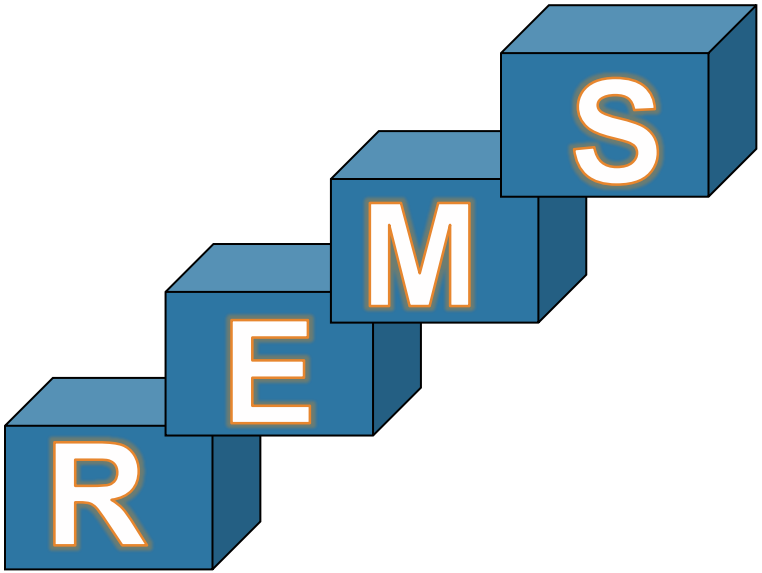
# Development of the 2012 Extended Release and Long-Acting (ER/LA) Opioid Analgesic REMS

# FDA Informs Sponsors a REMS is Needed




February 6, 2009

FDA notified holders of ER/LA opioid analgesics that their products would require a REMS to ensure that the benefits of those products continued to outweigh their risks.

March 3, 2009

FDA met with the application holders to discuss the REMS design to manage the risks while considering the burden on the health care system.

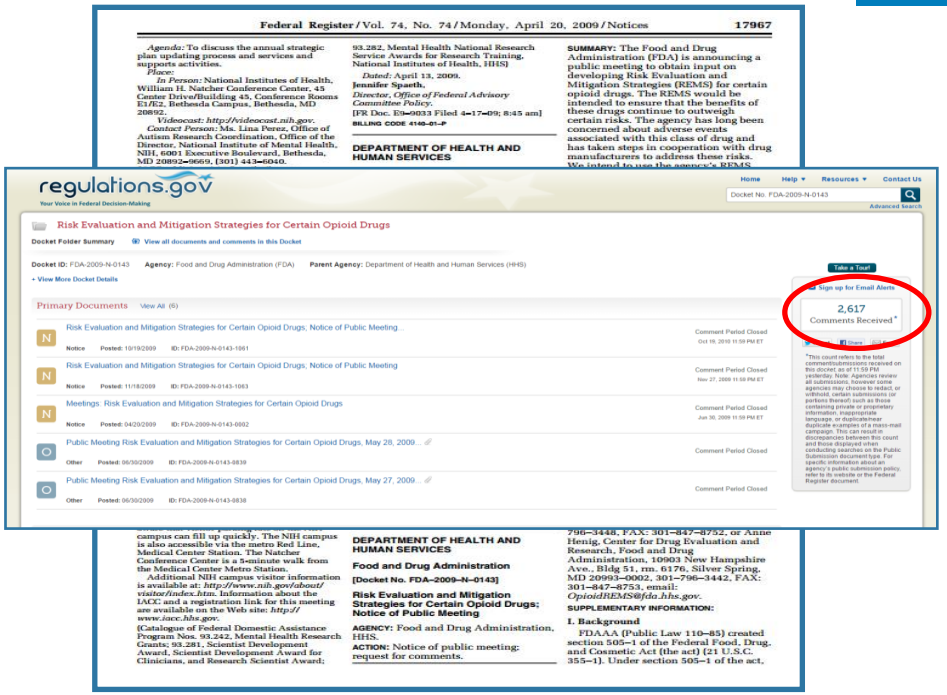
# Stakeholder Input: Public Docket

FDA opened a public docket on April 20, 2009.

FDA is interested in obtaining information and public comment on the following issues:

a. Elements of the REMS
b. System Issues

FDA received 2617 comments on the proposed REMS.



# Stakeholder Input: Public Meetings

| February 9, 2009 | May 4-5, 2009 | May 27-28, 2009 | December 4, 2009 | July 22-23, 2010 |
|---|---|---|---|---|
| Discuss the regulatory process and standards for review and approval of opioid products. | Obtain comments and opinions regarding the development of an opioid REMS | Hear about experiences with opioid drugs and suggestions for a REMS for ER/LA opioid products. | Hear from industry about their views on the specific features of the REMS. | Joint Meetings of ALSDAC and DSaRM to discuss FDA's proposal for a class-wide REMS for ER/LA opioids |

# Some Considerations in Developing the REMS

1. Scope of the REMS
2. Impact on the Health Care System
3. Impact on Patient Access to the Drug

# Some Highlights of Stakeholder Comments (1)

| | |
|---|---|
| **Size** | Largest and most complex program of its kind |
| **Drugs** | If the REMS only applies to ER/LA opioids, there will be shifts in prescribing to IR products or other potentially less effective pain relievers. Methadone should have a separate REMS. |
| **Prescriber Education** | Many comments supported prescriber education but comments were divided as to whether such education should be mandatory.<br>• Include safe use, storage, and disposal of opioid medications, pain management, benefits and risks of opioid treatment.<br>• If education is mandated, REMS certification should be linked to DEA registration to maximize participation, minimize cost, and streamline the prescription process. |

# Some Highlights of Stakeholder Comments (2)

| | |
|---|---|
| **Prescriber Certification** | Individual prescriber enrollment and real time verification of prescriber training at pharmacy level could cause “opting out.” Consider linking certification to DEA registration or state requirements (e.g. state Medical Board Licensure). |
| **Patient Education and Certification** | Patient education is vital to the safe use of REMS drugs. A REMS that employs a patient registration system would be overly burdensome and create a stigma for pain patients that could adversely affect patient access to necessary medications. |
| **Program Evaluation** | It is critical to assess the effectiveness of the program and its impact on appropriate access to pain medications. |
| **Other** | Less restrictive elements should be implemented first to determine if they are effective in mitigating risk while preserving access. |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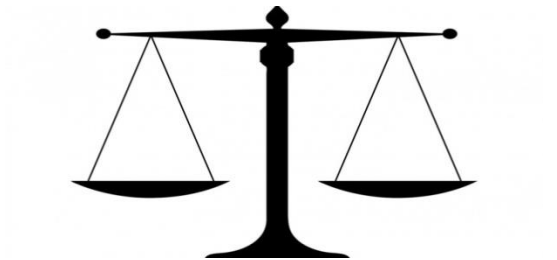
# Balancing Risk, Burden, and Patient Access

ETASU shall be commensurate with the specific serious risk listed in the labeling of the drug and considering such risk,

- Not be unduly burdensome on patient access to the drug
- And to the extent practicable minimize the burden on the health care delivery system



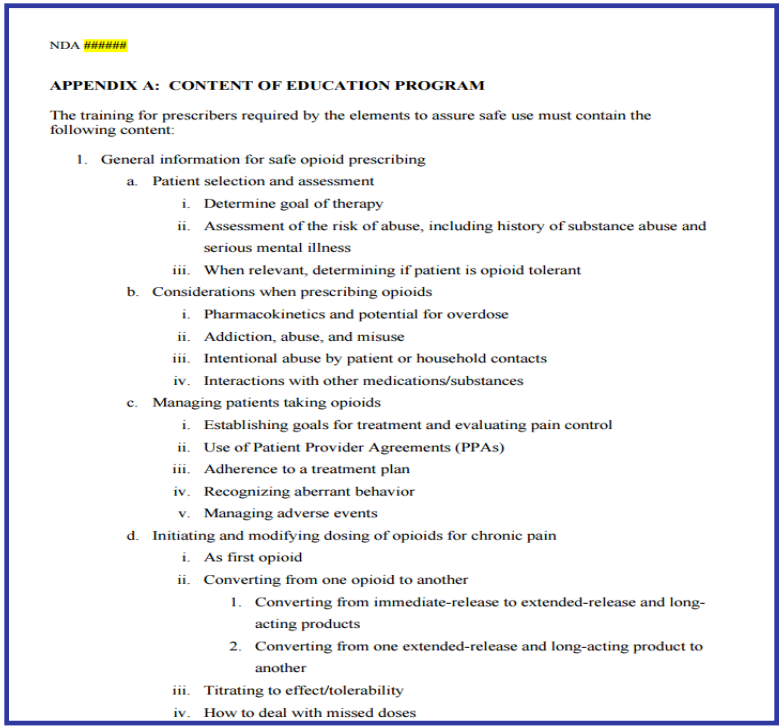
**April 19, 2011**

FDA sent REMS notification letters to application holders of ER/LA opioid analgesics. The notification letters specified requirements for

- Prescriber training/education
- Assessment plan and timetable for submission of assessments
- Medication Guide
- Patient Education Materials

Focus of the REMS was education and ER/LA products.

# Prescriber Education



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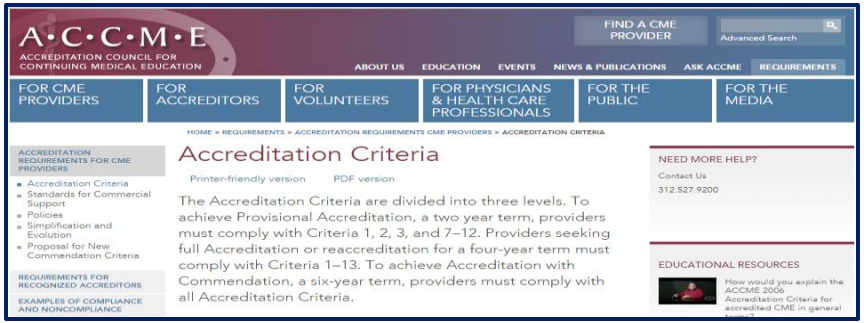
**APPENDIX A: CONTENT OF EDUCATION PROGRAM**

The training for prescribers required by the elements to assure safe use must contain the following content:

1. General information for safe opioid prescribing
   a. Patient selection and assessment
      i. Determine goal of therapy
      ii. Assessment of the risk of abuse, including history of substance abuse and serious mental illness
      iii. When relevant, determining if patient is opioid tolerant
   b. Considerations when prescribing opioids
      i. Pharmacokinetics and potential for overdose
      ii. Addiction, abuse, and misuse
      iii. Intentional abuse by patient or household contacts
      iv. Interactions with other medications/substances
   c. Managing patients taking opioids
      i. Establishing goals for treatment and evaluating pain control
      ii. Use of Patient Provider Agreements (PPAs)
      iii. Adherence to a treatment plan
      iv. Recognizing aberrant behavior
      v. Managing adverse events
   d. Initiating and modifying dosing of opioids for chronic pain
      i. As first opioid
      ii. Converting from one opioid to another
         1. Converting from immediate-release to extended-release and long-acting products
         2. Converting from one extended-release and long-acting product to another
      iii. Titrating to effect/tolerability
      iv. How to deal with missed doses

- Prescriber education program includes
  - General information about the use of the class of ER/LA opioid analgesics to aid in patient selection and counseling
  - Specific drug information
  - Information about how to recognize the potential for and evidence of addiction, dependence, and tolerance
  - Training conducted by accredited, independent CME providers
- Training is not mandatory under REMS.
  - FDA supported mandatory training linked to DEA registration as proposed in the Administration's comprehensive plan to address the epidemic of prescription drug abuse in April 2011.

# ACCME and FDA Collaboration





- FDA worked with the Accreditation Council for Continuing Medical Education (ACCME) and other accrediting bodies and CE providers.
- Goal was to help ensure that CE programs developed to comply with the REMS would be in
  - compliance with ACCME accreditation criteria and
  - standards for commercial support.

# FDA Lessons Learned re: CME

FDA and the CME community had different expectations for *The Blueprint for Prescriber Education*

## FDA

- FDA creates a *high level outline* to guide content of the Blueprint.
- FDA expected the *application holders to work together to develop the draft content* for FDA review and approval.
- This is analogous to how we handle the prescribing information in the label, i.e., sponsors may develop the draft, but FDA controls the content.

## CME Community

- *FDA would develop the Blueprint* for CE providers to use to develop the actual CE content.
- Application holders provide FDA with information about the scope of the content.
- CME Community wanted to be sure that the FDA "controlled" the content of the professional education.

# FDA Blueprint Available for Public Comment

- November 7, 2011 “Blueprint for Prescriber Education for Long-Acting/Extended-Release Opioid Class-Wide REMS”


- FDA received comments from about 65 individuals or organizations.
- Most comments were favorable and offered specific edits.
- The negative comments focused primarily on the REMS being ineffective in addressing the problem because
  - completion of the REMS training by prescribers is voluntary
  - industry is involved
  - the ER/LA opioid analgesic focus is too narrow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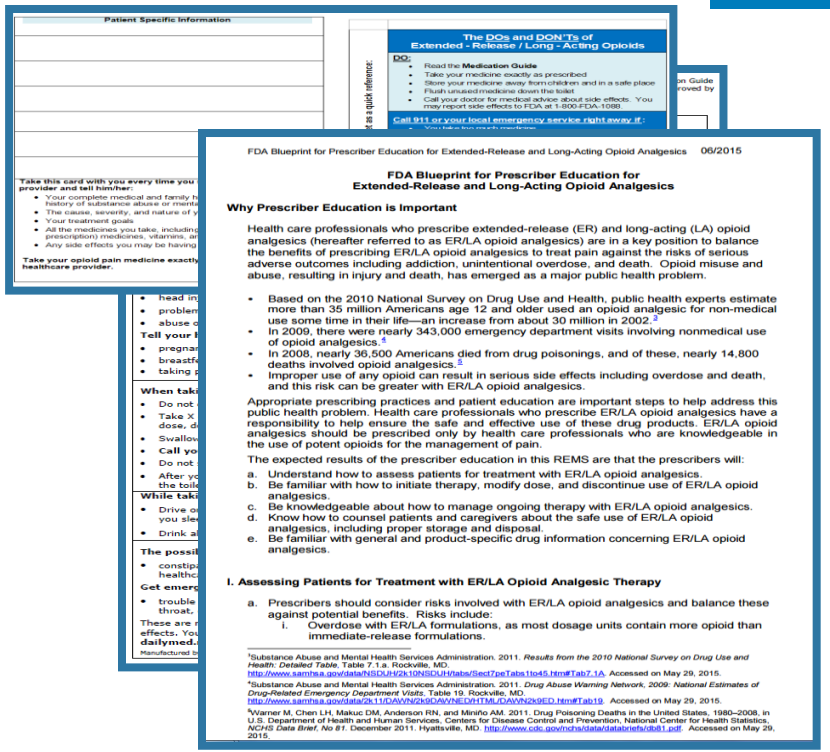
# REMS Approval

- FDA considered comments received and approved the ER/LA Opioid Analgesics REMS on July 9, 2012 .
- The REMS included a
  - A Patient Counseling Document for a prescriber to give to a patient
  - One-page Medication Guide
- Final FDA “blueprint”
  - Posted on FDA website for accredited CE providers to develop training supported by independent educational grants from ER/LA opioid manufacturers.
  - Content focuses on safe prescribing of ER/LA opioid analgesics.
  - Directed to prescribers of ER/LA opioid analgesics but may be relevant for other healthcare professionals.



# Summary

- Pharmaceutical companies, FDA, medical specialty groups, CME accreditors and accredited providers collaborated to include CME as a component of the ER-LA opioid analgesic REMS.
- Multiple companies successfully collaborated on the establishment, governance and operational aspects of a shared system REMS program with a CME component
- Lessons learned from creating the ER-LA opioid analgesic REMS CME program can be applied to the developing REMS requirements for immediate-release opioid analgesics.