REMS Reimagined

Leveraging integration, AI, and patient engagement across a REMS ecosystem improves patient outcomes and safety while decreasing stakeholder burden.

Since the inception of Risk Evaluation and Mitigation Strategies (REMS) to monitor patient safety related to high-risk and novel drugs, life science organizations (LSOs) have been forced to continue adapting outdated technologies in lieu of the option to adopt technologies specifically built for REMS. As a result, systems have become increasingly disconnected, resulting in issues for all involved actors. Alternatively, an integrated platform built around the patient and their safety can benefit REMS solutions through automated processes; real-time, real-world data; and direct reporting of patient outcomes.

This paper is designed to illustrate the ongoing issues facing risk managers administering REMS and what is needed to resolve these issues to create a safe, automated platform for their REMS and for involved patients, prescribers, and pharmacists.

INTRODUCTION

The Food and Drug Administration Amendments (FDAA) Act of 2007 legislated a new program—Risk Evaluation and Mitigation Strategies (REMS)—which mandated that mechanisms be put in place to monitor any drug with serious safety concerns to ensure benefits to patients outweigh the risks. Elements of a REMS vary, but include a medication guide and package insert for patients, as well as a communication plan for healthcare professionals (HCPs). Higher-risk drugs also require Elements to Assure Safe Use (ETASUs) to mitigate known risks. Since this mandate, the FDA has revisited their guidelines multiple times in an attempt to standardize and integrate REMS with existing systems.

> "Ultimately, REMS should be linked to electronic medical records, to health plans and programs, and to adverse event surveillance systems in order to bolster the collection of needed information on drug response and clinical effects of treatment for different patient populations."
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> **(Weschler, 2010)**

As concluded by Jill Weschler in 2010, clear suggestions were outlined a decade ago, yet REMS managers and administrators have struggled to find the necessary pieces and supporting technologies to enable a streamlined, frictionless REMS for all actors.

The challenges that LSOs with REMS face demand a comprehensive and integrated solution. Any viable solution must ensure patient safety, prescriber and pharmacy satisfaction, and compliance to reduce the burden of REMS and risk management. Lastly, to be wholly effective, the new approach must be patient centric.

Since the rollout of the FDA's REMS program, many have felt "as [if it is] something new tacked on at the end." (Weschler, 2010) This sentiment remains the same 14 years later. To manage REMS, traditional systems are being utilized in ways for which they were not designed. The utilization of these legacy systems has resulted in a myriad of issues and complications, the majority of which include lack of integration and lack of streamlined communication, limited real-world data, and burdensome manual processes for administrators and other stakeholders.

INTEGRATION

There is no standardized method of communicating or sharing information between life sciences and healthcare professionals, as each industry operates on its own infrastructure and standards.

- Prescribers, pharmacies, and LSOs use different, disconnected systems for patient information
- These disconnected systems operate on

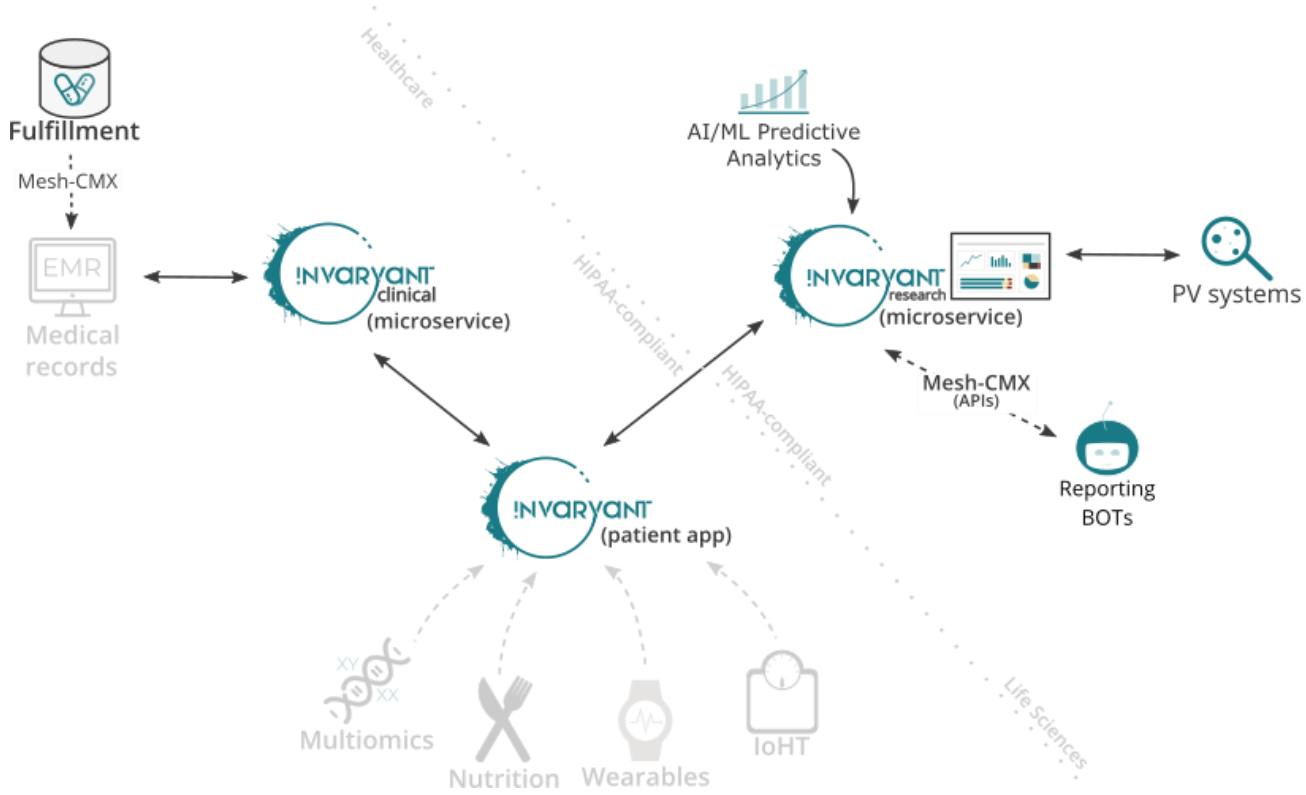
different standards

- Without a shared standard or integration, stakeholder communication and patient safety are compromised
- Patient centricity is key to a robust and viable REMS solution

To view patient information, doctors and pharmacists rely on electronic medical records (EMRs), the standard for which is FHIR (Fast Health Interoperability Resource). Each doctor's office, health system, and pharmacy has their own EMR system, none of which can communicate, except across individual iterations within a system (e.g., different doctors' offices within a single hospital system or individual pharmacies for a single retail company). Similarly, LSO risk managers rely on internal systems that are not created for REMS and that use standards (e.g., E2B(R3)) meant for pharmacovigilance.

Despite REMS being mandated by the FDA over a decade ago, no specific technology platforms exist for REMS. This has forced drug companies to modify their existing pharmacovigilance (PV) systems by developing new programs and acquiring additional tools to adapt to their REMS needs. The problems on each side are exacerbated by incompatible standards when information needs to be shared:

The lack of communication between systems creates a dangerous, expensive, and time-



consuming environment and neglects the most important stakeholder within a REMS program: the patient. Therefore, a standard through which both industries and their involved stakeholders can communicate and share information, without requiring massive integration initiatives and the associated costs, is necessary.

> "The resulting growing number of disparate programs lead to administrative, logistical, and workflow challenges for the health care system. The inconsistency that results from such 'siloed' programs leads to provider confusion, administrative inefficiencies in implementation, workflow inefficiencies, and burdens on the health care system."
>
> **(Lofton, 2009)**

For a REMS solution to be successful, it must integrate with existing systems and with multiple sources (EMRs, PV systems and their call centers, and regulatory agencies), rather than requiring stakeholders to abandon existing infrastructure to manage REMS through a new system. A viable solution must use the standards (E2B(R3) and FHIR) that are already in place, and each stakeholder must be able to easily and efficiently participate and complete required tasks.

REAL-WORLD DATA FOR PATIENT SAFETY

Real-world data is typically retrospective in nature; however, the industry requires data to be dynamic and real-time for effective risk management.

- LSOs have limited access to real-time, real-world data
- Disconnect leads to underreporting of adverse events
- Reactive approaches limit effectiveness and lack the benefits of proactive approaches

The lack of integration between healthcare and LSOs makes the roles of risk administrators and managers more difficult. Because drug companies primarily work through prescribers and pharmacies, critical information about patients is difficult to track, measure, and report. The resulting disconnect and inefficiencies lead to larger problems, such as underreporting of adverse events and serious adverse events (AEs and SAEs).

Some companies have retrospective real-world-data initiatives underway with, for example, data held in an EMR system. There are insights to be gleaned through this approach; however, drug companies have become dependent on retrospective data for a view into the lives of their product users. The real-world data required to provide evidence exists in siloed systems, including healthcare EMRs, apps, portals, and social media.

The reactive approach of retrospective reporting and analytics tools continues to limit the effectiveness of REMS and lacks the benefits of proactive measures. Any modern REMS solution must include access to real-time information to protect patients. The system should automatically alert all stakeholders involved in the REMS when the standards defined within the program are not met (e.g., required lab tests have not been run).

A fully integrated platform allows REMS to effectively utilize real-world data. A comprehensive platform with real-time, real-world data sharing improves patient safety while also reducing timelines and costs.

This comprehensive platform includes the ability to monitor prescription fulfillment and compliance, as well as the ability to track adherence and report adverse events (AEs) and serious adverse events (SAEs). If a patient experiences side effects, the system must allow them to report their symptoms quickly and easily through the use of current technologies. Additionally, for any solution to be fully patient centric and provide true real-

EXISTING PROBLEM	SOLUTION
Retrospective data	Proactive and predictive analytics: real-time, real-world data made available to risk managers to prevent patient-safety errors
Inability to proactively track prescription fulfillment	Real-time connections to patient medical records, which supply insight into fulfillment
Manual AE/SAE forms	BOT-driven and automated AE/SAE forms to increase event reporting
Paper forms and journals to collect patient-reported outcomes (PROs)	Real-time collection of PROs and digital surveys
No prescriber access to full patient medical records	REMS prescribers are provided with a full view into each patient's full medical record
Difficulty meeting ETASU requirements	Ability to trap non-compliance events and monitor the drug ecosystem, including, for example: ■ missing laboratory results ■ PROs ■ drug adherence ■ patient surveys ■ AI signals to identify positive and negative trends

world data, the system must have the ability to survey patients to acquire patient-reported outcomes (PROs) and other vital information directly from the patient. Surveys should be targeted and require minimal effort from patients, in addition to being able to identify risks, request key information from each patient, and disseminate that information from each patient to the appropriate stakeholders (e.g., risk managers).

For patients taking a drug with a REMS, it is vital that all stakeholders have access to the patient's relevant medical information to mitigate risk. Some REMS require specific tests, procedures, or conditions to be in place before the drug may be administered. The ability to easily access a patient's full medical record and/or receive relevant notifications allows enrolled prescribers and pharmacists to ensure the patient always meets defined criteria before the drug is administered or dispensed.

MANUAL VS. AUTOMATED PROCESSES

Manual, semi-automated, and ad hoc processes make accountability within a REMS difficult and "even undermine the actual purpose of a REMS (i.e., to protect patient safety), when roles and responsibilities are not clearly defined in communications about a REMS." (Food and Drug Administration, 2014)

- Patient and prescriber certification and education are managed manually
- Automated processes will aid prescriber participation
- Limited and slow exchange of information complicates ETASUs

The lack of REMS-specific platforms or standards means many processes that make up a REMS (e.g., enrollment, certification, education, safe-use management) remain mostly manual. As a result, stakeholders, such as patients and prescribers, are forced to communicate through inconvenient or unfamiliar channels (e.g., faxes and webforms), which leads to a breakdown of communication and a disconnect between manufacturers and their users.

> "Monitoring programs often require double and triple documentation, with redundant information added to medical charts, pharmacy records and the REMS database. Even in cases where an electronic medical record (EMR) is used, the information must still be entered separately into the REMS database. If the patient is on more than one medication with a REMS requirement, the amount of documentation increases exponentially."
>
> **(Lofton, 2009)**

Two key elements of a REMS are patient education and provider participation. Currently, patient education falls to prescribers, who are focused on diagnostics and treatment. Prescribers have limited time with their patients, and the educational demands of REMS reduce valuable time for patient interaction. As prescribers are not trained educators, risks associated with the REMS drug and the patient's responsibilities may not be properly conveyed. Additional components that amplify risk to the patient include the following:

- Higher-risk drugs with additional safety requirements, such as ETASUs
- A lack of diversity (including cultural and language) in available education materials that may cause patients to not fully understand the risk implications

In addition, the lack of integration across stakeholder systems limits availability of information and results in manual processes. This is especially apparent in the minimal direct exchange of data between pharmacies, labs, and prescribers in relation to ETASU requirements (e.g., notification of a specific lab result required for dispensing). Stakeholder burden would be alleviated through automation of these processes.

While integration with current systems is necessary, REMS programs must also begin to utilize current technologies (e.g., bots, computer-based training, etc.). Automation of mundane tasks is necessary to maintain accuracy and mitigate human error.

Education and certification should be streamlined as a part of the enrollment

EXISTING PROBLEM	SOLUTION
Manual education and certification for patients, prescribers, and pharmacists	End-to-end automation of enrollment, training, and certification, with dynamic notifications of program updates
Inability to successfully communicate contraindications and new AEs efficiently	Automated notification of contraindications combined with re-certification of prescribers via computer-based trainings (where appropriate)
Outdated modes of communication between stakeholders (e.g., call centers, fax machines, etc.)	Integration of chat bots, platform messaging, and PROs into the REMS platform, which decreases administrative burden
Manual prescriber reporting	Automatically generated reports and surveys, which minimize prescriber burden
Manual capture of AEs/SAEs in pharmacovigilance (PV) systems	Automatic notifications (including patient-reported AEs) sent to the drug-safety team via an E2B(R3) interface that feeds directly into the PV system

process, whereby newly enrolled patients, prescribers, and pharmacists can immediately participate in consistent, unbiased computer-based training and certification. This consolidation of steps will reduce timelines, minimize the demands on program administrators, and ensure program education is presented in a consumable form for all.

Traditional coordination tools, such as call centers and fax machines, must be upgraded to modern communication methods, such as PROs, chat bots, and platform messaging. This update to communication facilitates improved patient engagement and adherence, more efficient prescriber engagement, improved outcome reporting (e.g., capturing adverse events), and decreased administrative burden.

Unlike manually updated website bulletins and check-lists, bot-guided communications integrated into the provider workflow increase productivity and are less burdensome. Automated reports and surveys minimize the need for prescriber reporting and portal access and provide patients with a familiar platform to interact with the manufacturer. These advances facilitate proactive risk mitigation through the early identification of systemic failures.

WHAT'S NEXT?

Once a comprehensive REMS-specific platform is in place with full integration; real-time, real-world data; and automated processes for risk managers, patients, prescribers, and pharmacists, the way is paved for an advanced REMS platform. The following platform enhancements will optimize REMS efficiencies and overall patient safety:

Tri-level registry	Automatically generated and updated database of enrolled patients, prescribers, and pharmacies
Safety triggers and tripwires	Signals based on specific program criteria
ETASU monitoring	Bot-monitored checkpoints based on ETASU criteria
Script fulfillment & monitoring	Prescription tracking, from prescribing to dispensing
Bot-driven processes	Bot-driven processes that capture contraindicative conditions and treatments by constantly monitoring each patient's medical record and comparing additions to existing and active conditions, treatments, and medications Bot-driven custom reporting, stakeholder-compliance monitoring, and communication escalations to risk managers

Analytics	Custom range of data analysis, granular- to high-level, retrospective and predictive Trend detection Predictive analytics that go beyond retrospective event monitoring by detecting trends in the reported data and alerting risk managers when an adverse trend is signaled, which could, for example, identify technical product complaints, as well as adverse events, in population cohorts
Multiple-program monitoring	The ability to manage multiple drugs in a single REMS environment, with drug-specific configurations to meet the individual elements of each REMS program. Manage a shared REMS program (e.g., opioids). A dashboard that allows users to easily monitor the state of one or multiple REMS programs, including, but not limited to: ■ patient drug adherence ■ adverse events (AEs) ■ patient demographics ■ enrollment statistics

CONCLUSION

REMS have been plagued by issues ranging from lack of integration to manual processes since day one. These issues are attributed to the lack of a purpose-built REMS platform. This platform is a streamlined, integrated system that provides risk managers with a complete view into the lives of the patients served by their products. This system works with and leverages existing standards and platforms to positively impact workflows—and coexists with existing infrastructure and applications. The direct information made possible through this integration enables real-time, real-world data flow, including surveys/PROs and adverse-event reporting. Complete, cross-platform integration allows for program flexibility, increased prescriber and pharmacist participation, and greater communication between risk managers, patients, prescribers, and pharmacies.

Stakeholders are benefitted in the following ways:

Patients

- All REMS materials and health data are easily accessible

- Direct communication and event reporting
- Unbiased education in the patient's vernacular
- Efficient process that increases access to a drug
- Integrated systems providing real-time data that promote patient safety

Prescribers

- Reduced program education burden
- Single platform to manage patients on high-risk drugs
- Direct communication and event reporting
- Real-time notifications of patient adherence
- Integrated systems providing real-time data that promote patient safety

Pharmacists

- Reduced program education burden
- Clear and concise patient information
- Direct communication
- Real-time notifications of patient eligibility
- Integrated systems providing real-time data that promote patient safety

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Invaryant is a Georgia-based healthcare-technology company that is enabling safer healthcare through integrated, real-world-data technology. The unique platform connects and supports patients, healthcare providers, and clinical researchers. With AI and patent-pending technology, Invaryant will lead healthcare and life science into a new era of patient safety, access, and innovation. Founded in 2015 as a result of its founder losing a family member to a medical error, Invaryant is comprised of a passionate team that is reimagining healthcare to improve the lives of all people.

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