Duke | MARGOLIS CENTER for Health Policy

Challenges and Opportunities for REMS Integration, Innovation, and Modernization

Tuesday, October 11, 2022 | 1:00 p.m. – 5:15 p.m.

Workshop Summary

Introduction and Executive Summary

The Duke-Margolis Center for Health Policy, with support from the U.S. Food and Drug Administration (FDA) convened a workshop entitled "Challenges and Opportunities for REMS Integration, Innovation, and Modernization" on October 11, 2022. This workshop was the third in a series of Margolis-FDA workshops focused on Risk Evaluation and Mitigation Strategies (REMS), following two previous workshops in October 2021 and April 2022. While those workshops focused respectively on potential mandatory prescriber education and the content of prescriber education under the Opioid Analgesic REMS, this workshop was intended to present and solicit feedback on a new method for implementing requirements across a wide variety of REMS programs.

Speakers from FDA and the MITRE Corporation presented a proof-of-concept prototype for integrating REMS requirements into clinical workflows using modern health data standards. The proof-of-concept prototype is intended to improve patient outcomes by reducing the current burden associated with fulfilling REMS requirements. Then, a series of panel discussions featuring prescribers, pharmacists, health system representatives, patients, and other stakeholders explored challenges and opportunities associated with the prototype approach.

Key takeaways from this workshop included the following:

- The proof-of-concept prototype for REMS integration, supported by FDA and developed by MITRE, demonstrates how stakeholders can more efficiently exchange key data elements using modern health data standards. By integrating REMS requirements into clinical workflows, the prototype approach aims to alleviate burdens that prescribers, pharmacists, patients, and other stakeholders currently experience when fulfilling REMS requirements. The prototype is intended to model how these data transactions could be completed and lay out an approach for stakeholders to adopt, rather than being a finished product.

- Panelists were generally optimistic about the potential for the prototype to reduce burden and streamline the process of fulfilling REMS requirements. Many providers and patients especially supported the effort to reduce time spent handling administrative burdens, increase time available for direct provider-patient interactions, increase transparency in the prescribing and dispensing process, and ultimately reduce barriers to access for patients.

- In order to function effectively, the prototype approach will need to account for a vast range of complexities across the varied REMS programs and requirements, numerous sets of stakeholders interacting with them, and different sites of care they affect. To account for such complexities, panelists suggested piloting the prototype in diverse settings, training prescribers and pharmacists on the new system, soliciting end-user feedback on an ongoing basis, establishing clear metrics for success, and other steps to ensure effective implementation.

FDA Presentations

The workshop began with a presentation from Dr. Marta Sokolowska, Deputy Center Director for Substance Use and Behavioral Health in FDA's Center for Drug Evaluation and Research (CDER), providing context on previous Margolis-FDA workshops on REMS and this workshop's focus on implementing REMS requirements. While the two previous Margolis-FDA workshops on REMS centered on the Opioid Analgesic REMS, this workshop shifted focus to the challenges associated with implementing requirements across a wide variety of REMS programs.

Dr. Sokolowska detailed challenges with current systems for implementing REMS requirements – manual processes, lack of integration with prescriber and pharmacist workflows, lack of standardization and transparency – and highlighted opportunities for alleviating some of these challenges through a standards-based approach using modern health information technologies like Health Level 7 Fast Healthcare Interoperability Resources (HL7 FHIR) standards.

Speakers from the Office of Surveillance and Epidemiology in FDA's CDER further emphasized the burdens health care providers currently experience with REMS requirements, and the ways in which those burdens can reduce patient access. To address these challenges and improve patient outcomes, efforts are being made to integrate REMS requirements into clinical workflows using HL7 FHIR and National Council for Prescription Drug Programs (NCPDP) data standards. FDA's recent work on REMS integration includes ongoing engagements with the CodeX HL7 FHIR Accelerator – a group of health systems, specialty societies, government agencies, pharmaceutical manufacturers, researchers, electronic health records (EHRs) companies, and other organizations – that hosts monthly public forums focused on real-world applications of Minimal Common Oncology Data Elements (mCODE) and FHIR across a variety of use cases. Through collaboration with the MITRE Corporation and the CodeX FHIR Accelerator, FDA has championed a use case and MITRE has developed a proof-of-concept prototype, with stakeholder input, demonstrating how prescribers, pharmacists, health systems, REMS administrators, and patients can send and receive data needed to fulfill REMS requirements.

Prototype Demonstration

The MITRE team then provided a brief overview and recorded demonstration of the proof-of-concept prototype. The prototype was developed to model data transactions and workflows, and is not a fully-developed user interface. MITRE presenters reviewed the timeline of work to date on the prototype, from the initial version in late January 2022, through the latest version, released in late September 2022, the final iteration for the proof-of-concept stage.

The recorded demonstration (which is publicly available) showcased the functions available in the final version of the proof-of-concept prototype. At this stage, the prototype had been built to handle data transactions for the Turalio (pexidartinib), iPLEDGE (isotretinoin) and Transmucosal Immediate-Release Fentanyl (TIRF) REMS programs, though only Turalio and iPLEDGE were demonstrated during this presentation. For the Turalio REMS program, the demonstration walked through the processes for the prescriber, patient, and other providers to asynchronously complete necessary documentation. The completed documentation included the Patient Enrollment Form, Prescriber Enrollment Form, and Prescriber Knowledge Assessment Form. The demonstration then progressed to the process for the pharmacist to receive and verify this documentation before dispensing the medication. The

demonstration for the iPLEDGE REMS program displayed a similar process for synchronous completion of the Patient Enrollment Form.

Following the prototype overview, the MITRE team fielded questions from audience members. Several audience questions pertained to maintenance and updates to the prototype. The MITRE team explained that in practice, the REMS administrators will be responsible for maintaining the data and forms in the system, as well as updating the elements as needed if REMS requirements change. Other audience questions requested additional details on sign-ons and enrollment processes with the prototype. The MITRE team explained that the prototype approach can enable a single sign-on system in which the prescriber only needs to sign into the EHR system, not any additional external portals. They also clarified that the prescriber and patient enrollment processes shown in the demonstration will generally only be necessary the first time a new prescriber or patient participates in a REMS program. Another concern from the audience related to the role of manufacturers and distributors in the prototype's development and implementation, as it was noted that the demonstration and presentation had focused largely on the prescriber, patient, pharmacist and REMS administrator. The MITRE team responded by stating that the stakeholders included in the demonstration was just for ease of illustrating the data transactions. Additional stakeholders, including distributors, wholesalers, and manufacturers are planned to be included in the pilot and implementation processes.

Panel Discussion – Prescriber Perspectives

The first panel discussion of the workshop focused on how the prototype could alleviate the burden for prescribers of REMS drugs and whether there might be any disadvantages to this modernization approach for prescribers. Panelists felt the prototype had the potential to alleviate some prescriber burden related to the iPLEDGE and clozapine REMS programs (the programs with which the panelists were most familiar), and the standardized data elements could provide greater transparency into how well REMS programs function and where there might be opportunities for improvement. They also suggested that greater transparency for the patient to view lab results or the status of other requirements could be an important benefit of this approach.

Panelists also identified some key considerations and challenges related to implementing the prototype approach. Since there is a great deal of heterogeneity across different REMS programs, and even with how the patient journey plays out within individual REMS programs, the prototype would need to account for a wide range of complexities. Panelists suggested testing or piloting the prototype in diverse settings and accounting for different real-world challenges like switching providers or insurers to ensure it can account for these significant variations. They also mentioned that since not all healthcare sites may be equipped to adopt this approach, maintaining manual processes as a backup option would likely be necessary.

Panel Discussion – Pharmacy Perspectives

The next panel discussion shifted focus to the pharmacy setting. For both specialty and retail pharmacy settings, panelists said that the prototype approach could effectively streamline the process of fulfilling REMS requirements and promote patient access. They felt that the more seamless process of exchanging information with prescribers, REMS administrators, and patients enabled by the prototype could significantly reduce REMS-related burden for pharmacists. Pharmacies, they said, often bear a large portion of the administrative burden associated with REMS requirements. Since pharmacists act

as an intermediary between the prescriber, REMS administrator, and patient, they are responsible for verifying information with each party before ultimately dispensing the medication. As mentioned during the Prescriber Perspectives panel, reducing time spent managing administrative burdens means increasing time spent on patient care – and those effects could benefit all patients, not just those taking REMS drugs.

Panelists also emphasized the need for pharmacist training around the new approach as it is implemented. Training would teach pharmacists how to use a new system and ensure that the purpose and importance of REMS requirements is maintained as the process for fulfilling requirements is increasingly streamlined.

Panel Discussion – Health System Perspectives

The third panel discussion covered considerations for applying the prototype in the health system setting. Panelists were broadly optimistic about the prototype's potential to streamline and standardize processes across the health system setting. The health systems represented on the panel had each established internal processes for meeting REMS requirements, including similar prompts for prescribers and pharmacists that signify a drug has REMS requirements. Panelists felt the functions laid out in the prototype demonstration could further increase the efficiency of these processes – particularly through greater standardization and automatically pulling key information from EHRs.

Since health systems often include outpatient, inpatient, specialty, and even mail-order pharmacies, panelists said they observe significant ambiguity in how REMS requirements should be fulfilled across these different care settings. Panelists also suggested a more standardized approach offered by the prototype could clarify REMS requirement implementation and streamline the process of handling REMS requirements when patients receive both inpatient and outpatient care. One panelist also mentioned that provider and prescriber education requirements — often tracked through attestations or other manual processes — could be streamlined as well.

Panelists identified several points to consider for the implementation process in the health system setting. They generally agreed that making the prototype a "one-stop shop", with a single sign-on point, could replace existing processes for integrating REMS requirements and make adoption much more attractive for health systems. They also suggested soliciting end-user feedback, potentially through surveys, to engage the user community and make iterative improvements to the prototype as the approach is piloted. Though panelists were supportive of data collection on REMS programs and patient outcomes through the standardized approach offered by the prototype (supporting a shift toward "learning REMS" systems), they urged caution in complying with applicable privacy laws and ensuring adequate protection for patient information.

Panel Discussion – Implementation Considerations and Next Steps

Building on comments from the previous discussion, the final panel focused on how to encourage stakeholders to pilot the prototype approach and streamline the pathway to effective implementation. The significant complexity of REMS requirements across different drugs, sites of care, and pharmacy types was reiterated as a key challenge that will need to be addressed during implementation. Panelists recommended engaging closely with a variety of key stakeholders throughout the pilot and implementation stages to ensure that the prototype approach works effectively for all involved. They

suggested including disease advocacy groups for conditions often treated with REMS drugs and groups representing the full spectrum of the care team, including nurse practitioners and physician associates, who often take on much of the responsibility for ensuring REMS requirements are fulfilled. Panelists felt that ongoing stakeholder engagement would encourage uptake and also recommended dedicating further resources toward promoting awareness, mentioning targeted outreach to prescribers and pharmacists and potential incentives for adoption.

Finally, panelists stressed the importance of establishing metrics for success and formal efforts to evaluate the efficacy of the prototype during and after implementation. They proposed time spent on prescribing and dispensing REMS drugs as a potential metric for reduction in prescriber and pharmacist burden and time to treatment as a potential metric for improvement in patient outcomes.

Conclusion

Panelists consistently voiced support for the prototype's potential to reduce burden associated with REMS requirements. Prescribers and pharmacists noted significant burdens fulfilling REMS requirements under their current systems, which involve exiting clinical workflows to enter information into separate portals and in some cases manually verifying the necessary information. Streamlining those processes could reduce burdens and expedite medication access for patients. Still, panelists repeatedly acknowledged the challenges that may arise with implementing this new approach, emphasizing the need to ensure that the prototype can handle the complexities of differing REMS programs, patient populations, sites of care, and other variables. They encouraged FDA, MITRE and the broader communities involved with REMS to collaborate closely to shape the development of the prototype and build support for its adoption.

FDA and the Duke-Margolis Center for Health Policy thank the workshop participants and attendees for their insights and feedback related to the integration prototype. This valuable feedback will inform FDA's ongoing work to integrate, innovate, and modernize REMS programs to ensure safe medication use while reducing undue burden. With the transition to the pilot planning stage, FDA and the community participating in the CodeX REMS Integration Use Case continue to welcome feedback from the public and stakeholders through the use case public calls, leadership calls, and other fora. Information on this ongoing effort and further opportunities for community feedback can be found here.

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