Duke | MARGOLIS CENTER for Health Policy

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

Hotel Monaco • Washington, DC

Tuesday, June 7, 2016

Workshop Summary

Introduction

The Food and Drug Administration Amendments Act of 2007 (FDAAA) authorized the Food and Drug Administration (FDA) to require sponsors to develop a Risk Evaluation and Mitigation Strategy (REMS) when the Agency is concerned that the risks of a biomedical product might outweigh its benefits. FDA can require a REMS program as a condition of the product's approval, or as a post-approval requirement if new safety information becomes available showing a serious risk of adverse events. Since its authorization, the REMS program has become an important safety tool, and has enabled the Agency to approve a number of products that otherwise might not have been made available for patient use.

FDA launched a range of initiatives over the last several years to improve the design, operation, and assessment of REMS programs.[1] The latest of these initiatives, the "Common REMS Platform," was announced in October 2015. The goal of the Common REMS Platform is to encourage and stimulate the development of innovative health information technologies (health IT) to reduce the burden of REMS compliance, improve patient access to REMS drugs, and, most importantly, achieve better patient outcomes. The Common REMS Platform is envisioned as a set of open, electronic health data standards that REMS programs may use to operate within the healthcare system and communicate with stakeholders in a standardized way.[2] REMS programs that are compatible with these standards are referred to as "Platform REMS."

On June 7, 2016 the Robert J. Margolis, MD, Center for Health Policy at Duke University hosted two events supporting progress on the Common REMS Platform – a public meeting and an expert workshop. The public meeting recordings and materials are available on the Duke-Margolis website.[3] The objective of the public meeting was to communicate FDA's vision of the Common REMS Platform and highlight innovative tools and data standards that could be leveraged or developed to support this effort.

This document is a summary of the expert workshop focused on soliciting detailed input on how the Common REMS Platform could make the process of prescriber certification more efficient and also reduce the burden of compliance. Workshop participants included diverse experts from government agencies, standards development organizations (SDOs), health IT vendors, health care providers, and industry. The workshop discussion focused on how the Common REMS Platform for prescriber certification could:

- Allow for the exchange of necessary data,
- Support timely patient access to REMS drugs, and

[1] For more information on FDA REMS initiatives and implementation under the Prescription Drug User Fee Act (PDUFA V) commitments see: http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm

[2] 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.

[3] https://healthpolicy.duke.edu/events/building-common-risk-evaluation-and-mitigation-strategies-rems-platform-public-meeting

- Facilitate interoperable data exchange across a wide range of healthcare settings.

These events were convened as part of a cooperative agreement with FDA and the views expressed in this summary are those of the individual participants and do not necessarily reflect the official policies of the Department of Health and Human Services, nor does mention of specific projects or organizations imply endorsements by the U.S. Government or other organizations.

Supporting REMS Requirements with the Common REMS Platform

REMS programs are developed by the product's sponsor and may use a diverse set of materials and processes, called 'tools' to help mitigate potential product risks. Many of the current REMS tools are geared towards communicating risk through educational materials such as a Medication Guide or Patient Package Insert. Some REMS programs have more extensive requirements, which are referred to as "REMS with Elements to Assure Safe Use" (ETASU). These types of programs restrict the distribution and use of a product to providers or care settings that meet certain "safe use" requirements, and can include additional training, certification, or additional monitoring activities. Health care providers must complete these "safe use" requirements in order to prescribe, dispense, or order a REMS drug for a patient.

Some stakeholders are concerned that the additional burden placed on providers and health care systems seeking to comply with REMS with ETASU may negatively affect patient access to medically necessary drugs. Participants noted there is a wide variability across REMS requirements. This variability is driven by several factors including the unique safety profile of products, and the placement of responsibility for developing and implementing REMS programs on individual sponsors. Since REMS program requirements may differ between individual sponsors, providers may spend significant time finding and completing REMS requirements for different drugs, especially when the REMS program is paper-based.

The Common REMS Platform is intended to integrate REMS requirements into health IT systems and tools within a clinical workflow. Ideally, Platform REMS standards could allow prescribers to quickly download and complete the necessary forms to carry out REMS requirements through electronic health records (EHRs). Platform REMS standards could also support interoperability of health IT systems across care settings to streamline communication between stakeholders in order to carry out REMS requirements.

Integrating Prescriber Certification Requirements into Clinical Workflows

To advance the Common REMS Platform, workshop discussion was framed around an exemplar draft use case of prescriber certification. This was a compelling use case to consider given nearly all approved REMS with ETASU require some form of prescriber certification. During the certification process, health care providers enroll in the REMS and acknowledge that they: 1) understand the drug's risks and how to use the drug safely, and 2) agree to follow certain REMS requirements when treating patients with the drug. Once a healthcare provider or setting has met these requirements, they are referred to as certified. The process also commonly entails providers completing educational training and knowledge assessment.

Workshop discussion was specifically designed to identify the necessary data elements and refine the process steps needed to complete prescriber certification requirements using health IT. Participants were given a draft diagram of process steps to consider, which is depicted in Figure 1. Key actors engaged in the certification process include: Prescribers, REMS Administrators and Dispensing

Pharmacies. Color coded process steps 3, 4, 5 and 7 represent specific instances where data must be exchanged between them. Detailed sub-process steps for each process step in Figure 1 are provided in the appendix.

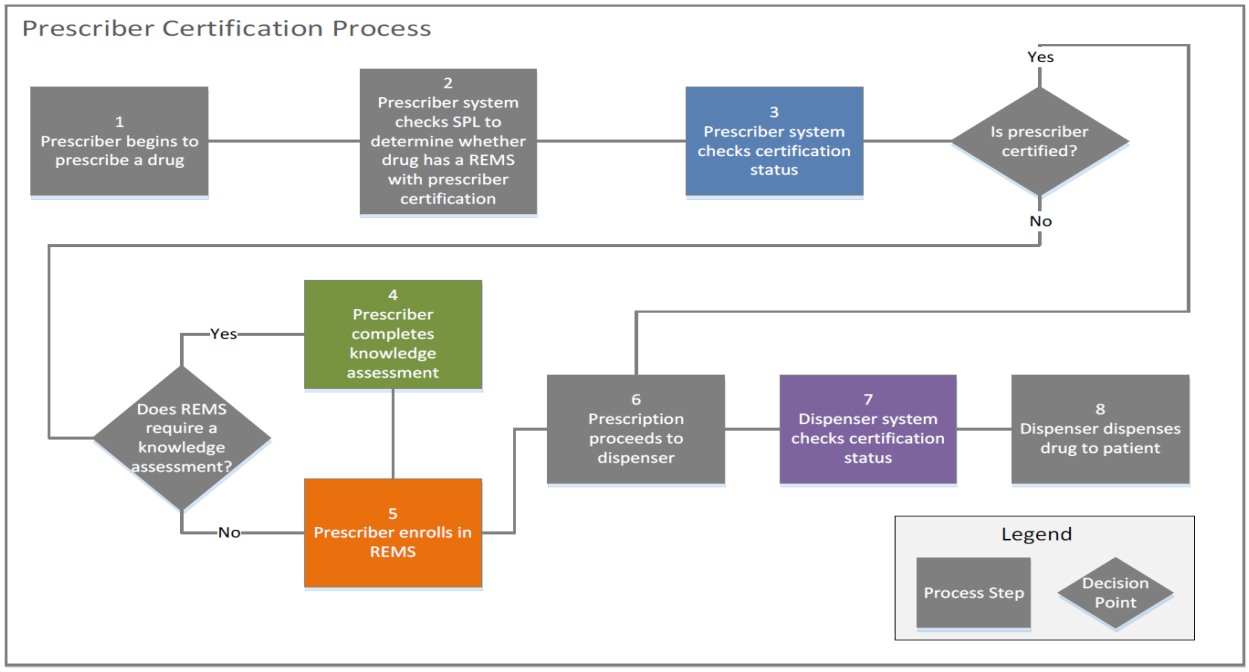


Figure 1. The Prescriber Certification Process

Identifying Necessary Data Elements

In developing the draft prescriber certification process, FDA staff identified a comprehensive list of data elements commonly exchanged in each process step (the list of data elements are provided in the appendix). This list was given to workshop participants to solicit their feedback on possible removals, modifications, and clarifications of data elements.

Prescriber contact information sourced from EHRs was identified as a data element for possible removal. This element is seen as unnecessary because existing provider identification numbers provide a more reliable source of contact information. Prescriber contact information is also a data element already captured by the REMS Administrator as part of the REMS enrollment process. Using contact information from the prescriber's EHR could introduce errors into the transaction through the exchange of incorrect or duplicate contact information. Such a scenario might occur especially when the prescriber has multiple addresses for different practices, which participants noted may not be accurately maintained in the EHR.

Prescriber identification numbers such as National Provider Identifiers (NPI) and Drug Enforcement Agency (DEA) numbers were data elements considered for further clarification and modification. Some prescribers such as medical residents may not yet have an identification number, while other prescribers may have multiple identification numbers. For more robust data exchanges, a combination of identifiers may be needed for each process step. Another opportunity discussed was adding unique prefixes to DEA numbers to facilitate use of the correct identifier in support of REMS requirements.

Use of NPIs for process step 7 (see Appendix D) when verifying prescriber certification may also need additional clarification. Since the dispensing pharmacy and pharmacist each have unique NPIs, potential errors could arise from incorrectly sending the pharmacy's NPI instead of the pharmacist's NPI. More discussion is needed to identify potential solutions to prevent the incorrect NPI from being sent.

Refining Process Steps

Prescriber workflow plays an important role in the successful completion of REMS certification requirements. If the prescriber is first learning of certification requirements at the point of prescribing, then workflow considerations such as the time needed to complete certification requirements may influence the prescriber's decision to prescribe the REMS drug. Ideally, the prescriber would already be certified prior to the patient visit. Participants thought that earlier awareness of REMS certification requirements could be achieved through "pre-certification" to pro-actively identify prescribers of REMS drugs. Pre-certification would occur prior to process step 1.

Criteria for pre-certification was explored for different settings of care. In large, closed practice settings, criteria could be established to identify eligible prescribers and tailor outreach efforts to promote certification. For open delivery systems, prescribing histories could help predict which prescribers are most likely to prescribe REMS drugs. Lastly, certain medical specialties and practices that commonly work with REMS drugs, regardless of practice setting, could also be considered for certification outreach efforts.

A process refinement was also proposed for dispenser verification of certification status (process step 7). Participants thought there could be instances where this requirement might unnecessarily impede patient access to their prescriptions. For example, dispenser verification may unnecessarily delay timely patient access to certain prescription refills that require only sponsor authorization. Instituting an 'exception pathway' with clearly defined criteria for when it is appropriate to use this pathway could help prevent these unnecessary dispensing hard stops. The exception pathway may be best placed after sub-process step 2. If an allowable exception is present in the transaction, then use case participants would skip to sub-process step 8. If no allowable exception is present, then the process continues with sub-process step 4.

Effective alert notifications are another process refinement that could help remind prescribers to certify for REMS products (process steps 4 and 5) or if their certification will soon expire. Participants discussed opportunities to leverage the provider task list function within the EHR. For example, a task list rule could be set up to auto-populate and trigger reminder alerts, which would continue until the prescriber becomes certified. Given the challenges of 'alert fatigue' providers face when receiving too many notifications, some participants thought case managers or other care team members responsible for coordinating patient care could also help remind the provider to certify to complement task list notifications.

Facilitating Interoperable Data Exchanges

Workshop discussion focused on potential opportunities to improve interoperable data exchanges in support of prescriber certification requirements. These uses included facilitating enrollment and knowledge assessment through electronic forms, supporting care continuity during transitions of care

via Structured Product Labeling (SPL), and creating a menu of data elements to streamline communications and data exchanges.[4]

Existing EHR capabilities could be adapted to receive, complete, and transmit knowledge assessments and enrollment forms to simplify workflow and minimize the burden of certification requirements. For example, the EHR or e-Prescribing module could facilitate completing knowledge assessments and REMS enrollment by auto-populating these forms, allowing them to be completed and exchanged in an electronic format. These functionalities would require use of established electronic data exchange standards.

Participants also discussed a potential role for SPL to help facilitate transitions of care. For example, if a patient was prescribed a REMS drug as part of inpatient care, then assuring the patient can continue receiving this drug in outpatient settings might be an important part of the discharge planning process. SPL could help support care continuity by determining whether certification checks (steps 3 and 7) are necessary for the REMS drug and help providers understand how to complete these checks.

Communication between different groups could be streamlined with a menu of standardized data elements. The data element menu could serve as a "data dictionary" comprised of definitions for each element helping prescribers, REMS Administrators, and pharmacists to quickly identify missing data elements and better understand their purpose in fulfilling prescriber certification requirements. Rather than adding extra data fields, however, participants thought a codified message with pop-up language describing the missing elements would be the most feasible option to develop through the EHR system.

Summary of Key Findings

Workshop participants identified a number of opportunities to improve how prescriber certification requirements can be supported by and achieved through the Common REMS Platform. These opportunities are divided into three domain areas: 1) identifying necessary data elements for data exchange between use case participants; 2) refining process steps; and 3) facilitating interoperable data exchanges, which are summarized in table 1.

To streamline data exchanges, participants recommended a few removals of and modifications to data elements. Prescriber contact information was a data element identified for removal because provider identification numbers is more likely to be up-to-date and a more reliable source of contact information. Adding unique prefixes to identifiers such as DEA numbers was recommended along with added clarification for NPIs to ensure the correct identifier is exchanged during the transaction.

Process step refinement recommendations include developing a pre-certification process, defining an exception pathway for dispenser verification of certification status (process step 7), and effectively leveraging EHR alert notifications. The goal of a pre-certification, which would occur prior to process step 1, is to prevent providers learning of REMS certification requirements at the point of prescribing. This could result in improved workflow and encourage prescribing of REMS drugs. An exception pathway under process step 7 was seen as a potential opportunity to support timely patient access to REMS drugs by developing a list of well-defined and appropriate exceptions to dispenser verification of

[4] Structured Product Labeling (SPL) is a Health Level Seven (HL7) standard adopted by FDA to support the exchange of product and facility information. FDA is currently piloting ways to integrate REMS into SPL format to share program requirements with existing pharmacy and health information systems. For more information on SPL, see: https://www.hl7.org/implement/standards/product_brief.cfm?product_id=156

certification status. Lastly, participants noted EHR technology, specifically the provider task list, could help improve provider certification by delivering automated reminder alerts triggered by a task list rule.

The last key domain of recommendations encompassed improved uses of health IT to facilitate interoperable data exchange. Leveraging electronic forms relying on established data standards could help facilitate the completion and exchange of certification enrollment and knowledge assessments under process steps 4 and 5. Another key recommendation identified was using SPL to improve care coordination during transitions from inpatient to outpatient care settings. SPL could determine the need for certification checks (process steps 3 and 7) and help providers understand how to complete these checks. The development of a standardized menu of data elements could also help facilitate data exchanges between use case actors by providing a central repository of data elements with definitions and their purpose in the data exchange. This menu would pop up with a codified message through the EHR system when missing data elements were detected.

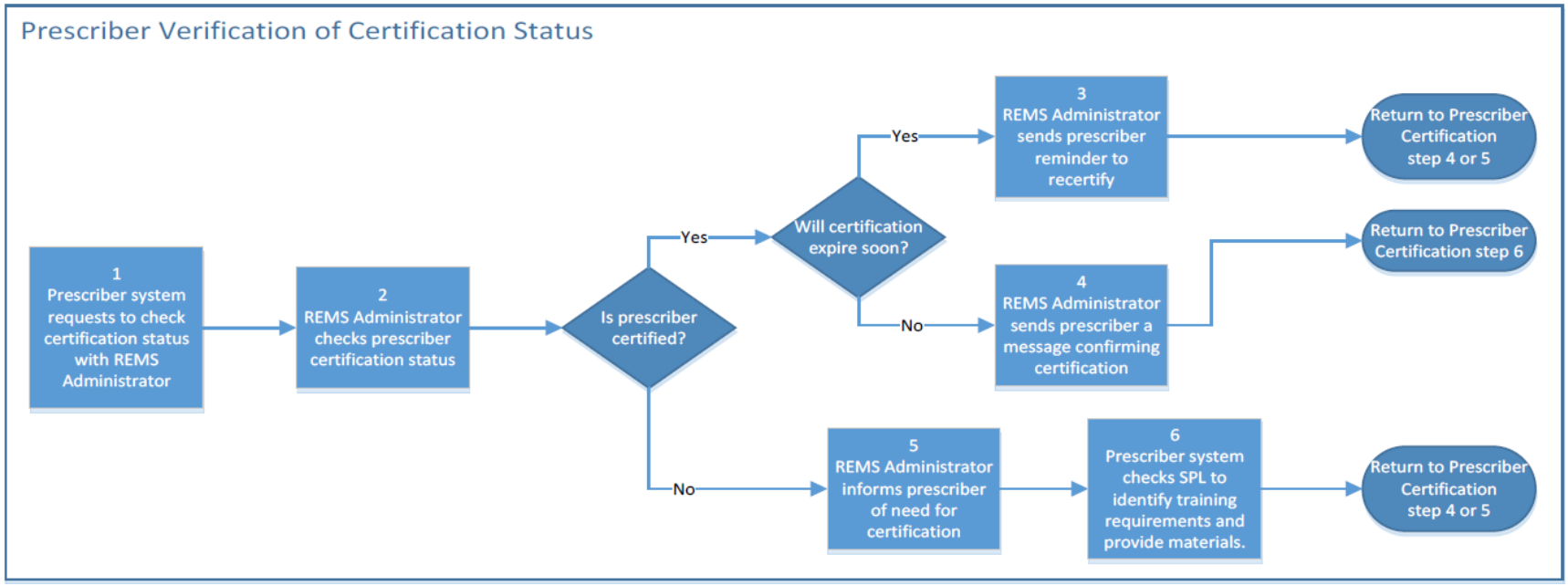
Input received at the workshop will inform the ongoing development of this use case and FDA's selection of an initial set of Platform Standards for prescriber certification. As FDA develops the Common REMS Platform, stakeholders are encouraged to continue collaborating and innovating with existing standards and health IT tools to improve prescriber certification as well as other components of REMS programs.

Table 1. Summary of Key Workshop Findings

Opportunity	Key Recommendations
Identifying Necessary Data Elements	Remove prescriber contact information as a core data element.
	Add unique prefixes to help improve correct use of identifiers especially when a combination of identifiers are needed.
	Provide additional clarification to reduce potential errors with sending the incorrect National Provider Identifier.
Refining Process Steps	Develop a provider "pre-certification" process to proactively identify eligible prescribers.
	Create an exception pathway to prevent in some circumstances unnecessary dispenser verifications of certification status.
	Leverage health IT to improve alert notifications at strategic points in the certification process.
Facilitating Interoperable Data Exchanges	Streamline and facilitate enrollment and knowledge assessment using electronic forms.
	Improve use of SPL to support transitions of care from inpatient to outpatient settings.
	Create a standardized menu of data elements to identify any missing data elements during exchange transactions.

Appendix A: Process Step 3 -- Prescriber Verification of Certification Status

Graphical Depiction of Process Step 3, Prescriber Verification of Certification Status



List of Data Elements for Prescriber Verification of Certification Status

Data Received by the Dispenser

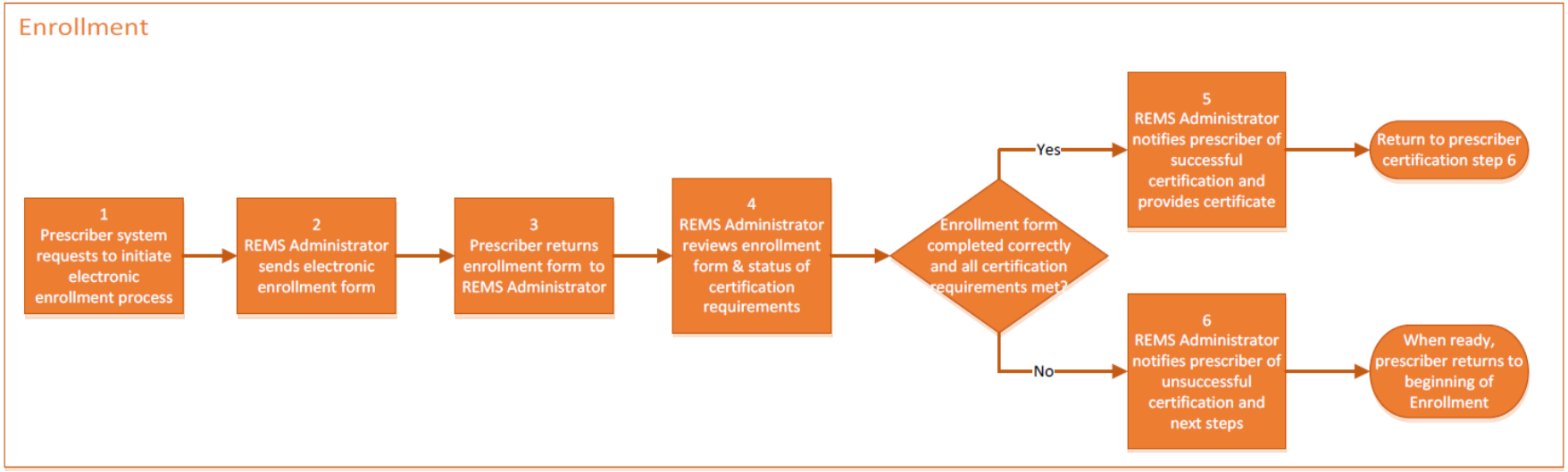
Element	Description / Purpose	Source
REMS Certification Requirements	Detailed list of REMS requirements prescriber must meet in order to be certified	REMS SPL (via EHR's drug database)
Certification Materials	Copies and/or links to materials prescribers may need as part of the certification process (e.g., training materials)	REMS SPL (via EHR's drug database)
Requirement completion status	Yes/no element that verifies whether training, knowledge assessment, and other requirements have been met.	REMS Administrator database
Requirements to be met	Text description of requirements that must still be met if the requirements are not complete	REMS Administrator database

Data Received by the REMS Administrator

Element	Description / Purpose	Source
Prescriber First Name	Prescriber identifier	Prescriber (auto-populated by their EHR)
Prescriber Last Name	Prescriber identifier	Prescriber (auto-populated by their EHR)
Prescriber NPI#	Prescriber identifier	Prescriber (auto-populated by their EHR)
Prescriber DEA#	Prescriber identifier	Prescriber (auto-populated by their EHR)
Prescriber Phone	Contact information	Prescriber (auto-populated by their EHR)
Prescriber Email	Contact information	Prescriber (auto-populated by their EHR)

Appendix B: Step 4 – Prescriber Enrollment and Knowledge Assessment

Graphical Depiction of Process Step 4, Prescriber Enrollment



List of Data Elements for Prescriber Enrollment

Data Received by the Prescriber

Element	Description / Purpose	Source
List of enrollment fields	List of fields that prescriber must complete in the enrollment form, as well as the type of information that each field should contain (see below for more details)	REMS Administrator
Enrollment errors	Description of errors that may have occurred when the prescriber attempted to enroll	REMS Administrator

Data Received by the REMS Administrator

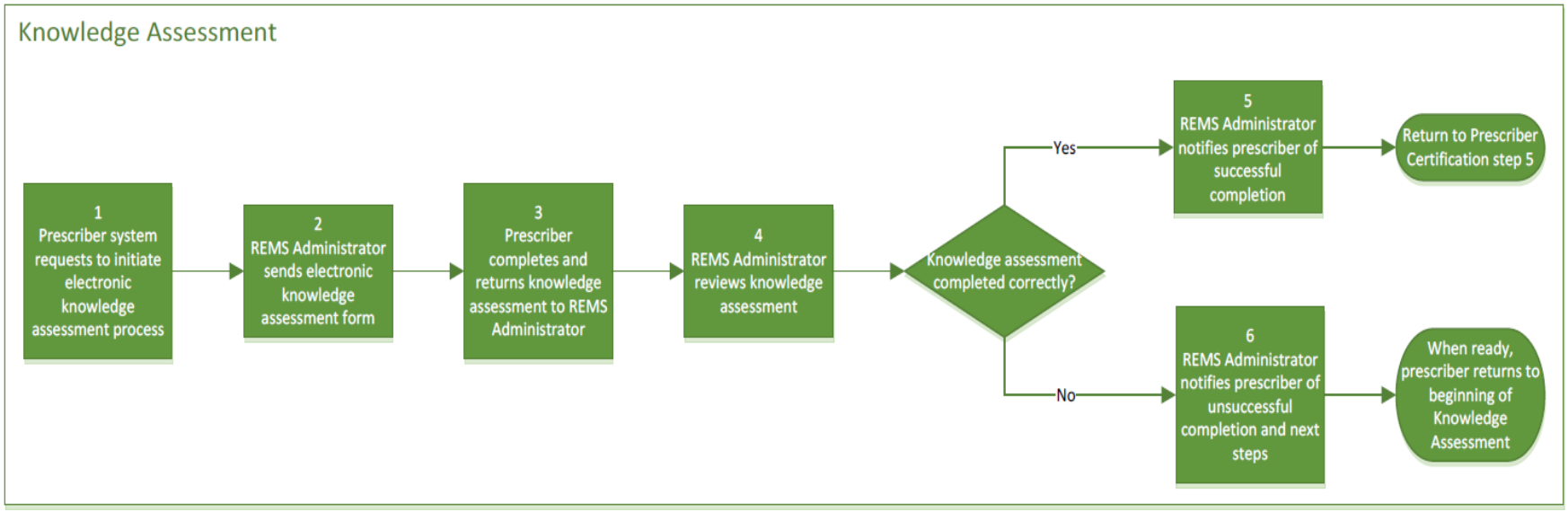
Element	Description / Purpose	Source
Signature	Validates prescriber agreement	
Date	Validates prescriber agreement	

First Name	Prescriber Identifier	Auto-populated by prescriber EHR
Middle Name/ Initial	Prescriber Identifier	Auto-populated by prescriber EHR
Last Name	Prescriber Identifier	Auto-populated by prescriber EHR
Degree		
Specialty		
NPI#	Prescriber Identifier	Auto-populated by prescriber EHR
DEA#	Prescriber Identifier	Auto-populated by prescriber EHR
State license #	Prescriber Identifier	Auto-populated by prescriber EHR
State of [license] Issue	Prescriber Identifier	Auto-populated by prescriber EHR
Practice Name	Identifies practice	Auto-populated by prescriber EHR
Practice Setting	Identifies practice	Auto-populated by prescriber EHR
Address	Contact information	Auto-populated by prescriber EHR
Address 2	Contact information	Auto-populated by prescriber EHR
City	Contact information	Auto-populated by prescriber EHR
State	Contact information	Auto-populated by prescriber EHR
Zip	Contact information	Auto-populated by prescriber EHR
Phone	Contact information	Auto-populated by prescriber EHR
Fax	Contact information	Auto-populated by prescriber EHR
Email	Contact information	Auto-populated by prescriber EHR
Preferred Method of Contact	Prescriber preference	
Office Contact First Name	Alternate contact information	
Office Contact Last Name	Alternate contact information	
Office Contact Email	Alternate contact information	
Office Contact Phone	Alternate contact information	
Office Contact Fax	Alternate contact information	
Alternate/ Mobile Phone #	3rd line contact information	
Confirm Email		Auto-populated by prescriber EHR
Additional Practice Location	Contact information	

Affiliated Hospital	Contact information	
Delegates	Identifies delegate	
Tax ID#		
Acknowledgment Field(s)	Yes/No (i.e., checkbox) field indicating whether prescriber acknowledges specific requirements	

Appendix C: Step 5 – Prescriber Knowledge Assessment

Graphical Depiction of Process Step 5, Prescriber Knowledge Assessment



List of Data Elements for Prescriber Knowledge Assessment

Data Needed by the Prescriber

Element	Description / Purpose	Source
Knowledge assessment questions	Questions that are part of the knowledge assessment	REMS Administrator
Answer choices	Possible answer choices for each question, as well as instructions	REMS Administrator
Instructions	Instructions for the knowledge assessment as a whole or for individual questions (e.g., whether prescribers should select only one answer or may select multiple answers for each question).	REMS Administrator

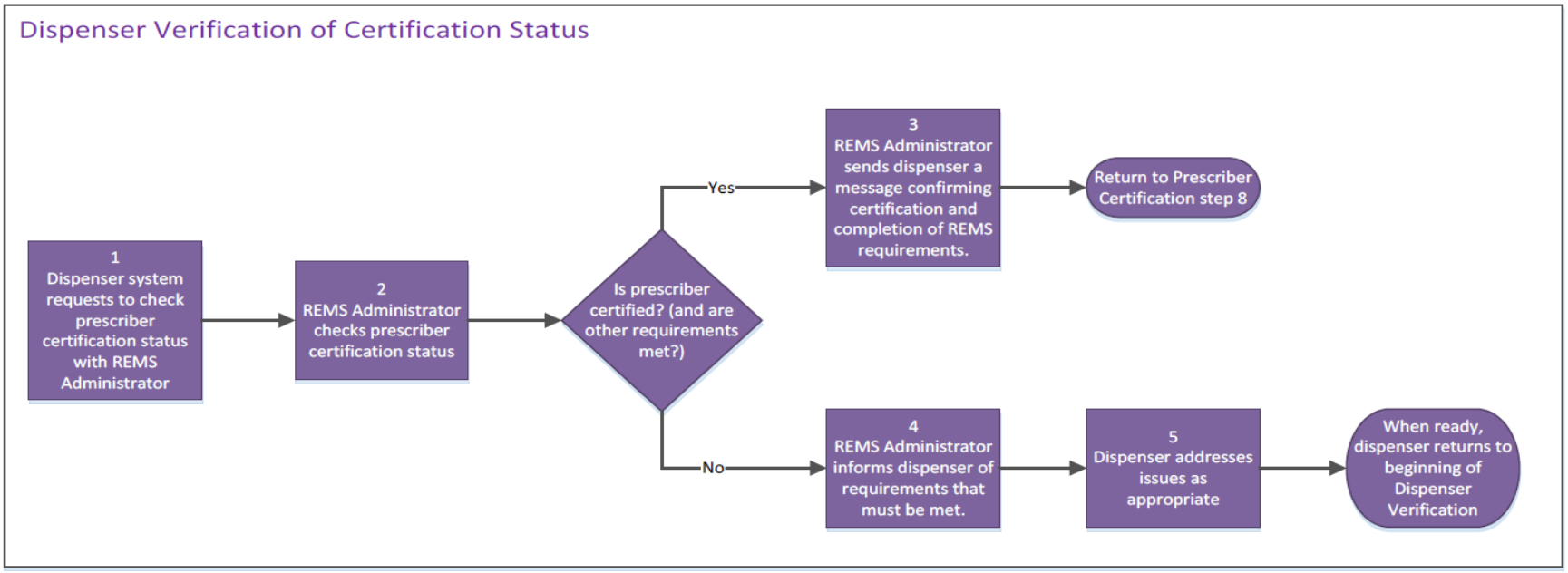
Data Needed by the REMS Administrator

Element	Description / Purpose	Source
Prescriber First Name	Identifies prescriber	Auto-populated by prescriber EHR

Prescriber Last Name	Identifies prescriber	Auto-populated by prescriber EHR
Prescriber NPI#	Identifies prescriber	Auto-populated by prescriber EHR
Prescriber DEA#	Identifies prescriber	Auto-populated by prescriber EHR
Prescriber Phone	Contact information	Auto-populated by prescriber EHR
Prescriber Email	Contact information	Auto-populated by prescriber EHR
Knowledge Assessment Answers	Allow the prescriber to submit an answer to a multiple choice question. Flexibility is needed both in terms of: • Total number of questions (and corresponding answers submitted) • Total number of answer options per question (e.g. a True/False question might only have two, whereas others could have 6+ options) For each question, one or more answers may be submitted	Manually entered by the prescriber

Appendix D: Process Step 7 – Dispenser Verification of Certification Status

Graphical Depiction of Process Step 7, Dispenser Verification of Certification Status



List of Data Elements for Dispenser Verification of Certification Status

Data Received by the Dispenser

Element	Description / Purpose	Source
Requirement completion status	Yes/no element that verifies whether training, knowledge assessment, and other requirements have been met.	REMS Administrator database
Requirements to be met	Text description of requirements that must still be met if the requirements are not complete	REMS Administrator database

Data Received by the REMS Administrator

Element	Description / Purpose	Source
Prescriber First Name	Prescriber identifier	Dispenser (received from prescriber)

Prescriber Last Name	Prescriber identifier	Dispenser (received from prescriber)
Prescriber NPI#	Prescriber identifier	Dispenser (received from prescriber)
Prescriber DEA#	Prescriber identifier	Dispenser (received from prescriber)
Prescriber Phone	Contact information	Dispenser (received from prescriber)
Prescriber Email	Contact information	Dispenser (received from prescriber)
Dispensing Pharmacy NCPDP ID	Identifies dispenser (for retail pharmacies)	Dispenser (auto-populated by pharmacy system)
Dispenser NPI#	Identifies dispenser	Dispenser (auto-populated by EMR / pharmacy system)