Standardizing and Evaluating REMS: Review of Draft Report Followed by Panel Discussion with FDA Participants

will begin at 12:01 pm ET…
Standardizing and Evaluating REMS: Review of Draft Report Followed by Panel Discussion with FDA Participants

October 8, 2014
Today’s Session

Standardizing and Evaluating REMS: Review of Draft Report Followed by Panel Discussion with FDA Participants

Speakers:

– **Jeff Fetterman**, President, ParagonRx
– **Panel Participants**, FDA
  - Adam Kroetsch
  - Cynthia LaCivita
  - Gary Slatko
  - Terry Toigo
Q&A

Submitting Questions:

» Type question in the Q&A box

» All submitted questions are only displayed to the Host and ParagonRx speaker

» Answers to your questions will be addressed verbally during Q&A

Submit questions here
Standardizing and Evaluating REMS: Review of Draft Report Followed by Panel Discussion with FDA Participants

October 8, 2014
Standardizing and Evaluating REMS Introduction

- FDA announced on Sept 23, 2014
  - “the availability of a draft report entitled
    “Standardizing and Evaluating Risk Evaluation and Mitigation Strategies (REMS). This report describes the Agency’s findings concerning strategies to standardize risk evaluation and mitigation strategies (REMS), where appropriate, with the goal of reducing the burden of implementing REMS on practitioners, patients, and others in various health care settings.”

- FDA is requesting comments to the draft report
  - by November 24, 2014
  - Docket No. FDA–2013–N–0502

Report Context: PDUFA V Reauthorization
Performance Goal XI(A)

By the end of FY 2013, FDA will:

- Develop and issue guidance on criteria for requiring a REMS
- Hold one or more public meetings to obtain stakeholder input on standardizing REMS to reduce the burden on the healthcare system
- Initiate one or more public workshops on methodologies for assessing REMS

By the first quarter of FY 2014, FDA will:

- Issue a report of its findings (related to standardization) and identify at least one priority project in each of the following areas including a workplan for project completion:
  - Pharmacy systems
  - Prescriber education
  - Providing benefit/risk information to patients
  - Practice settings

By the end of FY 2014, FDA will:

- Issue guidance on methodologies for assessing REMS

PDUFA = Prescription Drug User Fee Act

Focus of today’s webinar
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Overview - Background

- Mid-2000s, Risk Minimization Action Plans (RiskMAPs)
  - Intended to support safe use of products with certain serious risks
  - Guidance published addressing product safety concerns

- 2007, FDAAA authorized FDA to require REMS
  - RiskMAP principles informed the development and implementation of REMS
Overview - Background

REMS

• Must have a timetable for submission of assessments

• May include a communication plan, Medication Guide, patient package insert, and Elements to Assure Safe Use (ETASU)

• Once approved, the REMS document and appended materials serve as the basis for monitoring and enforcement

• As of date of publication, 72 REMS in place

• Sponsors must periodically assess REMS to determine if REMS is effectively meeting goals and if goals should be modified
Total REMS
2008 – September 23, 2014

Cumulative Individual REMS = 211
Single Shared System REMS = + 6
Released REMS = (145)
TOTAL Active REMS = 72

Overview – REMS Integration Initiative

Oversee the activities of three work groups with specific deliverables that will fulfill commitments FDA made under PDUFA V

- **The Policy Work Group**
  - Developing draft guidance to determine whether a REMS is necessary to ensure benefits of drug outweigh risks

- **The Design and Standardization Work Group**
  - Leads efforts to
    - identify best practices to incorporate into future REMS design,
    - standardize REMS tools, and
    - integrate REMS into the health care delivery system

- **The Evaluation Work Group**
  - Lead effort to develop an evidence-based approach to assessing the effectiveness and burden of REMS and developing draft guidance for assessing the effectiveness of REMS
## Stakeholder Outreach Activities

<table>
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<tr>
<th>Date</th>
<th>Outreach Activity</th>
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<tbody>
<tr>
<td>July 2010</td>
<td>FDA public meeting on issues associated with the development and implementation of REMS</td>
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<tr>
<td>June 2012</td>
<td>FDA public workshop to discuss survey methodologies and instruments used to evaluate patients’ and health care providers’ knowledge</td>
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<td>March 8, 2013</td>
<td>PDUFA Stakeholders meeting</td>
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<tr>
<td>April 2013</td>
<td>Roundtable discussion at the American Pharmacist Association Annual Meeting and a Global Alliance of Drug Information Specialist webinar</td>
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<tr>
<td>May 16, 2013</td>
<td>Update and discussion at Drug Safety Oversight Board Meeting</td>
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<tr>
<td>May 23, 2013</td>
<td>“Trends Emerging in Risk Management” seminar with Lehigh University’s Department of Industrial Systems Engineering</td>
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<tr>
<td>July 25-26, 2013</td>
<td>FDA-hosted 2-day meeting on Standardizing and Evaluating REMS</td>
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**FDA Public Meeting**  
**Standardizing and Evaluating REMS**

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<thead>
<tr>
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<th>Minimize Variation</th>
<th>Improve Quality</th>
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<tbody>
<tr>
<td>REMS Design</td>
<td>REMS that address similar risks with similar stakeholders / settings use similar tools</td>
<td>Rigorous and evidence-based approaches are used to set REMS goals and requirements</td>
</tr>
<tr>
<td>REMS Tools</td>
<td>REMS use similar tools drawn from a standardized REMS “toolkit”</td>
<td>REMS tools are informed by the latest science, stakeholder feedback, and established “best practices”</td>
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</table>

*FDA described tradeoffs in the standardization of REMS and tools*

Brookings Institute Expert Workshop
Strengthening REMS through Systematic Analysis, Standardized Design, and Evidence-Based Assessment

September 25, 2013

Agenda
• Welcome, Introduction, and Expert Workshop Objectives
  Mark McClellan, Health Care Innovation and Value Initiative
  Gregory Daniel, Engelberg Center for Health Care Reform
• Broad Goals for Standardizing REMS Design, Tools, and Assessments
• Systematic Approaches for Standardizing REMS Design
• Practical Considerations for Applying Systematic Approaches to the Development of Standardized REMS Tools
• Potential Mechanisms for Standardizing the Assessment of REMS
• Closing Remarks and Next Steps

Further pursuit of standardized methods for REMS design and assessment

Stakeholder Feedback: Opinions and Recommendations

- Health care stakeholders in various settings have successfully implemented REMS
  - Created systems to integrate REMS into their practice setting
  - Became more adept with REMS requirements for frequently prescribed drugs
- Stakeholders are not uniformly impacted by REMS requirements
  - Pharmacists
    - Need to understand who is accountable for each role or activity under a REMS
    - Have administrative burden to ensure appropriate REMS forms are completed
  - Some physicians said a REMS program may deter them from prescribing a drug that has a REMS
Stakeholder Feedback: Opinions and Recommendations

- Communication of REMS requirements should be improved
  - FDA communications of REMS are unclear, inadequate, inconsistent (most frequent response from stakeholders)
  - FDA should continue to provide general education to stakeholders about REMS programs and the reasons REMS exist (e.g., CE, “REMS 101”)
  - FDA should more clearly outline reasons why a product has a REMS
  - Professional medical associations and societies should be invited to communicate with their members regarding REMS
  - Patients perceive REMS as an extra, complicated step
  - Health care providers should be encouraged to help their patients understand REMS
Stakeholder Feedback: Opinions and Recommendations

- There should be some flexibility to implement a REMS program based on the nature and variety of health care settings
  - Wide variability exists among health care settings, particularly federal
  - Greater flexibility for health care setting enrollment and drug procurement

- REMS are vital tools that will be increasingly necessary, and content delivery must be streamlined without compromising the content itself
  - FDA should provide communications that lead to positive clinical outcomes
    - More comprehensive, evidence-based, and organized
Stakeholder Feedback: Opinions and Recommendations

- FDA should standardize REMS across platforms, media, and outreach technologies and work to fully integrate them into health care systems – which will increase access by both providers and patients and facilitate improved assessment to further inform standardization
  - Leverage existing technology systems to better integrate REMS into standard medical practice and ongoing health care delivery

- FDA should adopt and use a more standardized, systematic approach to REMS design, including human factors evaluation methods like Failure Mode and Effects Analysis (FMEA)
  - Utilize a framework for identifying and prioritizing drug-related risks
  - Characterize the process of medication use in “real world” settings and identify ways that care delivery and medication administration may fail
Stakeholder Feedback: Opinions and Recommendations

- FDA can improve REMS assessments with a variety of tools and techniques
  - Leverage data sources to conduct assessments
  - Assess programs earlier and more frequently
  - Apply information gleaned from these assessments to modify REMS
  - Consider pilot programs for REMS before full implementation to create a baseline

- FDA should structure and standardize REMS information
  - Suggest use of Structured Product Labeling (SPL)
Priority Standardization Projects

As part of the PDUFA V commitments, FDA agreed to at least one priority project in each of the following areas:

- Providing benefit/risk information to patients
- Prescriber education
- Pharmacy systems
- Practice settings
## Project 1: Patient Benefit/Risk Information Under REMS

### Providing Patient Benefit/Risk Information by Improving Tools for Prescriber-to-Patient Counseling under REMS

<table>
<thead>
<tr>
<th>Problem Statement</th>
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<tbody>
<tr>
<td>• Product labeling is FDA’s primary communication of benefit-risk information</td>
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<tr>
<td>• Patients want information and understanding about a product’s serious risks</td>
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<tr>
<td>• Patient-directed information should be conveyed via HCP – Pt counseling</td>
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<tr>
<td>• HCPs need to determine benefits and risks of each individual patient</td>
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<table>
<thead>
<tr>
<th>Project Overview and Approach</th>
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<tr>
<td>• Conduct research into existing REMS patient counseling tools</td>
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<tr>
<td>• Seek feedback</td>
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<tr>
<td>• Report findings and recommended counseling and tool attributes</td>
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<tr>
<td>• Develop a standardized counseling tool template</td>
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# Project 1: Patient Benefit/Risk Information Under REMS

*Providing Patient Benefit/Risk Information by Improving Tools for Prescriber-to-Patient Counseling under REMS*

## Project Goals and Deliverables

**Goals to achieve:**
- Support standardization and adoption of effective HCP – Pt counseling
- Enhance patient involvement, knowledge, and understanding
- Provide a basis for demonstrating the impact of effective counseling

**Deliverable:**
- A report of findings, including a summary of existing tools, feedback from stakeholders, and improvements for REMS patient counseling tools

## Project Scope

**Defining attributes of tools that enable implementation of standardized counseling instructions by HCPs to patients**

**Limitations include:**
- Unique drug-specific instructions for individual patients cannot be scripted
- Determining effectiveness of methods/tools without quantitative instruments
- Starting with existing tools and initiatives and consult with selected experts, rather than performing a comprehensive *de novo* assessment
- Patients vary in their ability to receive/understand/recall/act on HCP instructions
## Project 2: Health Care Provider Education Under REMS

### REMS and Continuing Education (CE) for Health Care Providers

<table>
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<tr>
<th>Problem Statement</th>
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<tr>
<td>• Variable effectiveness of communication plans (CP) and REMS education</td>
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<td>• Low participation rates and limited reach</td>
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<tr>
<td>• REMS-based CE training modules may improve participation and knowledge</td>
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<tr>
<td>• HCPs and drug sponsors report REMS training via CE courses is attractive</td>
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<tr>
<td>• Feasibility (time, resources, accreditation, channels) must be considered</td>
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<thead>
<tr>
<th>Project Overview and Approach</th>
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<tbody>
<tr>
<td>• Assess the feasibility of CE in REMS programs</td>
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<tr>
<td>• Define priorities, objectives, approaches, barriers, and whether barriers can be overcome for REMS CE programs</td>
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<tr>
<td>• Eliminate approaches whose barriers cannot be mitigated or overcome</td>
<td></td>
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<tr>
<td>• Engage a range of stakeholders</td>
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<tr>
<td>• Publish findings</td>
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Project 2: Health Care Provider Education Under REMS

REMS and Continuing Education (CE) for Health Care Providers

**Project Goals and Deliverables**

- **Goal:**
  - Determine feasibility of REMS-related accredited CE training
- **Deliverable:**
  - Issue report for comment

**Project Scope**

Evaluate feasibility of including REMS-related CE:
1. Phase 1: Define objectives for REMS-related CE
2. Phase 2: Identify optimum approaches and address barriers to implementation
3. Phase 3: Develop models for REMS-related CE
Project 3: Pharmacy Systems Under REMS

**Standardizing REMS Information for Inclusion into Pharmacy Systems Using Structured Product Labeling (SPL) under REMS**

<table>
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<tr>
<td>• REMS materials, tools, strategies, and requirements are inconsistent</td>
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<tr>
<td>• Materials and requirements are difficult to locate</td>
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<tr>
<td>• Difficult to integrate REMS materials and procedures into existing healthcare systems and process</td>
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<tr>
<th>Project Overview and Approach</th>
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<tr>
<td>• Work with standards development organizations (SDOs) to identify how to incorporate REMS information into SPL, which is potentially well-suited:</td>
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<tr>
<td>• Information easily shared and readily incorporated into health IT</td>
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<td>• Industry and FDA are both familiar with SPL</td>
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<tr>
<td>• Conduct gap analysis; propose new data elements and/or attributes</td>
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<tr>
<td>• Request SPL terminology for REMS data as necessary; get stakeholder input</td>
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<tr>
<td>• Update existing SPL Implementation Guide; update forms and style sheets</td>
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Project 3: Pharmacy Systems Under REMS

Standardizing REMS Information for Inclusion into Pharmacy Systems Using Structured Product Labeling (SPL) under REMS

**Project Goals and Deliverables**

- **Purpose:** develop a method to share clear, consistent information about REMS
- **Goal is to achieve:**
  - Structured REMS information available to HCPs, patients, and FDA
  - Integration of REMS into pharmacy systems and health IT systems
  - Improved efficiency of FDA’s review of proposed REMS
  - Enable cataloging of similarities and differences between REMS programs
- **Deliverable**
  - Revised SPL Implementation Guide

**Project Scope**

- **General information about REMS:**
  - Products with REMS; which are shared system REMS
  - When REMS was approved and/or modified
  - Elements included in each REMS
- **Content of REMS**
  - Text of REMS Document
  - Links to materials
- **Info about actions patients, health care providers, and distributors are to take**
- **Specific details on sponsor implementation of REMS are outside of scope**
Project 4: Practice Settings Under REMS

Providing a Central Source of REMS Information for Practice Settings under REMS

Problem Statement

FDA’s REMS web page does not have the necessary information

- Needs to provide more information about the content of REMS programs and what is required of specific stakeholders
- Should be in a user-friendly format and provide a concise overview

Project Overview and Approach

- Make site more user-friendly
- Add additional information about individual REMS programs
- Leverage information captured through SPL
- New features and information added to the page
- Iteratively refine page layout and content
Project 4: Practice Settings Under REMS

Providing a Central Source of REMS Information for Practice Settings under REMS

**Project Goals and Deliverables**

- Goals to achieve:
  - Help stakeholders more quickly learn
  - Help stakeholders understand and comply
  - Minimize confusion
  - Provide access to convenient, up-to-date and comprehensive REMS information
- Deliverable:
  - Centralized, standardized, reliable, and user-friendly repository of information about REMS

**Project Scope**

- Web page changes will be broad, including:
  - More user-friendly page with key information at a glance; REMS FAQS
  - Ability to identify and locate information about specific REMS programs
  - Provide regulatory history even after REMS are modified or released
  - Identify parties that must become certified or enrolled
  - Make information on page available for download and machine readable
Conclusion

FDA remains committed to systematic evaluation and improvement of REMS program implementation, informed by stakeholder feedback and reflecting the dynamic and evolving nature of the drug development process.
Observations and Considerations for Risk Management Professionals

- Is your perspective appropriately captured in the stakeholder feedback?
  - Post your comments to Docket No. FDA–2013–N–0502 by November 24, 2014
- This draft report from Design and Standardization Work Group seems to focus on communications; e.g.,
  - Doctor-patient communications
  - Physician training and CE
  - Communication and documentation via SPL
  - Communicating REMS information in practice settings
- How is standardization achieved in REMS design?
  - Standardized methods of risk assessments are available
- Quality Risk Management standards (ref. ICH Q-9) feature a connected cycle among risk assessment, risk control, risk communication, and risk review
  - This draft report does not help to “thread” these elements
Panel Discussion

FDA Panel Participants:

» Adam Kroetsch
» Cynthia LaCivita
» Gary Slatko
» Terry Toigo

» QUESTIONS?
Type question in the Q&A box to submit a question

Submitted questions are only seen by the Host and ParagonRx Speaker
FoREMS & More

- Occurs the **second Wednesday of every month at 12:00 pm ET**
- Topic ideas? Guest speaking opportunities? Feedback?
  - Contact us:
    - Jeff Fetterman
    - jfetterman@paragonrx.com
    - 888.459.8080
- **Next webinar:**
  - Wednesday, November 12, 2014