FDA Meeting on REMS Standardization and Evaluation

will begin shortly…
FDA Meeting on REMS Standardization and Evaluation

August 14, 2013
Today’s Session

*FDA Meeting on REMS Standardization and Evaluation*

Speaker:
- Jeff Fetterman – President, ParagonRx
- Marc DeLuca – Client Services Manager, ParagonRx
Today’s Session

*FDA Meeting on REMS Standardization and Evaluation*

Highlights:
- Overview of meeting events
- Recap of recurring themes and insightful recommendations
- Identify important trends
Today’s Session

FDA Meeting on REMS Standardization and Evaluation

Submitting Questions:

- Click once on ParagonRx Host under the users tab and click on Private Chat to initiate the chat feature

Resize slides:

- Click “Fit to Screen”
- Ability to zoom in & out
FDA Meeting on Standardizing and Evaluating REMS
FDA Objectives for Meeting

- Obtain feedback from stakeholders on:
  - Issues and challenges associated with standardizing and assessing REMS for drug and biological products
  - Identifying potential projects that will help standardize REMS and integrate them into the health care delivery system
- Meet performance goals included in the fifth reauthorization of the Prescription Drug User Fee Act (PDUFA)

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

Meeting Topics

FDA Presentations

- Meeting overview and REMS update
- Standardizing REMS
- Prescriber-directed tools
- Patient-directed tools
- Dispensers and dispenser tools
- REMS assessments: A summary of FDA’s experiences and challenges
- Building a framework for future REMS assessments

Stakeholder Presentations

- General standardization issues (2 panels)
- Prescriber and patient directed tools
- REMS tools used in dispensing settings
- Standardization projects
- General evaluation issues
FDA Cited Comments from Reviewers

“One company that does a particularly good job with REMS submissions provides an accompanying document that provides rationale for every change. This really helps to expedite the review process.”

“Companies that actually do good pre-testing of materials and react, is such a gift to us.”

“Many last minute surprises could be avoided if sponsors conceptualized and communicated how pending labeling changes may affect REMS programs and materials downstream.”

“Something very basic is how sponsors submit documents ... we go back and forth to just get the documents in the correct format.”

“We’ve learned, and continue to improve upon the importance of directly linking REMS goals, to elements, to assessments.”

“We need to better understand the sponsor/vendor processes to establish best practices for developing and finalizing REMS documents.”

FDA Cited Comments from Patients and Health Care Providers

“I like the repetitiveness that every time I have to talk about my usage. There’s no assumption that I’m doing it right just because I’ve used it a long time. I think that’s a good thing.”

“It is also important to recognize that while these tools may seem time consuming, they can be incredibly helpful.”

“But if we start adding 3, 4, 5, 6 of these REMS programs and they’re all different, different requirements, different websites, this has a much larger impact on [pharmacy] workflow.”

“Am I really doing anything other than just filling out paperwork?”

“We’re always afraid of things, but when you try it – it’s like eating your vegetables, you know, when you try it, it’s just a lot easier.”

REMS Challenges Cited by FDA

**Policy**
- When may an alternative to REMS be appropriate to address a serious risk?
- What are indicators that:
  - product labeling is insufficient to communicate the drug’s risks and conditions of safe use?
  - a REMS is no longer necessary to ensure the benefits of a drug outweigh the risks?

**Design/Standardization**
- What is the best way to balance customization and standardization?
- How much variation is necessary and unavoidable?
- How are the best interventions targeted to prevent or mitigate failures?
- What is the appropriate trade off between enhanced safety and additional burden to the health care system?

**Assessment**
- What are valid proxy measures of patient and provider behavior to determine if REMS goals have been met?
- How are particular REMS interventions associated with specific outcomes?
- How can limited data be used to determine whether REMS are effective?

Sources of Variation in REMS

- Risks vary
- Context of care varies
- Developers of REMS vary
- Best practices are evolving

Why REMS Have Varied

## Nomenclature Variations

<table>
<thead>
<tr>
<th>REMS</th>
<th>Form Name</th>
<th>Patient Agreement</th>
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<tr>
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**FDA seeks to include REMS information in Structured Product Labeling (SPL)**

The Structured Product Labeling (SPL) is a document markup standard approved by Health Level Seven (HL7) and adopted by FDA as a mechanism for exchanging product and facility information.

www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
REMS Standardization – What it Looks Like

<table>
<thead>
<tr>
<th>REMS Design</th>
<th>Minimize Variation</th>
<th>Improve Quality</th>
</tr>
</thead>
<tbody>
<tr>
<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>
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</tbody>
</table>

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<tr>
<th>REMS Tools</th>
<th>REMS tools are informed by the latest science, stakeholder feedback, and established “best practices”</th>
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<td>REMS use similar tools drawn from a standardized REMS “toolkit”</td>
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Identification of Best Practices

FDA is seeking stakeholder and expert feedback

– Building more effective and better-integrated tools
  ▪ Prescriber-directed tools for training and/or certification
  ▪ Patient-directed tools for education and counseling
  ▪ Tools in dispensing settings
    – Certification /enrollment
    – Distribution controls

– Methods to assess and characterize risks and select appropriate REMS tools
  ▪ e.g., Failure Mode and Effects Analysis (FMEA)
    – Expert workshop convened in Fall

Promising Best Practices Cited by FDA

Prescriber-directed tools
- CE credit for REMS training
- Checklists and quick summaries
- Single web portal for similar programs

Patient-directed tools
- FDA encourages all sponsors to test their materials prior to submitting them for review

Dispensers and dispensing settings in REMS
- Integration into existing systems and workflow
  - Inpatient order sets, outpatient pharmacy management system/claims process used to verify documentation of safe-use conditions
  - REMS forms adapted to be compatible with existing health systems
- Setting-specific customization
  - Customized requirements for outpatient and inpatient pharmacies
  - Custom process for closed/integrated systems
  - Customized enrollment forms for independent, chain, and closed system pharmacies
# REMS Assessment Framework – The RE-AIM Framework

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Reach</td>
<td>Proportion of the target population who participate</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>Success rate (positive /negative outcomes)</td>
</tr>
<tr>
<td>Adoption</td>
<td>Proportion of settings that adopt the intervention</td>
</tr>
<tr>
<td>Implementation</td>
<td>Extent to which intervention is implemented as intended</td>
</tr>
<tr>
<td>Maintenance</td>
<td>Extent to which intervention is sustained over time</td>
</tr>
</tbody>
</table>

**Sources and References**

- [www.re-aim.org](http://www.re-aim.org)
- [www.termcommunity.com](http://www.termcommunity.com)
## REMS Assessment Framework

<table>
<thead>
<tr>
<th>Category</th>
<th>Possible REMS Assessment Domains</th>
<th>Standardized REMS Metrics for Each Tool</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reach</td>
<td>Distribution / availability / receipt Participation Medication access</td>
<td></td>
</tr>
<tr>
<td>Effectiveness</td>
<td>Knowledge: awareness / comprehension / understanding Outcomes: REMS goal, clinical, patient-reported Unintended effects</td>
<td></td>
</tr>
<tr>
<td>Adoption</td>
<td>Application of knowledge Attitude / intention Behaviors: adoption, actions, compliance</td>
<td></td>
</tr>
<tr>
<td>Implementation</td>
<td>Process: pretesting, functionality, navigability, sponsor, stakeholder workflow, integration</td>
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<tr>
<td></td>
<td>Consistency</td>
<td></td>
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<tr>
<td></td>
<td>Burden</td>
<td></td>
</tr>
<tr>
<td>Maintenance</td>
<td>Persistency</td>
<td></td>
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<tr>
<td></td>
<td>Failures</td>
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Key Themes in Presentations by Stakeholders

- **PhRMA and BIO**
  - Increase dialogue and transparency
  - Make sure risk minimization activities actually improve patient safety

- **Pharmacy associations**
  - Bigger role for pharmacists in medication safety
  - Make better use of pharmacy systems

- **Healthcare systems**
  - Healthcare is evolving into integrated model
  - REMS must integrate with care systems
  - REMS can negatively affect care if not integrated properly

- **Academic organizations and service providers**
  - Apply existing evidence-based methods
Important Trends and Takeaways

- **Standardization**
  - Of design with evidence-based methods such as FMEA
  - Of tools for patients and prescribers
  - Of integration into existing systems

- **Clear linkage between program goals, elements, and assessments**

- **Framework for assessments**
  - Domains of measurement
  - RE-AIM factors
QUESTIONS?

Click on ParagonRx Host and select Private Chat to access the chat dialogue box
FoREMS & More

- Occurs the second Wednesday of every month
- 12:00 pm ET
- Next session:
  - Wednesday, September 11, 2013
Upcoming Events

- ParagonRx is attending:
  - 29th International Conference on Pharmacoepidemiology and Therapeutic Risk Management
    - Montreal, Canada, August 25-28

If you are attending the ISPE Conference please send us an email. We would love to meet you!
Future FoREMS & More

- We encourage you to submit any future topics you’d like us to cover
- Do you want to be a speaker for a future FoREMS & More?
- Contact us:
  - Jeff Fetterman
  - jfetterman@paragonrx.com
  - 888.459.8080

THANK YOU!