

REMS Integration and Innovation

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CDER | US FDA

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Learning Objectives

- ***Learn about the FHIR data standard and how it can help to optimize REMS implementation***
- ***Describe the REMS Integration Use Case and how it can help to reduce REMS implementation burden***
- ***Discuss key challenges and opportunities in REMS integration***

A Risk Evaluation and Mitigation Strategy (REMS)

- Is a drug safety program to help ensure the benefits of the medication outweigh its risks
- May include a number interventions (safe use conditions) to help reduce the occurrence and/or severity of a serious risks
- Designed to achieve specific goals to mitigate risks associated with use of a drug
- Our REMS authorities have allowed for the approval of drugs that would not have been approved or may have been removed from the market
- However, there are significant challenges in implementing and evaluating the effectiveness of REMS programs



REMS burden may be impacting patient access

- Each REMS is customized and uniquely designed and implemented by the drug manufacturer.
- Because REMS with ETASU are not well-integrated into health system workflows or health information technology (HIT) systems, this creates burdens for providers and pharmacists because it requires them to step outside of their workflows.
- The additional burden placed on providers and healthcare systems seeking to comply with the REMS requirements may negatively affect patient access to REMS drugs.



"Thirty-four participants (54%) reported burdens accessing REMS-covered drugs unrelated to insurance coverage at some point during their course of treatment, ranging from additional but not prohibitive challenges to major obstacles."

Sarpawari, Ameet et al. "Patient and Caregiver Experiences With and Perceptions of Risk Evaluation and Mitigation Strategy Programs With Elements to Assure Safe Use." *JAMA network open* vol. 5,1 e2144386. 4 Jan. 2022, doi:10.1001/jamanetworkopen.2021.44386

Background/Definitions



HL7: Health data standards development organization (SDO)



Contemporary health data exchange standard



HL7 FHIR-based cancer data standard (a “lingua franca” for cancer care/research/public health purposes)



Collaborative, stakeholder driven initiatives focused on solving health problems with FHIR-based solutions



CodeX: HL7 FHIR Accelerator building a community around mCODE to solve problems through stakeholder-driven use cases

HL7[®] FHIR Data Standard

The logo for the U.S. Food and Drug Administration (FDA), consisting of the letters "FDA" in white on a blue square background.

F – Fast (to design & implement)

H – Healthcare

I – Interoperability

R – Resources (building blocks)

Fast, Efficient, & Flexible

- Uses 80/20 Rule: 20% of the requirements satisfy 80% of the needs
- **FREE** to use
- Uses mainstream web technology
- Solutions built from modular components called “Resources”
- Option to develop custom extensions

FHIR[®] is a standard for exchanging healthcare information electronically

- Standards establish a common language and process for all health information technology (IT) systems to communicate, allowing information to be shared seamlessly and efficiently
- FHIR[®] can be used as a stand-alone data exchange standard or with existing standards



What is a FHIR Accelerator?

“.. designed to assist communities .. across the global health care spectrum in the creation and adoption of high quality FHIR Implementation Guides .. to move toward the realization of global health data interoperability”

<https://www.hl7.org/about/fhir-accelerator/>



HL7 FHIR Accelerators



HL7 FHIR Accelerator



<http://hl7.org/CodeX>

A Member-driven **community** accelerating **interoperable** data modeling and **implementation** around the **FHIR** and **mCODE** HL7 standards, leading to **substantial improvements** in **health care** and **research** in cancer and beyond

CodeX™ Members (April 2022)

CodeX Founders ★

PREMIER



PRINCIPAL



BENEFACTOR



GOVERNMENT AGENCY



SPONSORED MEMBER



DEVELOPER/IMPLEMENTER



CodeX™ Community of Practice

A group of health systems, specialty societies, government agencies, pharmaceutical manufacturers, researchers, EHRs and supporting organizations, participating in a **monthly public forum focused on real-world applications of mCODE.**



Latest developments on mCODE, CodeX, and cancer data exchange



Ask questions and learn from the experience of other community participants



Develop and share best practices for clinical workflows, data modeling, and exchange



55
Health Systems



7
Payers



10
Pharma



85
EHRs and other tech companies



12
Medical Societies and Consortia



14
Government Agencies



12
Research Organizations



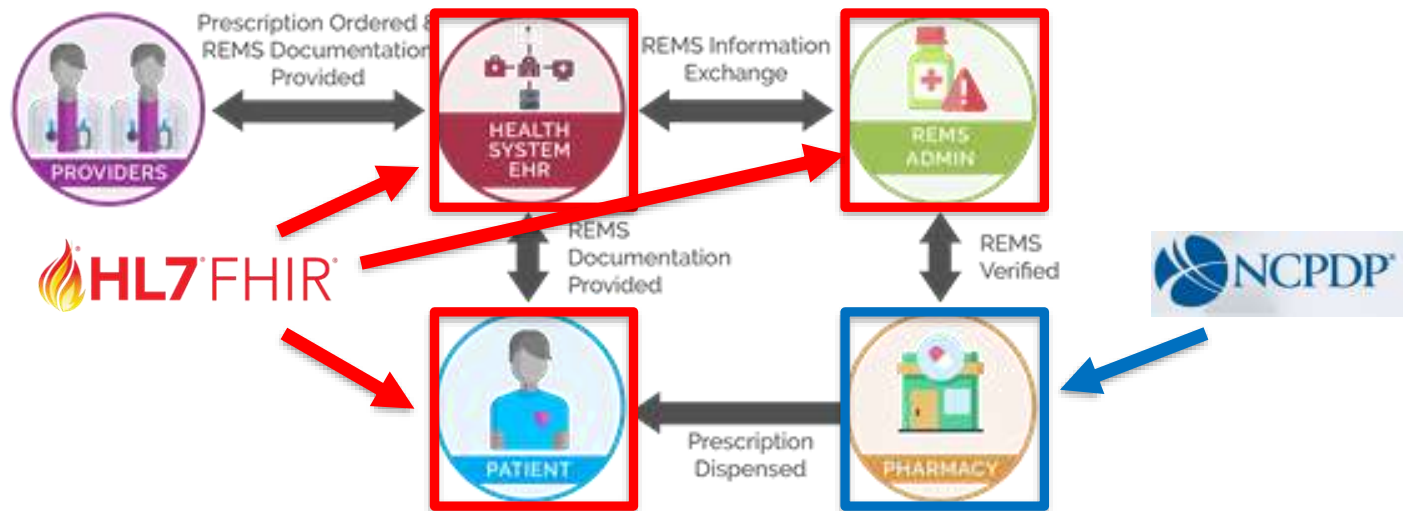
7
Nonprofits/Foundations



2
Patient Advocacy Organizations

<https://confluence.hl7.org/display/COD/mCODE+Community+of+Practice>

REMS Integration Proof-of-Concept/CodeX Use Case

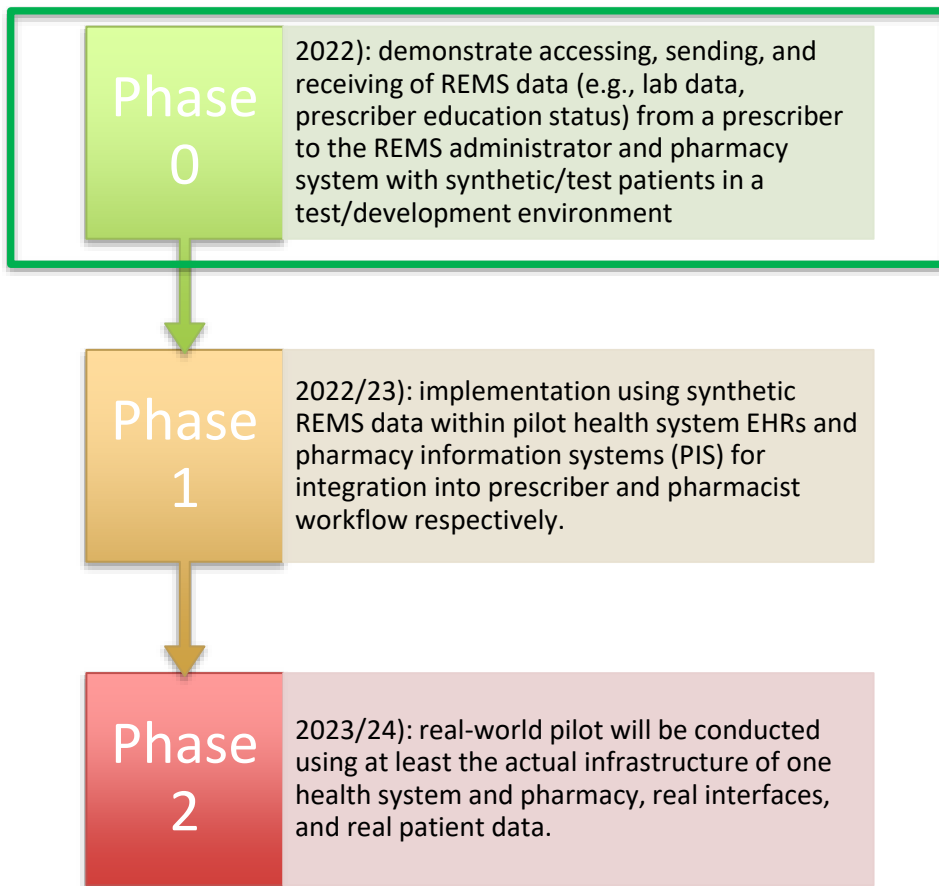


<https://confluence.hl7.org/display/COD/Risk+Evaluation+and+Mitigation+Strategies+-+REMS>

Think HL7[®] Software[®] working directly with Android NCPDP SCRIPT



Planned CodeX™ REMS Integration Use Case Phases



Scalable, standards-based solution for REMS integration & optimization

Structured Product Labeling (SPL) captures the essence of REMS documents



Data Element	Description	Examples
Stakeholder ("Who")	The party that must meet the REMS requirement	Prescriber, pharmacist, health care setting
Protocol ("When")	A particular "stage" in the treatment process around which REMS activities may occur	Certification, prescribing, pharmacy and administration
Requirement ("What")	A clinical or administrative activity that must be performed as part of the REMS	Counseling a patient, completing an enrollment form, lab testing
Material reference ("With what")	Reference to approved REMS material with which the requirement is carried out	Enrollment form, medication guide, educational pamphlet

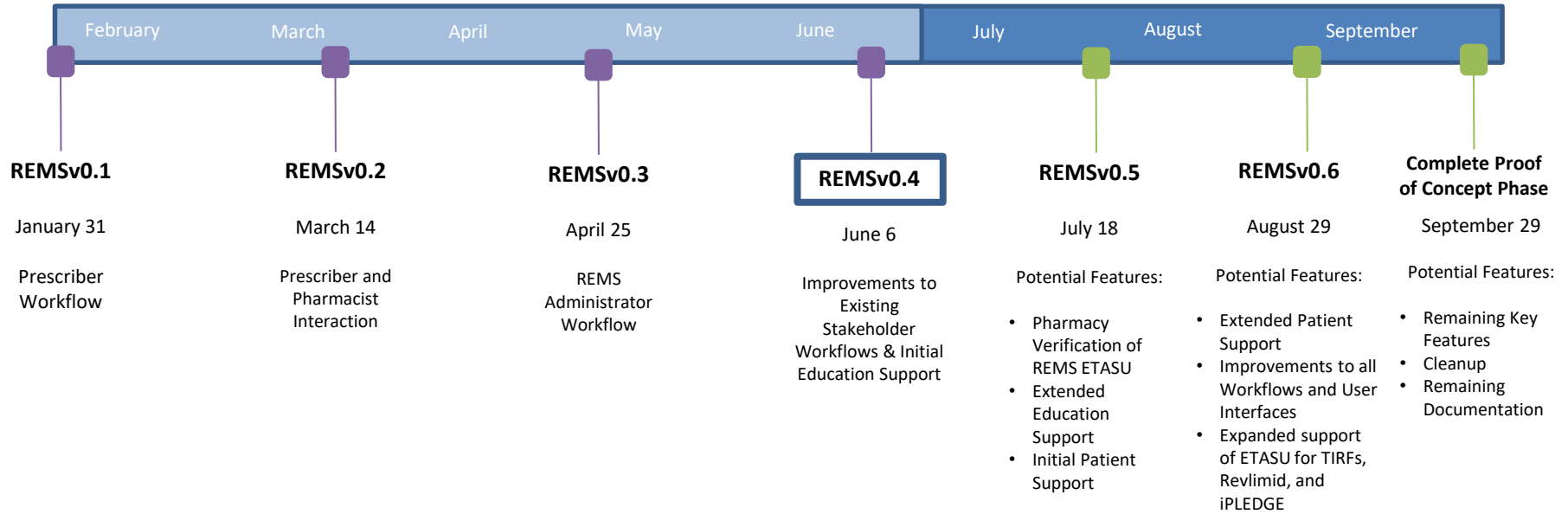
REMS SPL Submissions to FDA

- WHEN:
 - December 28, 2022
- WHO:
 - Applicants must submit the content of their REMS document electronically using SPL
- WHAT:
 - All REMS documents submitted to FDA on or after December 28, 2022, must be in SPL format, which include:
 - REMS documents associated with a **new** REMS
 - REMS documents submitted as part of REMS **modifications**
 - REMS documents that are **already in SPL format** must remain in SPL format
 - Components of a REMS required to be filed in SPL format:

Component of a REMS Submission	Submitted in SPL Format?
REMS document	Yes
REMS supporting document	No
REMS materials	Referenced in SPL file (see Structured Product Labeling Implementation Guide with Validation Procedures at https://www.fda.gov/media/84201/download)



REMS Integration Prototype Release Schedule





REMS Integration Project Status

- **REMS use case:** 5th and most recent public use case call on May 24
- **Prototype development:** 4th iteration (REMSv0.4) was made available on 6/6
- **FDA joined CodeX™**
- **Use case stakeholder groups:**
 - Pharmacies and health systems
 - Prescribers and ePrescribing Networks
 - REMS Administrators
 - Payers
 - Pharmaceutical companies
 - Other (e.g., wholesalers)

Select Patient and Medication

EHR Launch **Starbucke**

Patient Select: N/A

Demographics

- Name: N/A
- Age: N/A
- Gender: N/A
- State: N/A

Coding

- Code: N/A
- System: N/A
- Display: N/A

ID: pat015 Name: William Oster Gender: male Age: 6	Request: <input type="text" value="Choose an option"/>
ID: pat1234 Name: Bobby Tables Gender: male Age: 25	Request: <input type="text" value="Choose an option"/>
ID: pat014 Name: Theodor Roosevelt Gender: male Age: 75	Request: <input type="text" value="Choose an option"/>
ID: pat018 Name: Ada Wilson Gender: female Age: 45	Request: <input type="text" value="Choose an option"/>
ID: pat013 Name: Vlad Quinlan Gender: male Age: 65	Request: <input type="text" value="Choose an option"/>
ID: pat017 Name: Jon Snow Gender: male Age: 25	Request: <input type="text" value="(183)26 Turvilo 200 MG Oral Capsule"/>

Selection shows that drug has REMS

CHP Launch Standalone

Settings

Patient Select: pat017

Demographics	Prelisted
Name: Jon Snow	Patient: Patientpat017 ✓
Age: 25	MedicationRequest: MedicationRequestpat017-m-oral ✓
Gender: male	Coverage: Coveragecov017 ✓
State: Westeros	Practitioner: Practitionerpra1234 ✓

Coding	Other Resources
Code: 2183128	Organization/org1234 ✓
System: RxNorm	Location/loc1234 ✓
Display: Turabo 200 MG Oral Capsule	PractitionerRole/practf1234 ✓

Submit

Summary
Drug Has REMS: Documentation Required.

Details
Documentation Required, please complete form via Smart App link.

Source: Da Vinci CRD Reference

Documentation Requirements: [Patient Enrollment Form](#) [Patient Status Update Form](#)

Type:

Patient Enrollment Form Opens

Turalio Rems Patient Enrollment ⌵

Patient: Jon Snow Only Show Unfilled Fields Restoration Create Task

Patient Information

Address Line 2 Type a value

Telephone Type a value

Race Select one or type a value

Is the patient currently taking pexidartinib (i.e., started prior to REMS enrollment)?

If yes: Was this part of a clinical study?

Comment Type a value

Prescriber Information

Address Line 2 Type a value

Please visit www.turaliorems.com or contact the TURALIO REMS Coordinating Center at 1-833-TURALIO (833-867-2546) to designate up to two additional REMS certified prescribers who can view, edit, and submit REMS paperwork for your TURALIO patients.

Current Medication (including prescription, non-prescription and herbal or dietary supplements)

Check box if there are no current medications

Hepatic Medical History

Check box in this section if there is no hepatic medical history

Prescriber Agreement

I have reviewed and discussed the risks of TURALIO and the requirements of the TURALIO REMS with this patient.

Provider Signature

Signature *	Name (Printed) *	Date *	NPI *
<input type="text"/>	Jane B Doe	01/26/2022	1122334455

Patient Attestation

In order to receive TURALIO I must be enrolled in the TURALIO REMS. The TURALIO REMS will collect data to assess the risk of serious liver problems which can be severe and lead to death as described in the Patient Guide. • I agree to enroll in the Patient Registry. • I agree to review the Patient Guide. • I must get blood tests to test my liver as directed by my healthcare provider. • I agree to tell my healthcare provider if I have signs and/or symptoms of liver injury. • My personal information will be shared to enroll me in the Patient Registry so that my health and any liver injury can be evaluated while I am receiving TURALIO. • Daiichi Sankyo, Inc. and its agents, may contact me or my prescriber by phone, mail or email to manage the TURALIO REMS. • Daiichi Sankyo, Inc. and its agents, may use and share my personal health information, including lab tests and prescriptions as part of the TURALIO REMS. My information will be protected and will be used to enroll me into and manage the TURALIO REMS. My health information may be shared with the U.S. Food and Drug Administration (FDA) to evaluate the TURALIO REMS.

Patient Signature

Signature *	Name (Printed) *	Date *
Jon Snow	Jon S Snow	01/26/2022

Form Loaded: New

Patient Enrollment Form Prepopulated



Turalio Rems Patient Enrollment ⚙️ Only Show Unfilled Fields ⌵ Iteration ■ Create Task

Patient: Jon Snow

Prescriber Information

Last Name: Doe
 First Name: Jane
 Middle Initial: B
 NPI: 112234455
 Practice/Facility Name (where you see this patient): Boston Medical Center
 Address Line 1: 840 Seneca St
 Address Line 2: Type a value
 City: Buffalo
 State: NY
 Zip: 14210
 Telephone: 716-673-1957
 Email: jane.betty@myhospital.com

Please visit www.turaliorems.com or contact the TURALIO REMS Coordinating Center at 1-833-TURALIO (833-857-2546) to designate up to two additional REMS certified prescribers who can view, edit, and submit REMS paperwork for your TURALIO patients.

Baseline Labs

Assess the patient by obtaining liver tests as stated in the Prescribing Information. If Albumin or PT/INR were not obtained, indicate "not applicable." Please provide the results below.

Laboratory Test	Baseline Value (units, reference range)	Date
AST or SGOT	22 U/L	06/15/2021
ALT or SGPT	12 U/L	03/11/2021
GGT	15 U/L	12/04/2021
Total Bilirubin	0.8 mg/dL	04/11/2021
Direct Bilirubin	0.2 mg/dL	04/18/2021
Alkaline Phosphatase	27 U/L	06/15/2021
Albumin	4.8 g/dL	01/25/2020
PT/INR	9.7 s	12/25/2020

Current Medication (including prescription, non-prescription and herbal or dietary supplements)

Check box if there are no current medications

Medication:

Submit REMS Bundle



Type a value | Jane B Doe | 04/21/2022 | 1122334455

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Patient Signature

Signature *	Name (Printed) *	Date *
Jon Snow	Jon S Snow	04/21/2022

Form Loaded: New

Load Previous Form | Save to EHR | **Submit REMS Bundle**



Order Appears in Pharmacy System

Orders Grouped by Status

The screenshot displays the Pharmicare Pharmacy Management System interface. At the top, there is a navigation bar with the Pharmicare logo, the user role 'Pharmacist', a search bar, and a 'Log out' button. Below the navigation bar, there are three tabs: 'New Orders', 'Verified Orders', and 'Picked Up Orders'. The 'Picked Up Orders' tab is selected and highlighted in blue. Below the tabs, there is a table titled 'Picked Up Orders' with the following columns: Doctor Name, Doctor Contact, DoctorID, Doctor Email, Drug Names, Drug Prices, Quantities, Total, Scheduled Pickup Date, and Actual Pickup date. The table contains one row of data for Dr. Jane Betty Doe, with a scheduled pickup date of Thu Apr 21 2022 and an actual pickup date of Thursday, April 21, 2022. A green box highlights the tabs and the table area.

Doctor Name	Doctor Contact	DoctorID	Doctor Email	Drug Names	Drug Prices	Quantities	Total	Scheduled Pickup Date	Actual Pickup date
Dr. Jane Betty Doe	716-873-1557	1122334455	jane.betty@myhospital.com	Turalio 200 MG Oral Capsule	200	90	18000	Thu Apr 21 2022	Thursday, April 21, 2022



Summary

- FDA is working with stakeholders to leverage data standards for REMS implementation optimization.
- There are current and future opportunities for the public and stakeholders to contribute to the REMS integration use case.
- The REMS integration use case is demonstrating the art of the possible to integrate REMS into workflow, reduce undue burden, and optimize REMS outcomes.



Challenge Question #1

What data standards are being used in the REMS integration use case:

- A. CDISC
- B. NCPDP[®] SCRIPT
- C. HL7[®] FHIR[®]
- D. B and C above



Challenge Question #2

Which of the following statements is NOT true?

- A. FHIR stands for Fast Healthcare Interoperability Resources.
- B. A REMS data hub for sharing REMS information is being created as part of the REMS integration use case.
- C. The REMS integration use case is integrating into the workflow of prescribers, pharmacists, and REMS administrators.
- D. The public and interested stakeholders can join the REMS integration use case.



Resources

- [CodeX™ REMS Integration Use Case](#)
- [CodeX™ FHIR® Accelerator](#)
- [Minimal Common Oncology Data Elements \(mCODE™\)](#)
- [FHIR® data standard specification](#)
- [Approved Risk Evaluation and Mitigation Strategies \(REMS\)](#)
- [REMS Public Dashboard](#)

SPL Resources



- REMS SPL submission requirements begin Dec 28, 2022
 - [Providing Regulatory Submissions in Electronic Format -- Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling](#)
- FDA REMS SPL coding pages
 - [Structured Product Labeling Implementation Guide with Validation Procedures](#)
 - [REMS SPL Sample](#)
 - [REMS Approval](#)
 - [REMS Protocol](#)
 - [REMS Stakeholder](#)
- DailyMed SPL Indexing files
 - [DailyMed - Download All Indexing & REMS Files](#)



Closing Thought

To advance drug safety and bring REMS into the 21st Century, please consider joining the REMS Integration Use Case Community by visiting the use case page and signing up for the monthly Public Use Case Meetings:

[CodeX REMS Integration Use Case](#)

CodeX™ REMS Use Case Webpage



Project Overview

Problem

- There are a number of key stakeholders (Patients, Prescribers, Nurse/Office Administrators, Pharmacists, REMS Administrators and Pharmaceutical Manufacturers) who play an important role in the REMS workflow of prescribing a drug to the patient. This includes verification of completed REMS requirements and dispensing the drug to the patient. There currently is no unified way to share data between REMS stakeholders.
- Due to gaps in data interoperability, there is difficulty in communication and coordination of efforts amongst stakeholders in the REMS workflows.
- REMS are not built into current workflows and the complexity of these programs leads to additional burden on stakeholders and the overall healthcare system.
- All of these challenges can result in delays in therapy for patients, treatment abandonment, limited access to REMS drugs, time taken away from patient care, overwhelmed stakeholders and sub-optimal care for the patient.

Description

- REMS is integrated into prescriber and pharmacist workflows, allowing them to easily complete the necessary REMS requirements without having to open a separate portal or remember additional steps for handling a REMS
- REMS integration allows prescribers to be alerted that a drug requires REMS education and training and any additional clinical actions needed (e.g. monthly liver enzyme monitoring, lab tests, etc.) to adhere to the requirements of the REMS program without having to manually look up this information
- Prescribers are able to easily submit the necessary information in their current workflow, allowing them to fulfill or attest to REMS requirements
 - Structured data is used for populating REMS requirements, helping to automate the process and reduce the burden of manual entry
 - Capture of a completed REMS is integrated in a claim and documented in prescriber's clinical notes
- When a request is received to dispense a REMS drug, pharmacists are able to easily confirm, within their

REMS Use Case Quick Links

- CodeX REMS One-Pager
- REMS Use Case Public Call
- GitHub REMS Code Repository
- FDA_REMS_Landscape_Analysis

REMS Engagement Value by Stakeholder

- Prescribers
- REMS Administrators
- Pharmacists
- Patients

REMS Use Case Page Navigation

- Project Overview
 - Problem
 - Description
 - Target Outcome
 - Value
- REMS Proof-of-Concept Prototype
 - GitHub REMS Code Repository
- Project Plan
- Conference Call Information
- Use Case Team

Questions?

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Office of Surveillance and Epidemiology

CDER | US FDA

CodeX REMS integration use case link: [CodeX REMS Integration Use Case](#)