REMS Integration and Innovation

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CDER | US FDA

Regulatory Education for Industry (REdI) – June 7, 2022

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."

Sarpatwari, 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

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

Slide adapted from CodeX Community of Practice Presentation, "Introduction to FHIR," by MITRE on July 30, 2021.

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 ARGONAUT PROJECT

DA VINCI HL7 FHIR

CodeX™

HELIOS

carin
Creating Access to Real-time Information Now through Consumer-Directed Exchange

gravity PROJECT

VULCAN HL7 FHIR

FAST
FHIR AT SCALE TASKFORCE

Slide adapted from the CodeX™ Master Slide Deck titled, "Introduction to mCODE™ and the CodeX™ HL7® FHIR® Accelerator" available on the CodeX™ Confluence page.

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

Slide adapted from the CodeX™ Master Slide Deck titled, "Introduction to mCODE™ and the CodeX™ HL7® FHIR® Accelerator" available on the CodeX™ Confluence page.

CodeX™ Members (April 2022)

CodeX Founders ★

PREMIER

AMERICAN ASSOCIATION of PHYSICISTS IN MEDICINE ★
ASTRO ★
UnitedHealthcare ★
ALLIANCE ★
MITRE ★
EVERNORTH
HL7 International ★
Syntropy ★
ontada
Pfizer ★

PRINCIPAL

Cancer Action Network ★

BENEFACTOR

CIBMTR ★
Telligen
TrialJectory

GOVERNMENT AGENCY

CDC ★
FDA U.S. FOOD & DRUG ADMINISTRATION
University of Nebraska Medical Center
MCSP MICHIGAN

SPONSORED MEMBER

COMP Canadian Organization of Medical Physicists
OCPM Organisation canadienne des physiciens médicaux
HC FARNING HEALTH COMMUNITY
SIIM
ONS
AMGEN

DEVELOPER/IMPLEMENTER

Cancer Insights
MASSIVEBIO
mcg
Mettle SOLUTIONS
NeuralFrame
varian
patientlink
PRINCIPIA HEALTH SCIENCES
QL HC Quantum Leap Healthcare Collaborative
Wemedoo Clinical Information Specialists

CodeX™

Slide adapted from the CodeX™ Master Slide Deck titled, "Introduction to mCODE™ and the CodeX™ HL7® FHIR® Accelerator" available on the CodeX™ Confluence page.

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

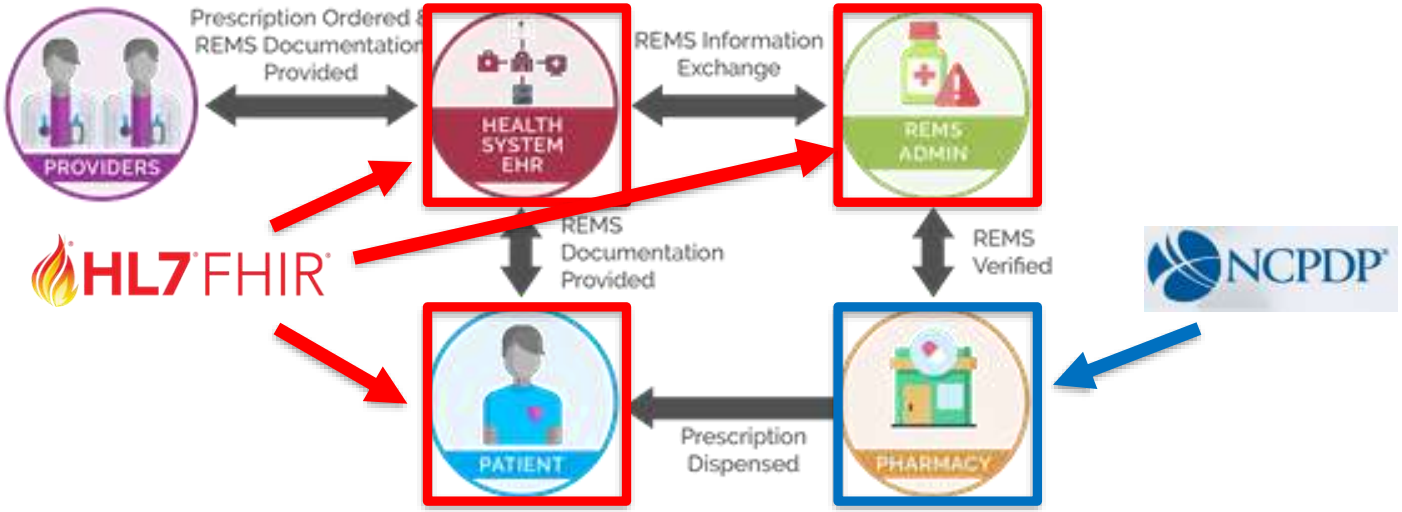
2 Patient Advocacy Organizations

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

Slide adapted from the CodeX™ Master Slide Deck titled, "Introduction to mCODE™ and the CodeX™ HL7® FHIR® Accelerator" available on the CodeX™ Confluence page.

CodeX™

REMS Integration Proof-of-Concept/CodeX Use Case



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

Think HL7® FHIR® working directly with NCPDP SCRIPT

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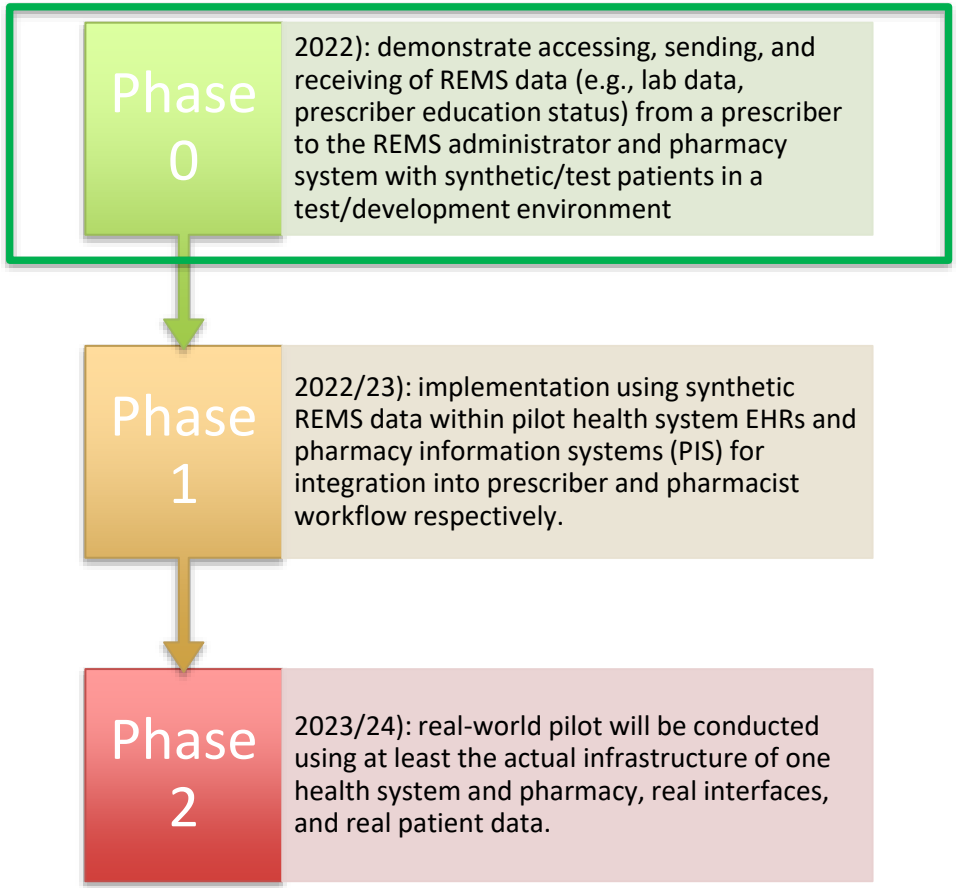
Planned CodeX™ REMS Integration Use Case Phases



HL7 FHIR

CodeX™
Common Oncology Data Elements eXtensions

Scalable, standards-based solution for REMS integration & optimization

* These phases do not include the development of a REMS data hub/platform or database for prescriber education and REMS data and information. This will need to be developed in the future.

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

REMSv0.1

January 31

Prescriber Workflow

REMSv0.2

March 14

Prescriber and Pharmacist Interaction

REMSv0.3

April 25

REMS Administrator Workflow

REMSv0.4

June 6

Improvements to Existing Stakeholder Workflows & Initial Education Support

REMSv0.5

July 18

Potential Features:

- Pharmacy Verification of REMS ETASU
- Extended Education Support
- Initial Patient Support

REMSv0.6

August 29

Potential Features:

- Extended Patient Support
- Improvements to all Workflows and User Interfaces
- Expanded support of ETASU for TIRFs, Revlimid, and iPLEDGE

Complete Proof of Concept Phase

September 29

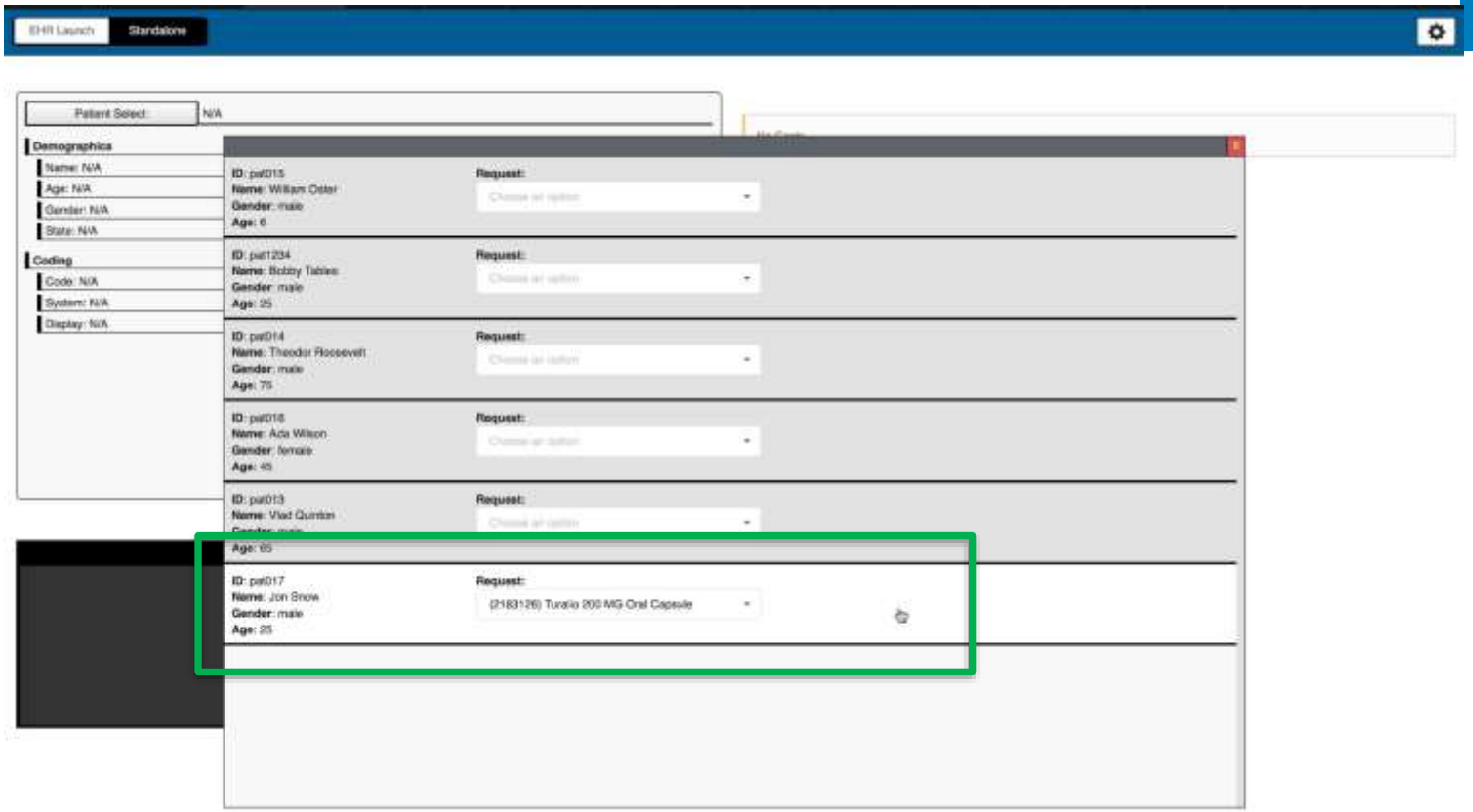
Potential Features:

- Remaining Key Features
- Cleanup
- Remaining Documentation

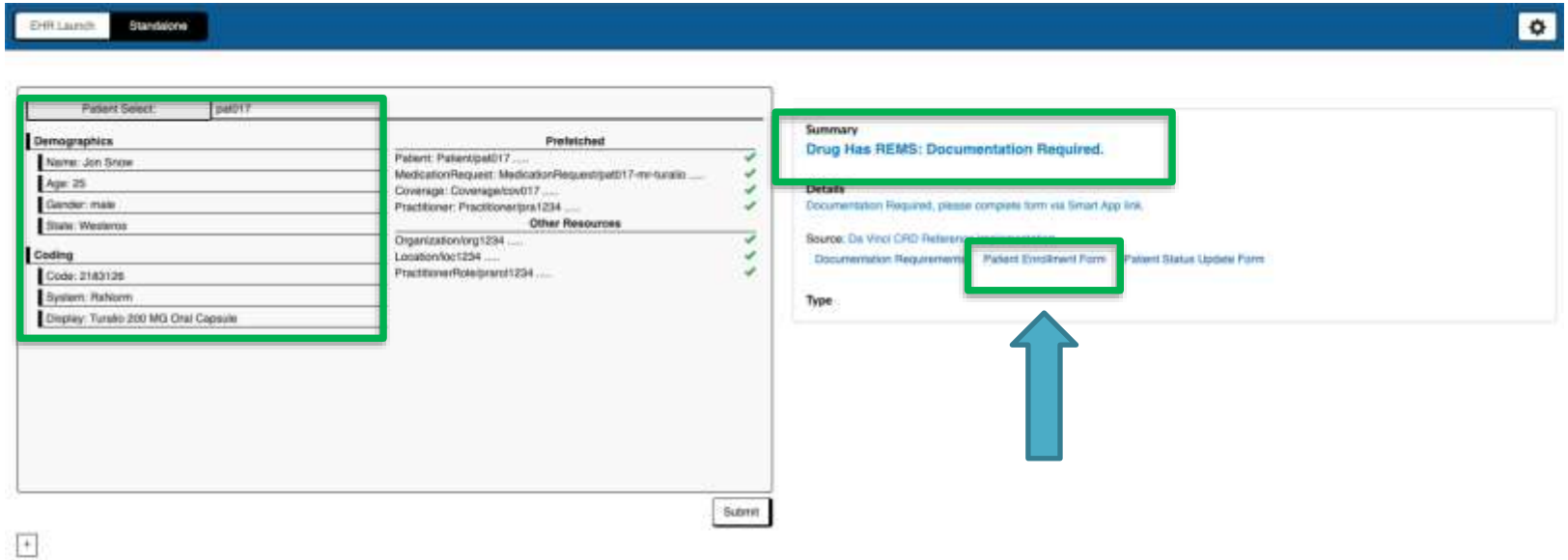
REMS Integration Project Status

- **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)

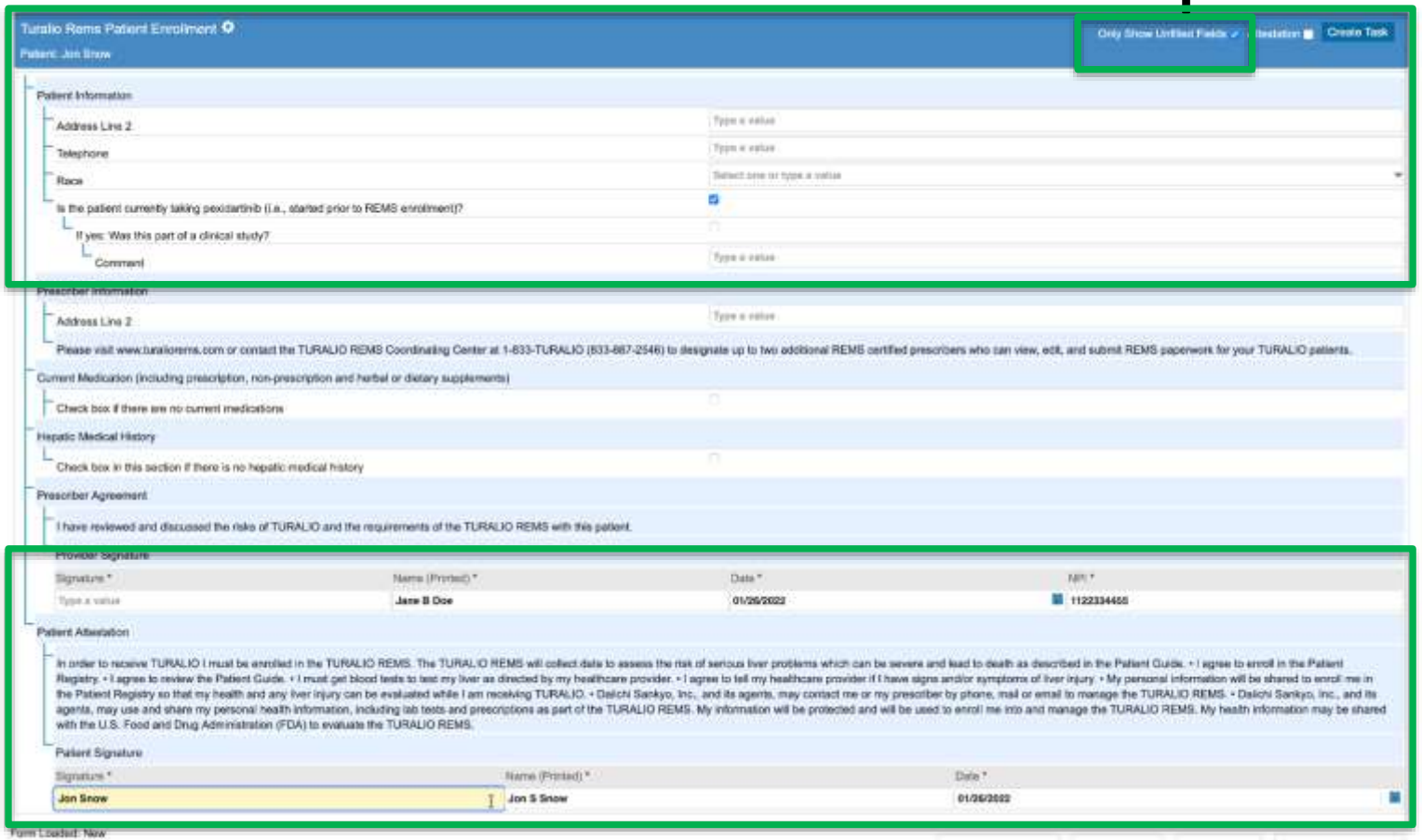
Select Patient and Medication



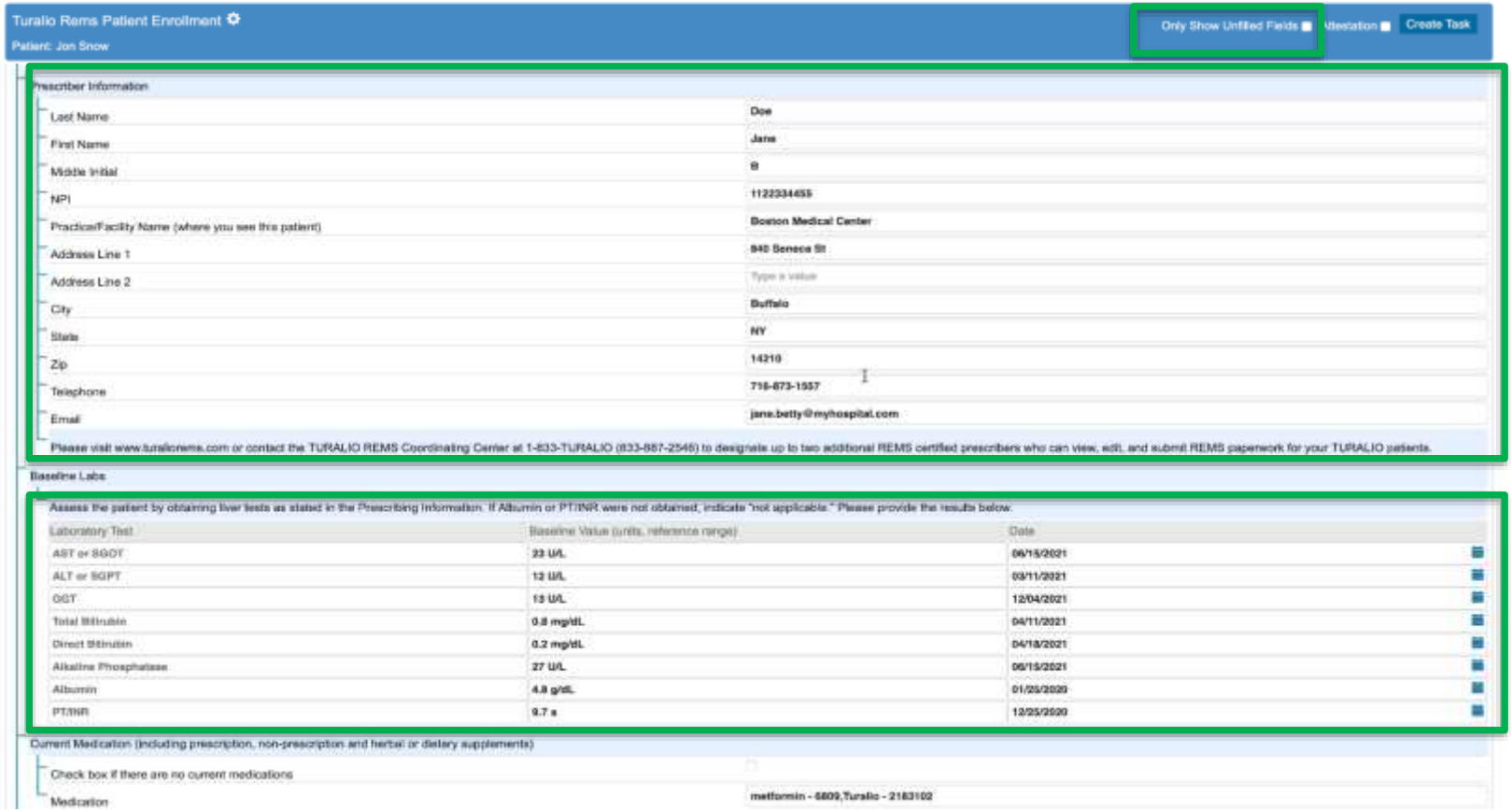
Selection shows that drug has REMS



Patient Enrollment Form Opens



Patient Enrollment Form Prepopulated



Turalio Rems Patient Enrollment

Patient: Jon Snow

Only Show Unfilled Fields | Attestation | Create Task

Prescriber Information

Last Name	Doe
First Name	Jane
Middle Initial	B
NPI	1122334455
Practice/Facility Name (where you see this patient)	Boston Medical Center
Address Line 1	940 Seneca St
Address Line 2	Type a value
City	Buffalo
State	NY
Zip	14210
Telephone	716-873-1557
Email	jane.betty@myhospital.com

Please visit www.turalionems.com or contact the TURALIO REMS Coordinating Center at 1-833-TURALIO (833-887-2546) to designate up to two additional REMS certified prescribers who can view, edit, and submit REMS paperwork for your TURALIO patients.

Baseline Labs

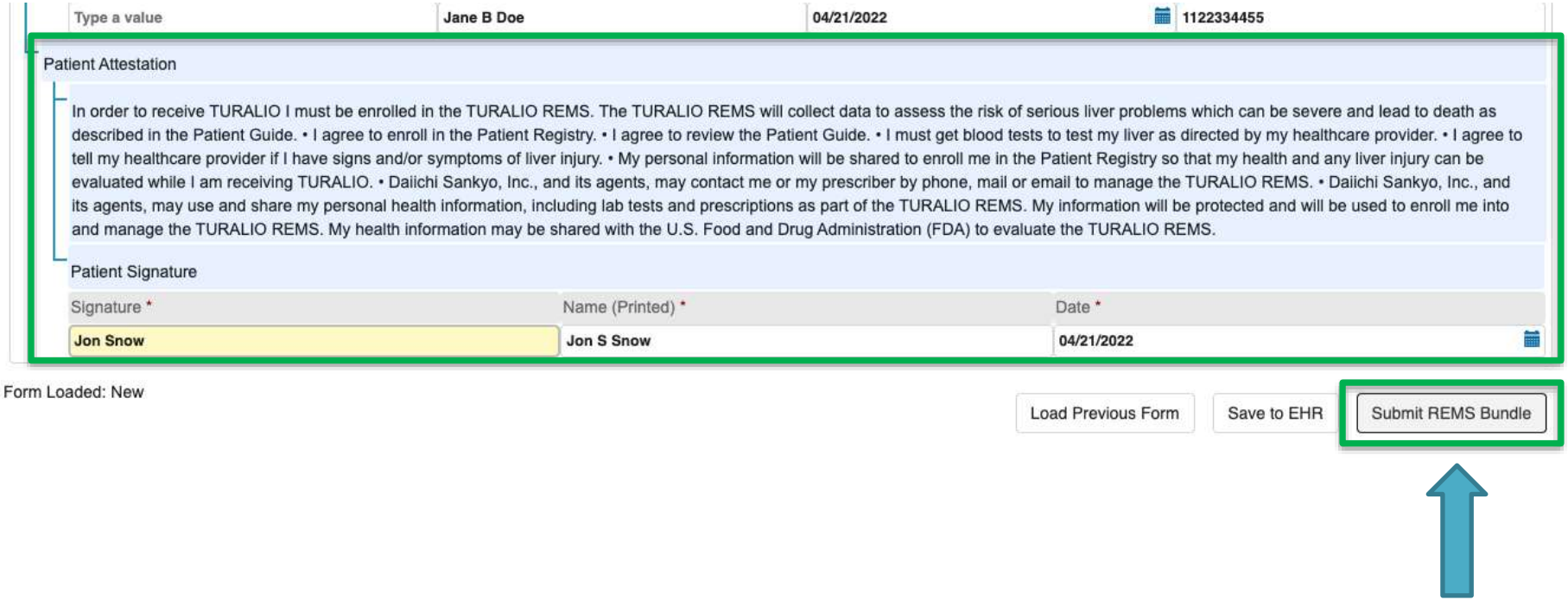
Assess the patient by obtaining liver tests as stated in the Prescribing Information. If Albumin or PT/INR were not obtained, indicate "not applicable." Please provide the results below.

Laboratory Test	Baseline Value (units, reference range)	Date
AST or SGOT	23 U/L	06/15/2021
ALT or SGPT	12 U/L	03/11/2021
GGT	13 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)

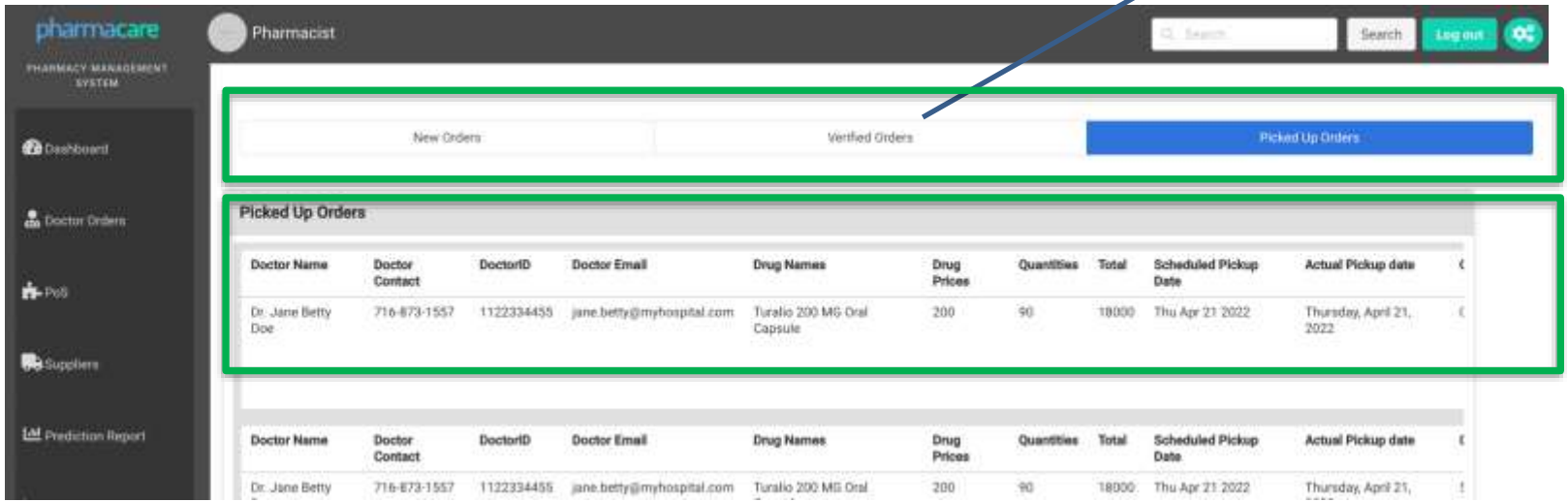
Check box if there are no current medications	
Medication	metformin - 6809,Turalio - 2183102

Submit REMS Bundle



Order Appears in Pharmacy System

Orders Grouped by Status



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

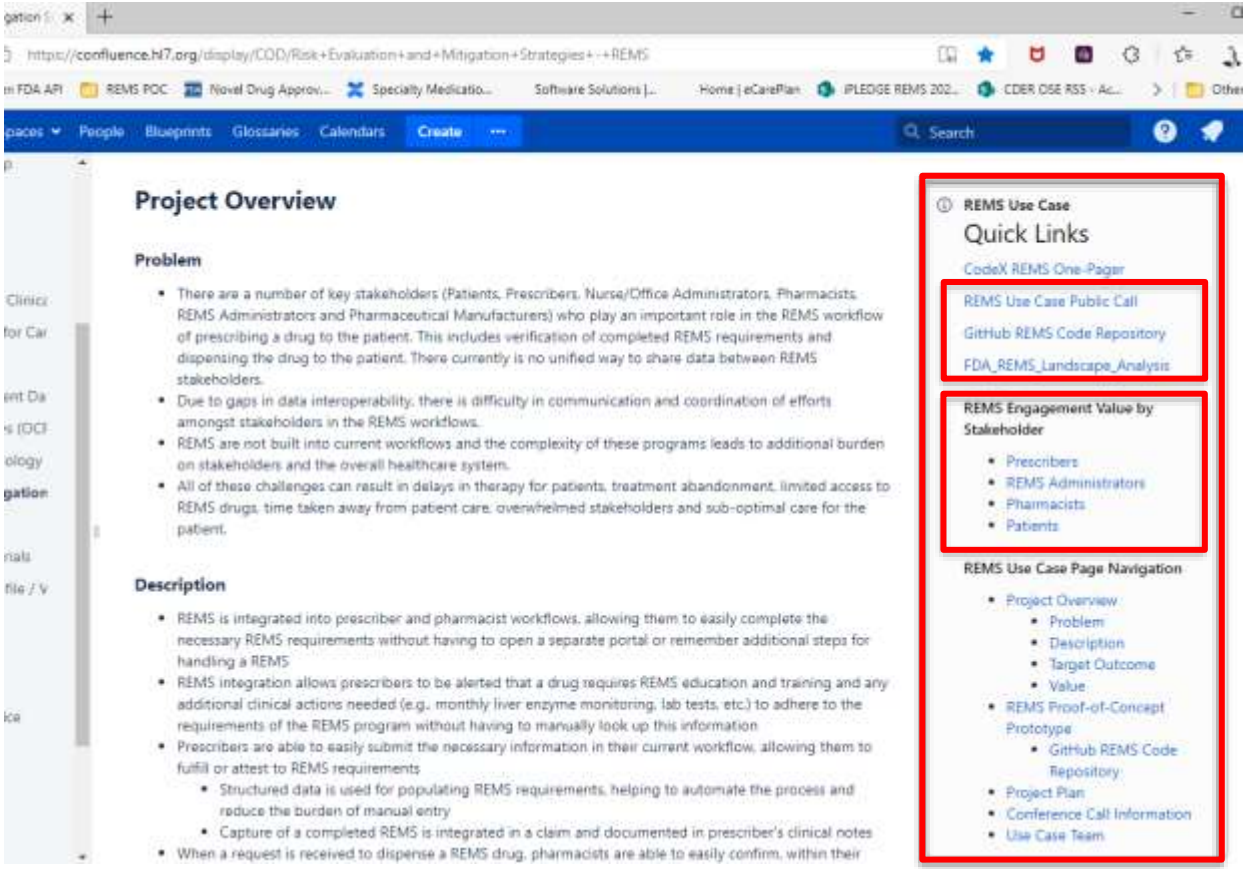
SPL Resources

- 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



https://confluence.hl7.org/x/HQXUB

Questions?

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Office of Surveillance and Epidemiology

CDER | US FDA

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