

## Building a Common Risk Evaluation and Mitigation Strategies (REMS) Platform

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### Discussion Guide

#### Introduction

Risk Evaluation and Mitigation Strategies (REMS) are programs designed to ensure that certain drugs and biologics with serious risks are used safely. The U.S. Food and Drug Administration (FDA) requires a drug's sponsor to establish a REMS when the Agency is concerned that the risks of a biomedical product might otherwise outweigh its benefits. Since the inception of REMS in 2008, stakeholders have raised concerns over REMS' burden on providers and the health care system more broadly, as well as the potential barriers it may create for patient access to REMS products. In an effort to address these concerns, FDA has pursued a number of initiatives aimed at improving the design, operation, and assessment of REMS programs. Among these initiatives is the development of a Common REMS Platform, a system-wide effort to facilitate the standardization and integration of REMS programs into the health system.

#### Risk Evaluation and Mitigation Strategies (REMS)

The Food and Drug Administration Amendments Act (FDAAA) of 2007 expanded the ability of the FDA to ensure the safety of drugs and biologics on the market. Within the scope of this new authority was the power to require a REMS for a drug or biologic if the Agency determines that additional safeguards are necessary to ensure that the benefits of that product outweigh its risks.<sup>1</sup> FDA may require a REMS as a condition of a drug's approval, or may require it post-approval if new safety information becomes available that shows a serious risk of adverse events associated with the drug.

A given REMS program can include one or more elements as well as a diverse set of materials and processes (collectively referred to as 'tools') to help mitigate the risks of a particular drug. (See Table 1) Many REMS tools are geared principally towards communicating risk through educational materials or letters. However, some REMS restrict the distribution and use of a drug to providers or care settings that have met certain "safe use" requirements, such as additional training or certification, or performing additional monitoring activities. REMS with these more extensive requirements are collectively referred to as "REMS with Elements to Assure Safe Use" (ETASU).

The process of designing, implementing, and evaluating a REMS program is the responsibility of the drug's sponsor (i.e., its manufacturer). In some cases—for example, when a class of drugs share a common risk or when there are generic versions of the drug available—multiple sponsors may participate in a "shared system REMS". As of May 2016, there are 67 REMS and 6 shared REMS.

Sponsors submit periodic assessments to FDA (typically 18 months, 3 years, and 7 years following approval of the REMS program though more frequent assessments may be required for ETASU REMS) in order to determine how well the REMS is meeting its goals. Based on these assessments, the REMS may be modified or discontinued if the REMS program is not functioning as intended, if new safety

information becomes available, or if the burden of the program on the health care delivery system is too great.<sup>2</sup>

**Table 1: Available REMS Elements**

REMS Element	Definition	Example tool
<b>Medication Guide or Patient Package Insert</b>	Paper handouts that address issues that are specific to particular drugs and drug classes. These handouts contain FDA-approved information that can help patients avoid serious adverse events.	<ul style="list-style-type: none"> <li>• Paper handout provided to patient by pharmacy</li> </ul>
<b>Communication Plan (CP)</b>	Strategies to inform targeted health care providers and professional societies of the REMS requirements, encourage implementation, and/or explain the serious risks and appropriate safety measures associated with the drug’s use.	<ul style="list-style-type: none"> <li>• “Dear Healthcare Provider” Letters</li> <li>• Websites</li> <li>• Factsheets</li> <li>• Journal Information Pieces</li> </ul>
<b>Elements to Assure Safe Use (ETASU)</b>	Specific interventions or other actions required by health care providers before they may prescribe or dispense the drug. ETASU may also be necessary throughout a course of treatment of the drug.	<ul style="list-style-type: none"> <li>• Health care providers who prescribe the drug have specific training or experience or are specially certified;</li> <li>• Pharmacies, practitioners, or health care settings that dispense the drug are specially certified;</li> <li>• Drug is dispensed to patients only in certain health care settings (e.g., infusion settings, hospitals);</li> <li>• Documented evidence of safe-use conditions before dispensing (e.g., lab test results)</li> <li>• Patients using the drug are subject to certain monitoring</li> <li>• Patients using the drug are enrolled in a registry</li> </ul>
<b>Implementation Plan</b>	A system to monitor and evaluate those who are responsible for implementing certain ETASUs.	<ul style="list-style-type: none"> <li>• Certification of distributors who distribute the drug to certified pharmacies or other certified settings</li> </ul>

**Efforts to Standardize and Improve REMS**

The requirements of a given REMS vary depending on the risks of the drug, and there is little standardization across different REMS programs. Similar REMS tools may have different names, use different terminology, or require different processes, and in general they are not well-integrated into health system workflows or health IT systems, creating burdens for providers and barriers to efficient communication about REMS products.

In response to these concerns—and as part of FDA’s commitments under the Prescription Drug User Fee Act of 2012— FDA announced four priority projects to move towards an improved and integrated REMS standardization strategy. These efforts have included improving tools for prescriber-to-patient risk-benefit counseling, integrating REMS into accredited continuing education for providers, and standardizing REMS information for inclusion into pharmacy systems using Structured Product Labeling (SPL). SPL is a data standard designed to capture and share key information (e.g., product name, dosage form, packaging, etc.) about FDA-approved products. FDA is currently piloting REMS SPL submissions, with the hope that sponsors, health care information system developers, and other stakeholders will all

eventually share REMS information through the SPL standard. On October 6, 2015, the agency announced its newest effort to promote standards-based approaches to integrating REMS into health information technology (health IT) processes: the Common REMS Platform.

### **Building a Common REMS Platform**

As envisioned by FDA, the Common REMS Platform will be a list of electronic health data standards that REMS may use to operate within the healthcare system and communicate with participants in a standardized way.<sup>3</sup> Once established, FDA would work with sponsors to make their REMS compatible with these standards to the extent feasible. REMS that are compatible with the standards would then be referred to as “Platform REMS”.

The FDA will not develop these standards independently. Instead, it will rely on existing Standards Development Organizations (SDOs) to develop or leverage existing standards in close coordination with sponsors, patients, prescribers, health systems, health IT vendors, and government partners. FDA will help to facilitate and encourage this process in a variety of ways. First, the agency will help to promote ongoing standards development efforts. The National Council for Prescription Drug Programs (NCPDP), ASC X12, and Health Level 7 are examples of SDO’s developing standards that could potentially be leveraged for Platform REMS. Each organization uses an open and transparent process that usually involves soliciting public comment and balloting to develop and approve standards.

FDA will also promote the development of Platform REMS more directly through identifying and developing Use Cases for certain common REMS activities such as healthcare provider enrollment and certification. These Use Cases will model how stakeholders and systems interact to perform these activities, and define the data elements and standards needed to support this workflow. FDA would then work with SDOs and other stakeholders to identify standards that can meet the requirements laid out in the Use Cases. It is anticipated that existing standards will likely be adapted or modified to meet these requirements. For example, the NCPDP Telecommunications D.0 standard, which was developed to provide a standard format for the electronic submission of third party drug claims and other transactions between pharmacists, payers, and other responsible parties, is already being used to help pharmacists verify that REMS safe use conditions are in place before they dispense the drug to a patient. In the future, this standard could be recognized as a Platform REMS Standard.

Once a data standard has been identified as a possible candidate for a given Use Case, FDA will work with the relevant SDO to develop implementation guides and specifications, which would describe in detail how the standard would be used to carry out the specified REMS activities, and what steps stakeholders could undertake to accommodate these standards. FDA will maintain the finalized list of official Platform REMS Standards and will seek to promote their broader adoption by sponsors and other health system stakeholders. Figure 1 below depicts common workflows entailed with implementing REMS and possible standards that could be leveraged in outpatient settings for Platform REMS. In addition to the implementation guide, another important tool that could help facilitate uptake is through REMS Structured Product Labelling (REMS SPL). REMS SPL can integrate standardized, structured information about REMS requirements into pharmacy and health IT systems. This will make it easier for pharmacy and health IT systems to give providers the information needed to understand and comply with REMS requirements.<sup>4</sup>

### ***Advantages of a Common REMS Platform***

The Common REMS Platform offers several benefits. First, it would facilitate the integration of REMS tools and processes into provider and health system workflows. Adopting these standards would

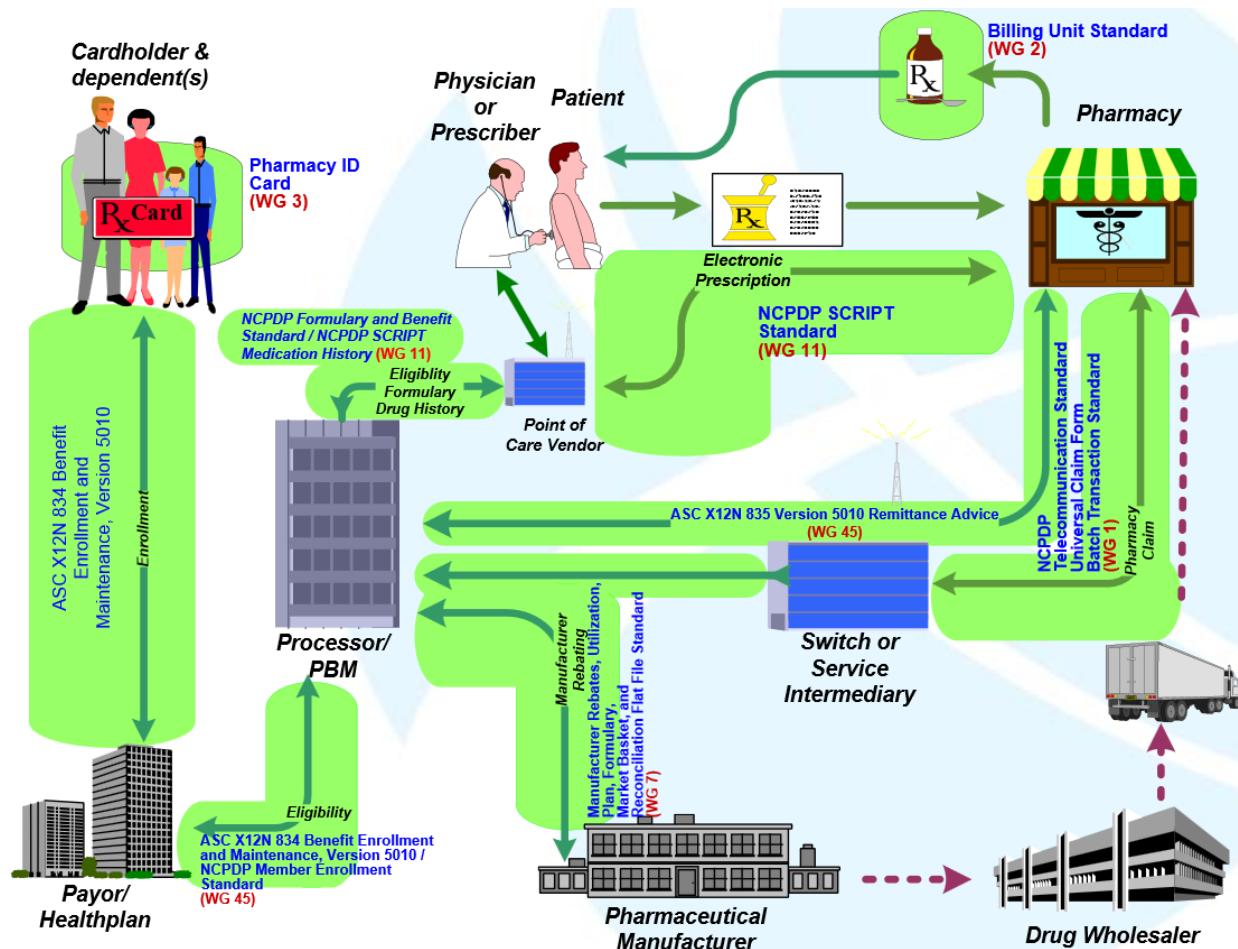


Figure 1. Landscape of NCPDP standards to support REMS processes in outpatient settings. (Slide adopted from NCPDP materials with full permission).

require health systems and other stakeholders to make a single initial modification to their internal health IT systems and processes in order to accommodate the platform. After this, any REMS that relies on these standards can be more easily integrated into the system. A Common REMS Platform could also reduce the complexity and cost to sponsors developing and implementing REMS, reduce operational and administrative burden on FDA reviewers, and facilitate compliance with REMS requirements across health systems. A common platform built on open standards would also simplify and encourage the creation of new and innovative REMS health IT tools and resources.<sup>5</sup>

### Workshop Objectives and Questions for Discussion

In support of next steps in this effort, and under a cooperative agreement with FDA, the Duke-Margolis Center for Health Policy is hosting a half-day public event to: 1) present FDA’s vision for a common REMS platform and obtain feedback on those aspects of the platform that are ready for further development, 2) identify existing data standards and partnerships that may be leveraged in order facilitate the development and broader uptake of REMS common data standards, and 3) explore innovative new tools and systems that may be developed under the common REMS platform.

### Session I: Fostering Innovation under a Common REMS Platform

*Objective:* Discuss potential innovative tools and health IT systems that could be developed under a common REMS platform as envisioned, and identify strategies that can help to facilitate their development.

*Questions to address:*

- What are the potential REMS tools and health IT systems that may developed using the data standards once they are available?
- How can FDA and other stakeholder best facilitate and encourage the development of these REMS tools and resources?
- How might the common REMS platform be leveraged to better inform evaluations of the effectiveness and impact of REMS?
- How might the resulting REMS tools fit within/support the development of a learning health care system?

## **Session II: Leveraging Existing Data Standards and Partnerships to Facilitate the Development and Implementation of the Common REMS Platform**

*Objective:* Discuss the existing data standards that may be leveraged to develop REMS tools and relevant health IT systems and identify any gaps/barriers that may need to be addressed in order to facilitate the development of common REMS Platform Standards.

*Questions to address:*

- What existing standards may be leveraged to achieve the objectives of the common REMS Platform?
- How can FDA best partner with stakeholders to encourage development of standards and implementation guides to meet the objectives of REMS use cases?
- How can the agency and other partners ensure broad uptake of REMS data standards once developed?

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<sup>1</sup> See Section 505-1 of the FDCA and FDA guidance: Format and content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications (September 2009), p. 5. Retrieved from <http://www.fda.gov/downloads/Drugs/Guidances/UCM184128.pdf>.

<sup>2</sup> See Section 505-1 of the FDCA and FDA guidance: Format and content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications (September 2009), p. 5. Retrieved from <http://www.fda.gov/downloads/Drugs/Guidances/UCM184128.pdf>.

<sup>3</sup> See FDA background document: Impact of REMS on the Healthcare Delivery System & Patient Access (October 2015) p. 14. Retrieved from <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM466329.pdf>.

<sup>4</sup> See document number 2015-25349 in Docket No. FDA-2015-N-3402. Federal Register Notice of SPL Pilot: Electronic submission of final approved risk evaluation and mitigation strategies and summary information in a standard structured product labeling format; pp. 60391-60393. (October 2015) Retrieved from <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm470964.htm>.

<sup>5</sup> See FDA background document: Impact of REMS on the Healthcare Delivery System & Patient Access (October 2015) p. 15. Retrieved from <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM466329.pdf>.

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