistent “4 W’s format”.

2. Makes REMS information more accessible.

3. Helps integrate REMS into the care process.
SPL captures all REMS documents in a consistent “4 W’s” format

<table>
<thead>
<tr>
<th>Data Element</th>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stakeholder (“Who”)</td>
<td>The party that must meet the REMS requirement</td>
<td>prescriber, dispenser, health care setting</td>
</tr>
<tr>
<td>Protocol (“When”)</td>
<td>A particular “stage” in the treatment process around which REMS activities may occur</td>
<td>certification, prescribing, dispensing, administration</td>
</tr>
<tr>
<td>Requirement (“What”)</td>
<td>A clinical or administrative activity that must be performed as part of the REMS</td>
<td>counseling a patient, completing an enrollment form, lab testing</td>
</tr>
<tr>
<td>Material reference (“With What”)</td>
<td>Reference to approved REMS material with which the requirement is carried out</td>
<td>enrollment form, medication guide, educational pamphlet</td>
</tr>
</tbody>
</table>
In SPL, old format REMS Documents are transformed into REMS Summaries

**REMS Document Text**

To become certified, each prescriber must activate registration, by completing the Prescriber Enrollment Form, via the iPLEDGE website or the automated phone system.

The healthcare provider completes the Healthcare Provider Enrollment Form.

To become certified, each prescriber must complete the Prescriber Enrollment Form.

**REMS Summaries**
4 W’s in REMS SPL

REMS SPL presents the “4 W’s” for all REMS in tabular format:

<table>
<thead>
<tr>
<th>1. Healthcare Providers who prescribe drug X must:</th>
</tr>
</thead>
<tbody>
<tr>
<td>To become certified to prescribe</td>
</tr>
<tr>
<td>1. Review the drug’s Prescribing Information.</td>
</tr>
<tr>
<td>2. Enroll in the REMS by completing the Drug X REMS Enrollment Form and submitting it to the REMS Program.</td>
</tr>
<tr>
<td>Before treatment initiation (first dose)</td>
</tr>
<tr>
<td>3. Counsel the patient using Drug X REMS Counseling Material.</td>
</tr>
<tr>
<td>4. Assess the patient’s [condition(s) or health status(es)].</td>
</tr>
</tbody>
</table>

REMS Summaries are not necessary for REMS Documents that follow the new REMS document template.
Comparison: Old vs New Template

<table>
<thead>
<tr>
<th>Old Template</th>
<th>New Template</th>
</tr>
</thead>
<tbody>
<tr>
<td>Header</td>
<td>REMS Administrative Information</td>
</tr>
<tr>
<td>REMS Goals</td>
<td>REMS Goals</td>
</tr>
<tr>
<td>REMS Elements</td>
<td>REMS Requirements</td>
</tr>
<tr>
<td>Medication Guide</td>
<td>REMS Participant Requirements</td>
</tr>
<tr>
<td>REMS Communication Plan</td>
<td>REMS Sponsor Requirements</td>
</tr>
<tr>
<td>REMS Elements to Assure Safe Use</td>
<td>REMS Assessment Timetable*</td>
</tr>
<tr>
<td>REMS Implementation System</td>
<td>REMS Material</td>
</tr>
<tr>
<td>REMS Assessment Timetable*</td>
<td></td>
</tr>
<tr>
<td>REMS Summary</td>
<td></td>
</tr>
<tr>
<td>REMS Material</td>
<td></td>
</tr>
</tbody>
</table>
Why SPL?

1. Presents information about REMS in a consistent “4 W’s format”.

2. Makes REMS information more accessible.

3. Helps integrate REMS into the care process.
REMS SPL information is shared across the healthcare system

SPL data is transmitted from the sponsor to patients, healthcare providers, and the public.
FDA will be using REMS SPL for its own REMS website

<table>
<thead>
<tr>
<th>Name</th>
<th>REMS Approved</th>
<th>Last Updated</th>
<th>MedGuide (MG)</th>
<th>Comm. Plan (CP)</th>
<th>ETASU</th>
<th>Imp. System (IS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adasuve (loxapine), aerosol, powder</td>
<td>12/21/2012</td>
<td>10/10/2017</td>
<td></td>
<td></td>
<td>ETASU</td>
<td>IS</td>
</tr>
<tr>
<td>NDA #022549</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Addyi (fibanserin), tablet</td>
<td>08/18/2015</td>
<td>08/16/2017</td>
<td></td>
<td></td>
<td>ETASU</td>
<td>IS</td>
</tr>
<tr>
<td>NDA #022526</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adempas (riociguat), tablet, film coated</td>
<td>10/08/2013</td>
<td>01/17/2017</td>
<td>MG</td>
<td></td>
<td>ETASU</td>
<td>IS</td>
</tr>
<tr>
<td>NDA #204819</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Drug Name, NDA number, dosage form**
- **Approval Date**
- **REMS Elements**
Why SPL?

1. Presents information about REMS in a consistent “4 W’s format”.

2. Makes REMS information more accessible.

3. Helps integrate REMS into the care process.
In REMS SPL, “4 W’s” are mapped to standardized data elements

4W’s: REMS Summary / REMS Participant Requirements

- **Stakeholder**: Prescribers
- **Protocol**: To be able to prescribe
- **Requirement**: Enroll in REMS
Data elements allow REMS to be integrated into health IT systems

1. Healthcare Providers who prescribe drug X must:

<table>
<thead>
<tr>
<th>To become certified to prescribe</th>
<th>1. Review the drug’s Prescribing Information.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Enroll in the REMS by completing the Drug X REMS Enrollment Form and submitting it to the REMS Program.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Before treatment initiation (first dose)</th>
<th>3. Counsel the patient using Drug X REMS Counseling Material.</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Assess the patient’s [condition(s) or health status(es)].</td>
<td></td>
</tr>
</tbody>
</table>
To become certified, each prescriber must activate registration, by completing the Prescriber Enrollment Form, via the iPLEDGE website or the automated phone system.

The healthcare provider completes the Healthcare Provider Enrollment Form.

To become certified, each prescriber must complete the Prescriber Enrollment Form.
Illustrative Diagram: New Template

Stakeholder: Prescribers
Protocol: To be able to prescribe
Requirement: Enroll in REMS

REMS Document Text

Standardized Data Elements

3. Pharmacies that dispense Drug X:
1. Designate an authorized representative to carry out the certification process on behalf of the pharmacy.
2. Have the authorized representative review the educational materials for dispensers, including Program Overview.
3. Train all relevant staff involved in the dispensing of Drug X using the Program Overview.
4. Establish processes and procedures to verify dispensing to certified pharmacies.

Before dispensing Drug X:
6. Obtain Prescription Ordering Forms from the Drug X REMS Program.
7. Obtain authorization to dispense by calling the Drug X REMS Program.
8. Re-enroll in the Drug X REMS Program every 2 years.
9. Do not distribute, transfer, loan, or sell product except to certified dispensers.
10. Cooperate with audits carried out by the sponsor to ensure that all processes and procedures are in place and are being followed.

Ongoing:
REMS Data Elements

The <stakeholder> Data Element uses a standard terminology to describe the role of the participant in the REMS:

- Prescriber
- Dispenser
- Patient
- Distributor
- Other Healthcare Providers (e.g., nurses who treat patients on the drug)
REMS Data Elements

The `<protocol>` Data Element uses a standard terminology to describe the steps in the REMS and medication use process, such as:

- REMS Certification
- Treatment Initiation
- Dispensing
- Discontinuation

These terms are combined with “modifiers” to specify when a requirement needs to happen: e.g., “before REMS Certification”, “after Treatment Initiation”, “one week after Dispensing”, etc.
REMS Data Elements

The <requirement> Data Element uses a standard terminology to describe the clinical or administrative activities that stakeholders need to carry out in the REMS, such as:

• Enroll in the REMS
• Counsel patient
• Review Prescribing Information
• Get lab test or monitoring
REMS Data Elements

The `<documentReference>` Data Element identifies the material used to carry out the REMS activity. In general, there are three types of “materials” that may be referenced in an SPL document:

- A REMS material (e.g., a form or educational material) – typically attached as a PDF
- A website, referenced as a URL
- An electronic data standard
  - Currently NCPDP’s Telecommunications Standard is the only standard available, but more will be added in the future as needed.
Example of codified REMS within SPL

When: - While prescribing

What: - Counsel patient

Who: - Prescriber

With What: - documentReference
Codified REMS SPL information can be displayed in many different ways.

<table>
<thead>
<tr>
<th>Before/During/After</th>
<th>Activity</th>
<th>Stakeholder</th>
<th>Requirement</th>
<th>Document</th>
</tr>
</thead>
<tbody>
<tr>
<td>before</td>
<td>all activity</td>
<td>dispenser</td>
<td>designate authorized representative</td>
<td></td>
</tr>
<tr>
<td>before</td>
<td>all activity</td>
<td>dispenser</td>
<td>Have representative review educational materials</td>
<td>Program Overview</td>
</tr>
<tr>
<td>before</td>
<td>all activity</td>
<td>dispenser</td>
<td>train staff</td>
<td>Program Overview</td>
</tr>
<tr>
<td>before</td>
<td>all activity</td>
<td>dispenser</td>
<td>Establish processes and procedures to verify safe use conditions</td>
<td>Program Overview</td>
</tr>
<tr>
<td>before</td>
<td>all activity</td>
<td>dispenser</td>
<td>Enroll in REMS</td>
<td>Pharmacy Enrollment Form</td>
</tr>
<tr>
<td>before</td>
<td>dispensing</td>
<td>dispenser</td>
<td>obtain dispensing authorization</td>
<td></td>
</tr>
<tr>
<td>every 2 years during</td>
<td>dispensing</td>
<td>dispenser</td>
<td>Enroll in REMS</td>
<td></td>
</tr>
<tr>
<td>during</td>
<td>dispensing</td>
<td>dispenser</td>
<td>ensure dispensing only to certified provider</td>
<td></td>
</tr>
<tr>
<td>during</td>
<td>dispensing</td>
<td>dispenser</td>
<td>Cooperate with audits</td>
<td></td>
</tr>
</tbody>
</table>
Use of REMS SPL in the Healthcare System

Structured REMS data in a format like SPL can help integrate REMS into the healthcare system and ensure stakeholder awareness of and compliance with REMS.

Source: Journal of Managed Care Pharmacy.
http://www.amcp.org/JMCP/2013/May/16524/1033.html
Use of SPL in the Healthcare System  
Prescriber Example

Scenario: A doctor is about to start a patient on a drug that has a REMS. The prescriber does not realize that the drug has a REMS. Fortunately, the prescriber’s EHR contains SPL data.

- Using the `<stakeholder>` data element, the EHR notifies the prescriber that they have a role to play in the REMS.
- Using the `<protocol>` and `<requirement>` data elements, the EHR notifies the prescriber that there are several steps they have to take when initiating therapy with the patient, including providing the patient with counseling materials.
- Using the `<documentReference>` data element, the EHR presents a copy of the counseling material to the prescriber to print and give to the patient.
Use of SPL in the Healthcare System
Dispenser Example

Scenario: A pharmacist is about to fill a prescription for a drug with a REMS. The pharmacist is aware that a REMS exists for the drug, but is not aware that the REMS has recently changed. Fortunately, the pharmacist’s pharmacy system contains SPL data.

• Using the <protocol> and <requirement> data elements, the pharmacy system notifies the pharmacist that they must now confirm that a specific lab test result is on file before dispensing the drug.

• Using the <documentReference> data element, the pharmacy system learns that the lab test results can be requested electronically.

• Thanks to the “trigger” provided by SPL, the pharmacy system can now, using a different data standard, check with the REMS program to determine whether there is a negative lab test on file.
Next Steps

• Sponsors are now able to submit their REMS in SPL format

• Once REMS SPL files are approved, they will be made available on DailyMed

• We have issued a draft guidance under FD&C 745A(a) that would require REMS submissions in SPL format
  – We are now soliciting comments on the draft guidance, which will be considered as we develop a final guidance. Comments are due
  – Electronic submission requirements take effect 2 years from the publishing of a final guidance.
  – We will continue to have opportunities for stakeholder feedback prior to issuing final guidance.
Acknowledgments

• FDA Colleagues: CDER and Office of the Commissioner

• National Library of Medicine

• National Cancer Institute: Enterprise Vocabulary Services

• Pilot Participants and Applicants
Conclusion

• The REMS Integration Initiative was launched in 2011 to evaluate and improve the implementation of REMS authorities, and to reduce the associated burden.

• It ended in October 2017 after:
  – Implementation of the 4 ‘W’s REMS document template to standardize how REMS requirements are described.
  – Creation of the REMS@FDA website for easy access to individual and program-wide REMS information.
  – Incorporation of REMS into SPL format for integration with existing healthcare systems.
  – Publishing 5 guidances and 3 reports to establish and discuss best practices in REMS implementation.

• Efforts continue to evaluate and improve REMS:
  – REMS Platform Standards Initiative.
For more information...

- For more information the REMS Integration Initiative, including access to guidances and reports published, please visit the initiative’s [website](#).
- The new REMS document template and associated guidance can be found [here](#).
- For instructions on creating REMS SPL documents, consult the SPL implementation guide, available [here](#).
- If you have questions, please contact the DRISK Policy Team at [REMS@fda.hhs.gov](mailto:REMS@fda.hhs.gov).

- The [REMS@FDA](#) website
Resources

Click for:

- Email questions to: REMS@fda.hhs.gov
- REMS Integration Initiative website
- REMS Overview
- FDA SPL Website
- REMS@FDA
- PDF of today’s slides

Open Q&A begins shortly – type in your questions now.

Click Here for Evaluation and Certificate

Learn about other resources from CDER Small Business & Industry Assistance: Visit Our Website!