Current Developments in REMS
McKesson
Who We Are

• Administrator for the majority (60%) of the approved single shared REMS and individual product REMS with ETASU.

• Industry’s first:
  – FDA-approved REMS (with ETASU)
  – REMS Assessment report to FDA
  – Unwind FDA released REMS with ETASU
  – Develop and maintain all approved REMS leveraging pharmacy adjudication systems

• Manage 68% (78 of 116) of products that fall under a single shared REMS

• 750,000 claims processed annually through REMS Pharmacy Network ...and growing
Objectives

• Discuss current developments in U.S. risk evaluation and mitigation strategies

• Provide updates on the ongoing REMS SPL Pilot program to streamline REMS summary development

• Learn about recent developments in shared REMS programs

• Offer best practices and emerging trends in patient education associated with REMS programs
General Trends in REMS
General Trends in REMS

• Greater Clarity: Multiple Draft Guidance Documents expected in 2016
  – Applying the Statutory Criteria for Requiring a Risk Evaluation and Mitigation Strategy (REMS)
  – REMS Program Evaluation: Assessment Planning and Reporting
  – Submission of Study Protocols for Drug Products with Certain Risk Evaluation and Mitigation Strategies for Review by the Office of Generic Drugs
  – Survey Methodologies to Assess Risk Evaluation and Mitigation Strategies (REMS) Goal Related to Knowledge
  – Use of a Drug Master File for Shared System Risk Evaluation and Mitigation Strategies (REMS)

• Standardization
  – SPL Pilot leading into SPL implementation in REMS
  – Single Shared REMS Programs
  – Patient education

• Integration into healthcare technology
  – Related to standardization, but opportunities for innovation exist
  – Includes integration into patient-friendly technology (i.e. smartphone)
  – Increasingly user-friendly REMS requirements – reduced burden for stakeholders
REMS SPL Pilot


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Structured Product Labeling

- SPL is a data standard used to capture and share structured information about drug products. SPL is maintained by Health Level Seven (HL7), an SDO that develops numerous standards for the transmission of information about health care and medical product regulation.

- The majority of information currently included in SPL, including general product information, the content of drug labeling, and registration and listing information, is entered by a sponsor and submitted to FDA.

- FDA has committed to evaluating SPL as a standardized format for submitting and maintaining REMS submissions
  
  - SPL use in REMS is one of 4 key projects that FDA has committed to pursuing, to standardize the structure, format, and content of REMS through the REMS Integration Initiative (Pharmacy Systems Under REMS Project: Standardizing REMS Information for Inclusion Into Pharmacy Systems Using Structured Product Labeling (SPL))

  - Intent is to use standard fields to allow for clear dissemination and integration of REMS information into different healthcare settings, and to develop a REMS Summary that would be written for the general public

  - The REMS Summary is intended to address stakeholder and public confusion about the components, location, and requirements of individual REMS programs

REMS Summary

- For REMS with ETASU, the REMS Summary will be presented in a tabular format that facilitates coding of REMS data elements and allows stakeholders to quickly obtain a reader-friendly overview of what the REMS requires.

- REMS Summary uses language that is similar to that found in existing REMS documents and the summaries.

- Detailed instructions for creating the REMS Summary are available in the Draft REMS SPL Implementation Guide Excerpt on FDA's SPL Web site.

- The REMS Summary does not replace the approved REMS document, which will continue to be the enforceable document establishing the REMS requirements.

Details of the REMS SPL Pilot

• The REMS SPL Pilot was announced by FDA at the Oct. 5-6, 2015 REMS Public Meeting

• FDA allowed up to 9 participants for voluntary participation in the SPL Pilot

• The pilot is running from from October 6, 2015 to February 3, 2016, and be extended as resources and needs allow. The first submission deadline was January 15, 2015.

• Both the REMS Summary and the data elements will capture four basic pieces of information about each requirement:
  – Who is required to carry out the requirement: For example, a requirement may be carried out by the healthcare provider who prescribes the drug or dispenses it.
  – What that individual is required to do: This could include a clinical activity, such as counseling a patient, or an administrative one, such as completing an enrollment form.
  – When the activity must be carried out: For example, a REMS activity may need to be completed before a drug is prescribed or dispensed, or before a patient is able to receive the drug.
  – References to REMS materials that may contain additional information about the requirement, such as forms and educational materials.

• Requirements of SPL Pilot participants include appropriate software, knowledge of terminology and standards, and access to FDA’s Electronic Submissions Gateway (ESG)
REMS SPL Pilot Goals and Deliverable

This project’s purpose is to develop a method to share clear, consistent information about the content of REMS programs, including REMS documents, requirements, and materials to achieve the following goals:

• Make structured REMS information available to health care providers, patients, and FDA.

• Provide a single conduit of comprehensive information about REMS programs.

• Facilitate the integration of REMS into pharmacy systems and health information technology, including systems for electronic prescribing.

• Improve the efficiency of FDA’s review of proposed REMS by allowing the Agency to receive REMS submissions in a consistent format.

• Support FDA’s ongoing REMS standardization efforts by enabling the cataloging of similarities and differences between REMS programs.

The project’s final deliverable will be a revised SPL Implementation Guide that describes how sponsors, health care information system developers, and other stakeholders can share REMS information leveraging the existing SPL standard. This project also may lead to the creation of new SPL data elements and attributes, if needed.

Further Information on the REMS SPL Pilot

• FDA staff working on the REMS SPL Pilot can be reach directly by email at REMS_Standardization@fda.hhs.gov.

• FDA is seeking comment from any stakeholder on its proposed approach for capturing REMS information in SPL format in this pilot.


Single Shared REMS Programs
# Currently Approved Single Shared REMS

<table>
<thead>
<tr>
<th>Shared REMS Name</th>
<th>Last Updated</th>
<th>REMS Approval</th>
<th>Med. Guide</th>
<th>Comm. Plan</th>
<th>ETASU</th>
<th>Imp. System</th>
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<tr>
<td>Buprenorphine Transmucosal Products for Opioid Dependence (BTOD)</td>
<td>8/10/2015</td>
<td>2/22/2013</td>
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<td>Yes</td>
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<td>Extended-Release and Long-Acting (ER/LA) Opioid Analgesics</td>
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<td>iPLEDGE (isotretinoin)</td>
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<td>10/22/2010</td>
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<td>Transmucosal Immediate-Release Fentanyl (TIRF) Products</td>
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<td>12/28/2011</td>
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Evolution of Shared REMS
Rosiglitazone-Containing Medicines

• Shared REMS for Rosiglitazone-Containing Medicines was originally approved in December 2008 with prescriber training/enrollment, patient enrollment, and restricted distribution
  – Postmarketing data and analysis suggested an increased risk of cardiovascular events with rosiglitazone usage in Type 2 diabetics vs. alternative therapies
  – Data and analysis were inconclusive, and an FDA Advisory Committee in July 2010 was split on the recommendations to address the risk

• REMS restrictions were eased in May 2014 to remove patient and prescriber restrictions after a reanalysis of the postmarketing data

• The REMS requirements were eliminated in December 2015 after continued review and FDA “identified no new pertinent safety information”

Evolution of Shared REMS

Continued Consolidation

• Shared REMS Waiver(s)
  – FDA may approve a waiver for an ANDA under specific circumstances¹
    - Burden outweighs benefit of single, shared system for HCPs, patients, ANDA applicant(s), and/or RLD holder
    - Existing patent protection of one or more aspects of the REMS, for which a license could not be obtained
  – Alosetron is the only currently-approved waiver for a shared REMS
  – Multiple waiver programs currently under consideration/development by manufacturers and/or FDA

• Clozapine REMS Program was approved in September 2015 with prescriber, pharmacy and patient requirements, as well as restricted distribution²

¹ Risk evaluation and mitigation strategies, 21 CFR 355-1.i.1.B. (2016).
Patient Education in REMS
FDA Focus on Patient Education

- Improving Tools for Prescriber-to-Patient Counseling under REMS
- FDA proposes to:
  - Conduct research into existing REMS patient counseling tools, other patient counseling initiatives, and counseling literature to identify the current state of patient counseling regarding medication benefits and risk
  - Seek feedback (e.g., from Advisory Committees, risk communication experts, health care intervention specialists, federal partners, health care providers and others) to identify opportunities to improve upon the content, format, processes, techniques, tools, and delivery of effective counseling within REMS programs
  - Develop a report for stakeholders of findings, counseling processes, and tools that could serve as the basis for designing new tools and validating them in demonstration projects

Best Practices in REMS Patient Education

- Apply consistent/equivalent rigor to development of patient safety materials as any other patient-directed materials (e.g. marketing)

- Accessibility
  - Physical (easily obtainable)
  - Educational (low literacy/illiterate)

- Enlist trusted HCP relationships

- Verify usefulness
  - Pre-test with an equivalent population
  - Comprehension
  - Usability
  - Visual appeal
  - Pictures/pictographs
Discussion