WHITE PAPER: US FDA REMS Standardization; a prerequisite to improving healthcare provider application of patient-directed tools and medication risk reduction strategies for reducing patient harm

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Risk evaluation mitigation strategies otherwise referred to as REMS originated out of the Food and Drug Administration Amendments Act of 2007, which further granted the U.S. FDA authority to require REMS programs as a means to ensure that the benefits of a drug or biological product outweigh its risks. The purpose of REMS programs are to draw attention to, raise awareness of, command respect for, and ensure appropriate use of certain medications that possess a higher potential for causing harm compared to other medications. REMS Logic serves to promote this initiative as well as other national and global efforts aimed at decreasing preventable harm from medications.

REMS Logic Goals are to develop technologies that support global medication risk reduction, to improve prescriber compliance with U.S. FDA REMS drug program requirements and to empower patients with access to information that improves knowledge, experience, satisfaction and health outcome.

REMS Logic is a company deeply rooted in medication safety and risk reduction. The company’s objective is to continually evaluate medication use practices by all clinical disciplines to improve healthcare quality and patient safety worldwide. REMS Logic is a healthcare information technology platform offering solutions in the following areas.
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<thead>
<tr>
<th>Problem</th>
<th>Solution</th>
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<td>U.S. Health and Human Services, Office of Inspector General audit published February 2013 found that U.S. compliance with REMS is only 14%</td>
<td>REMS Logic™ provides a simple, mobile solution to improve national compliance with FDA REMS drug law</td>
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<td>Lack of REMS standardization and large number of REMS requirements are barriers to prescriber compliance and prevent healthcare organizations from implementing strong REMS management programs</td>
<td>REMS Logic™ standardizes REMS requirements and offers a simple, interactive tool for tracking medication risk reduction training, compliance and certification</td>
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<td>Healthcare providers lack adequate training and experience in risk reduction management and REMS education is minimal in medical schools and academia</td>
<td>REMS Logic™ is a federal drug law and medication risk avoidance education tool that can be applied in colleges, universities and healthcare settings. It provides risk management training, continuing education and professional development.</td>
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<td>Pharmacy benefit management (PBM) systems lack comprehensive processes for verifying prescriber compliance with REMS requirements during claim adjudication and prior to issuing prescriptions to patients</td>
<td>REMS Logic™ system establishes a reference database for PBMs and insurance companies to verify prescriber compliance, ensure patient safety, and decrease liability</td>
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<td>Since FDA REMS program inception, there remains a need for conclusive evidence and research data to determine the effectiveness of risk mitigation programs in reducing risk and preventing patient harm</td>
<td>REMS Logic™ data collection and industry utilization research will yield data that can be evaluated over time to establish REMS program effectiveness and guide decisions for future program improvement</td>
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<td>Substandard patient satisfaction rates and ineffective patient-provider communication strategies impede healthcare successes and outcomes</td>
<td>REMS Logic™ provides a mobile tool that encourages communication with patients to foster patient–provider relationships and improve patient satisfaction</td>
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REMS Logic Users and Industry Stakeholders

- Prescribers (MD, DO, CNP, PA, Resident) – compliance and certification management
- Hospitals and Healthcare systems – organizational oversight; audit and liability protection
- Pharmacies (Inpatient, Long-term care, Mail Order, Retail, Specialty) – compliance information & verification
- Pharmacy benefit managers (PBM’s) – prescriber compliance validation
- Drug companies – REMS program management
- Patients - education and communication
- Universities/Colleges and Students – federal compliance teaching tool
- Insurance companies – healthcare industry compliance data
- Federal and governmental agencies – medication risk reduction program outcome data

Background

The science of pharmaceutical development has become highly sophisticated, innovative and broad in capability to treat. With such advancements in medicine come higher degrees of risk and potential for harm. Today, protecting patients requires extreme diligence compared to just 10 to 15 years ago. Anticoagulant drugs accounted for 1,734 reports to the FDA in the second quarter of 2012, including 233 patient deaths (1). Coroner’s records across Southern California identified 3,733 fatal overdoses from 2006 through 2011 and determined that nearly half stemmed from drugs prescribed for the deceased by his or her physician (2).

Additionally, there is an alarming trend within the United States due to medication misuse, abuse and non-compliance. In 2011 the White House announced a public health threat based upon information from the U.S. Centers for Disease Control (CDC) declaring preventable prescription drug harm and death a national epidemic (3). The White House launched the U.S. Prescription Drug Abuse Prevention Plan of 2011 and released a commitment to action titled “Epidemic. Responding to America’s Prescription Drug Abuse Crisis”. (4) As part of the national campaign, the FDA was directed to strengthen Risk Evaluation and Mitigation Strategies (REMS) drug programs.

The first REMS program was implemented in 2008 and the number of REMS drugs grew to approximately 100 drugs by 2011. From 2011 through 2013 many drugs from the less restrictive Non-ETASU category were released; yet the total number of REMS drugs remained the same because several novel drugs were brought to market and assigned to the more stringent ETASU REMS category. The trend over the past 5 years has demonstrated growth and expansion of FDA REMS. There has been a significant increase in the number of ETASU REMS drugs and numerous program revisions that further broaden requirements for prescribers, hospitals, healthcare providers and patients.

In the span of history, REMS programs remain in their infancy and are considered a new concept. Conversely, the practice of medicine has existed for thousands of years. Therefore, efforts toward integration of these regulatory changes have been difficult. Lack of awareness and
slow acceptance has caused REMS compliance to fall below government expectations. Like many federal regulations, adoption and full enforcement will take time.

U.S. Health and Human Services (HHS) Office of the Inspector General (OIG) audited the FDA’s REMS programs and released their findings in February 2013. (FDA Lacks Comprehensive Data To Determine Whether Risk Evaluation and Mitigation Strategies Improve Drug Safety) The audit found only seven of 49 areas to have met compliance goals and stated that the “FDA most often determined that REMS were not meeting their goals because of deficiencies in patient and prescriber awareness of drug risks”. This translates to prescribers issuing prescriptions and authorizing patient use of REMS drugs while unknowingly being out-of-compliance with federal requirements. The HHS OIG audit was the first of its kind to shed light on the current issues surrounding REMS programs. It provides transparency and a heightened awareness of REMS non-compliance.

Each day patients are exposed to risk due to non-compliance with FDA standards intended to mitigate preventable adverse drug events and medication errors. The FDA classifies the highest risk medications as REMS based upon data from harm reports and medication profiles that demonstrate a narrow harm-to-benefit ratio. In its current state, REMS drug prescriptions are being issued without proper adherence to REMS program requirements. This impacts risk and liability to the organization and drives up the cost of care. Patients, healthcare employers and insurers are unaware of prescriber compliance status.

Prevalence of Adverse Drug Events and Medication Errors

In January 2014, Global Record Systems (GRS) announced their research collaborative with the FDA to combine and gather data to create the Electronic Health Data Initiative (EHDI) for improved reporting of safety and clinical outcomes. GRS stated current REMS are predicated on the passive reporting of adverse drug events and “given this current approach, it is estimated that only 10% of actual important adverse events are reported to the FDA. The GRS’ EHDI proposes to address these issues by interacting directly with patients and, with patient consent, leveraging the health care information stored in Electronic Medical Records (EMRs)... It is projected that the EHDI will collect approximately 100 million patient records over the next 3-4 years thus creating the largest database of its kind in the world.”

REMS Logic understands that adverse drug events are severely underreported and recognizes the significance of the GRS-FDA data collection project. It can be anticipated that the GRS research will be profoundly revealing and necessitate mitigation plan deployments. REMS Logic offers healthcare organizations a proactive means to impact preventable medication errors and patient harm prior to release of GRS FDA data findings.
Cost of Risk and Liability

The Aon/ASHRM Hospital and Physician Professional Liability Benchmark report “estimates that in 2014 medical malpractice claims will represent $0.60 per every $100 of hospital revenue or an average of $135 per hospital admission. Using simple, accessible statistics such as revenue and admissions translates benchmark statistics into tangible terms with direct meaning for health care financial managers.”

The cost savings are achieved by promoting patient safety, uniformity of risk management and jointly defending claims, when they happen. However, Erik Johnson, health care practice leader for Aon’s Actuarial and Analytics Practice warns, “some costs that would have traditionally been covered by the physician are now shifted to the hospital.” Ron Calhoun, managing director of Aon Risk Solutions Health Care practice added, “Risk management involvement and investment in patient safety have translated into improved medical malpractice results.” Data from Aon’s self-assessment tool, the Risk Maturity Index, indicates that hospitals are advanced in their approach to risk but reveal the need to integrate additional risk management processes throughout their organizations.

About FDA REMS Requirements

Risk evaluation mitigation strategies provide a new process to counteract the number of deleterious events caused by prescription medications. Prior to REMS, physicians have had the unconditional authority to prescribe the majority of the 10,000+ prescription drugs regardless of the varying levels of risk. FDA REMS regulations have been instituted to raise awareness of the important risk considerations in order to foster appropriate use of high-risk drugs.

REMS requirements for a certain drug may necessitate certification or compliance prerequisites are met prior to prescribing or dispensing a medication. There may be as many as seven independent REMS components for a given drug. REMS laws are complex, cumbersome and lack standardization. Healthcare providers do not have adequate time to perform the REMS research needed to stay up-to-date with program changes. Traditional processes require a physician to follow inconsistent, confusing and time-consuming steps. Healthcare organizations lack oversight capability to allow a better understanding of how to support prescriber compliance. In the event of patient harm, both the prescriber and the organization are exposed to liability.

Recognition of the Need to Standardize REMS

From the time of REMS inception in 2008, those who have taken strides to comply have exposed barriers and program limitations. Well over 100 cases have been submitted from large industry stakeholders, national associations and healthcare organizations advocating for REMS improvement and standardization. In 2009 the Journal of the American Pharmacists Association published a white paper outlining recommended strategies for standardizing REMS. In 2011 the American Pharmacists Association (APhA) published a proposal compiled from 34 stakeholders in support of an improved risk evaluation and mitigation strategies (REMS) system.
for maximizing effective and safe patient medication use while minimizing burden on the health care delivery system. (11)

The U.S. FDA has held several public meetings to collect stakeholder feedback on how to better integrate REMS into the evolving health care system and to explore strategies to standardize REMS and reduce the burden of implementing REMS on practitioners, patients, and others in various health care settings. (12) In July 2013, forty-two industry stakeholders submitted comments and testimonies to the FDA Docket in response to the U.S. FDA meeting “Standardizing and Evaluating Risk Evaluation and Mitigation Strategies”. (13) The sessions were well attended and those who presented offered rationale advocating for the FDA to implement additional measures to improve REMS programs through greater standardization. Companies and associations who submitted comment included, but were not limited to the following:

1. Biotechnology Industry Organization (BIO)
2. Pharmaceutical Research and Manufacturers of America (PhRMA)
3. American Society of Clinical Oncology
4. International Society for Pharmacoepidemiology (ISPE)
5. CVS Caremark
6. JoAnn Stubbings - REMS and the ACO
7. National Council for Prescription Drug Programs (NCPDP)
8. American Pharmaceutical Association
9. Celgene Corporation
10. United Biosource Corporation
11. Biocentric Inc
12. UBC: An Express Scripts Company
13. United Biosource Corporation
14. Society for Women's Health Research (SWHR)
15. Biogen Idec Inc.
16. Pharmaceutical Research and Manufacturers of America (PhRMA)
17. AbbVie
18. Frommer Lawrence & Haug LLP
19. Pfizer Inc
20. American Association of Nurse Anesthetists
21. ParagonRx
22. Biotechnology Industry Organization (BIO)
23. Microbiologics
24. National Community Pharmacists Association
25. McKesson Corporation
27. American Academy of Family Physicians (AAFP)
28. Kaiser Permanente
29. United BioSource Corp.
30. Amgen Inc
31. Academy of Managed Care Pharmacy (AMCP)
32. American Society of Health System Pharmacists (ASHP)
Why Hospital and Industry Attempts to Foster REMS Compliance are Unsuccessful

There are two main components to REMS programs that often go unrecognized, but that have a significant impact on healthcare provider efficiency and workflow. Healthcare organizations commonly attempt to support their prescribers and pharmacists with FDA REMS compliance by attempting to integrate all REMS requirement information into EHRs, prescribing and pharmacy systems. This is carried out with the rationale that by making REMS drug information available at the point-of-care or while processing prescriptions, processes will be more efficient. Doing so however has proven less than optimal and such attempts have contributed to barriers to REMS compliance, workflow and efficiency; all of which create "push-back" from clinicians and overall frustration with REMS.

Although, the push is to maintain all drug-related warnings, alerts, and information in one system, it would be impractical to integrate all DEA and medical compliance information, drug law books and comprehensive physician desk references into an EHR at the point of prescribing or drug dispensing. Integrating comprehensive FDA REMS drug law compliance requirements and professional development education at the point of order entry and clinicians may interpret these notifications as counter productive, dissatisfactory and a contributor to alert fatigue.

How REMS Logic has Standardized REMS

REMS Programs are federal laws that are complex, multi-faceted and difficult to navigate. To support healthcare organizations in efforts to successfully implement a process for compliance, REMS Logic has separated REMS program requirements into two main components:

1) Education/training and professional development

2) Patient/bedside care and ongoing compliance

Application of the two REMS Logic components provides organizations with a streamline process for prescriber and pharmacist REMS compliance in a manner that does not inhibit or disrupt workflow. REMS Logic further allows healthcare providers to easily understand what REMS actions apply during direct patient care encounters.

REMS Logic understands healthcare provider workflow and has standardized REMS in a manner that allows prescribers and pharmacists to quickly identify and understand what baseline compliance prerequisites (pre-prescribing & pre-dispensing requirements) exist for a given drug. The tool manages education, training, certification and enrollment while being non-disruptive to workflow and patient care. The REMS requirements that remain after the prerequisite actions are fulfilled are those that pertain to direct patient care and ongoing FDA REMS compliance. REMS Logic has organized the direct patient care information separately so that it is quickly and easily accessible from any mobile device for incorporation into patient care as appropriate.
The REMS Logic Solution

Healthcare reform breeds' uncertainty and hospitals are tightening budgets and expected to do more with less. Focus centers on avoiding risk and cost not directly tied to caring for patients. REMS Logic helps to decrease the number of adverse drug events, improve drug management outcomes, avoid patient harm intervention expense and lessens liability related to federal drug law non-compliance and patient harm litigation. Compliance success can be included as part of a risk mitigation program to help reduce insurance cost. Hospitals are able to demonstrate risk reduction over time to insurers and gain access to data to rationalize decreases in liability rates.

REMS Logic makes non-compliance a non-issue and provides healthcare providers with a practical tool for application within the current workflow environments. REMS Logic is sensitive to patient care, efficient and non-disruptive. It offers an interactive, mobile guide for prescriber compliance that augments workflow at the bedside. The user-interface is simple to use. REMS Logic consolidates all REMS drug requirements, compliance prerequisites and certification information into one single source to eliminate confusion and prescriber burden.

Additional Benefits of Using REMS Logic

- Promotes patient-provider relationships and patient satisfaction
- Expanded communication strategies
- Workflow efficiency
- Simplified communication plans to aid care delivery
- Organization risk reduction measure
- Impact morbidity and mortality statistics
- Decrease medication adverse events
- Single source access to FDA approved risk reduction education
- Compliance tracking and facility oversight
- Audit and liability protection
- Keeps healthcare staff up-to-date with the ever-changing REMS information
- Limits risk and patient harm
- Physician performance indicators; comparison of compliant and non-compliant prescribers
- Supports public health initiative to decrease medication abuse and misuse

REMS Logic helps to cut cost, reduce risk, improve quality and patient outcome at the same time!
Medication Risk Reduction; A Global Initiative

“The work of protecting the health and safety of the American people cannot be done in isolation,” says Janet Woodcock, Director, M.D., director of the FDA’s Center for Drug Evaluation and Research. “It is part of a larger collaborative global effort between the FDA and its international regulatory partners to ensure the health and safety of all our citizens.”

Pharmacovigilance is a shared responsibility that requires interaction among global regulatory agencies. The U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have announced an international collaboration toward this end. Canadian and Japanese regulatory authorities will also participate as observers.

“In an increasingly globalized pharmaceutical market, collaboration between medicines’ regulators is essential,” explains Guido Rasi, the EMA’s Executive Director. “Medicines’ regulators are inter-dependent: any action taken in one territory has repercussions on the rest of the world. International cooperation is a key area of work for the agency.” REMS Logic employs a global economy perspective and recognizes that medication risk reduction strategies have relevance regardless of location.

REMS Logic supports efforts of medicines’ regulators to harmonize medication safety initiatives and encourages collaborative efforts in order to ensure the safety and quality of medication use throughout the world.
References

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3. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6101a3.htm