



A PHARMACY CONTINUING EDUCATION PROGRAM

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## JANUARY 2012 "ANNUAL PHARMACY LAW LESSON"

34<sup>TH</sup> YEAR



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Pharmacists have opportunities within Risk Evaluation & Mitigation Strategies Programs. That's the reason for presenting this topic. As professionals, sometimes we're trained or taught to fear or stay away from narcotic analgesics. But what about patients who truly need them for legitimate reasons. The overall goal of this lesson is to convey how pharmacists can interact and impact this area of concern. Additionally, this is our annual lesson that concentrates on a contemporary issue related to pharmacy law & practice.

This lesson provides 3.0 hours (0.3 CEUs) of credit, and is intended for pharmacists in all practice settings. **The program ID # for this lesson is 707-000-12-001-H03-P. Pharmacists completing this lesson by January 31, 2015 may receive full credit.**

**To obtain continuing education credit for this lesson**, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

If you have any comments, suggestions or questions, contact us at the above address, or call toll free 1-800-323-4305. (In Alaska and Hawaii phone 1-847-945-8050). **Please write your ID Number (the number that is on the top of the mailing label) in the indicated space on the quiz page** (for continuous participants only).

**The objectives of this lesson are such that upon completion the participant will be able to:**

1. List principles of risk mitigation established under FDA guidelines.
2. Describe options for using REMS to assure safe drug use (ETASUs).
3. Discuss steps that have been taken to implement REMS for opioid analgesics.
4. Discuss improvements to REMS that may take place pursuant to PDUFA 2012.

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Federal law was modified significantly in 2007 when the Food and Drug Administration Amendments Act (FDAAA) was passed. One of the most significant aspects of FDAAA was the establishment of a program known as Risk Evaluation and Mitigation Strategies (REMS) that was designed to keep on the market those drugs that are inherently safe and effective but have not consistently been used safely and effectively.<sup>1</sup> Prior to the availability of REMS, the FDA had often been forced to remove from the market those drugs that were being used inappropriately and dangerously for some, but not all, patients. The only authority the FDA had was either to continue product approval or withdraw the drug from the market. There was no middle ground. The “all-or-nothing” approach was frustrating for regulators, as well as health care professionals and patients, because it meant that the many suffered due to the misdeeds of the few.

Because some prescribers were using drugs irresponsibly and their patients were experiencing preventable adverse effects, many safe and effective drugs were made unavailable—even for those prescribers who were using the drug responsibly and whose patients were experiencing improved outcomes from drug use. The FDA had earlier developed a voluntary program called RiskMaps, on which REMS was based, seeking to encourage safe product use, and recognizing that even the safest products can be used unsafely by those who do not follow accepted standards. REMS is a mandatory version of RiskMaps that has teeth in it, and it uses various specific methods of assuring that accepted standards for medication use are being adhered to. The REMS program gives the FDA a mechanism for allowing a drug to continue on the market, while steps are taken to control the drug so that dangerous and risky use is minimized.

One of the most closely watched REMS activities has been a series of meetings held by the FDA to consider how to mitigate the risks of using opioid analgesics. The agency does not want to be overly restrictive in regulating these drugs, because some physicians and pharmacists are already reluctant to provide chronic pain patients with the opioids they need. On the other hand, opioid misuse and abuse, resulting in injury and death, has emerged as a major health problem.<sup>2</sup> Public health experts estimate that more than 35 million Americans age 12 and older used opioid analgesics for non-medical purposes during 2010, up from 29 million in 2002. In 2009, nearly 342,000 emergency room visits were associated with nonmedical use of opioid analgesics. In 2007, nearly 28,000 Americans died from unintended consequences of drug use, and of these, nearly 12,000 involved prescription drug pain relievers. Despite these frightening figures, the FDA continues to recognize the safety and efficacy of opioid analgesics when used appropriately. These drugs continue to be approved by the agency for the treatment of acute and chronic pain. The fundamental regulatory goal is to achieve balance in restricting access to opioids, so that pain patients who need them can get them and use them safely, while dangerous and even deadly inappropriate use is eliminated.

### **FUNDAMENTAL APPROACHES TO REMS COMPLIANCE**

Most currently established REMS rely primarily on the distribution of either a Medication Guide (MedGuide) or a patient package insert (PPI) for drugs that have risks capable of being mitigated through the actions of informed patients.<sup>3</sup> Within the MedGuide or PPI are instructions for patients on the use of medication in ways that enhance safety of use, and precautions regarding the types of effects that can be noticed by patients and reported to health care professionals. This is perhaps the most basic method through which REMS assure drug safety, by providing patients with information that can promote self-monitoring and effective self-care.

REMS strategies may focus on health care professionals rather than on patients. There are pharmaceutical products for which REMS programs impose requirements for communication of risk-related information to health care professionals in several different ways. The goal of these communications is to emphasize certain aspects of product safety and the manner in which a product can be used to enhance the safety of it. One way for this communication to occur is through letters sent directly by the manufacturer to the health care professional. A second option is to use collaborations between manufacturers and professional societies. Through these collaborations, professional organizations can use continuing education programs and other alerts to members that spread the word about safety protocols, such as medical monitoring by periodic laboratory tests, as may be necessary to assure the safe use of a product.

### **ASSURING ACCESS AND MINIMIZING BURDEN**

One key aspect of REMS is recognition that programs implemented to reduce risk should not overly burden or restrict access to care.<sup>4</sup> This principle recognizes that the easiest way to reduce risk is to decrease access to a medication for all who use it. Unfortunately, this approach has the detrimental consequence of reducing access not only for those who are at risk from inappropriate use, but also for those who need the medication and are not at significant risk. Recognizing the principle of balance in regulation, the REMS program requires that restrictions on drug use not be unduly burdensome on patient access, considering particularly patients with serious life-threatening diseases or conditions, as well as patients who have difficulty accessing health care (such as patients in rural or medically underserved areas).

The REMS program also requires that measures taken to mitigate risk minimize the burden on the health care delivery system. Risk mitigation measures must be designed to be compatible with established distribution, procurement, and dispensing systems for drugs. In this regard, the REMS program acknowledges that the pharmacy profession has already established ways to assure product safety, and that these established systems should be used to meet requirements of the program rather than reinventing the wheel.

The overall intent of the REMS program is to help those people who need help in mitigating drug risks, but not to impose requirements that interfere with use of medication by people who are already doing quite well and who do not need additional assistance. Sometimes government programs can be so intrusive into individual decisions that they figuratively "throw out the baby with the bath water" by going too far to protect people from themselves. Within the REMS program there is specific guidance on how not to allow this to occur. Risks are to be mitigated for those who are at risk, but the measures taken to mitigate risk must not be so restrictive that people who do not require government protection are put at a disadvantage.

### **ELEMENTS TO ASSURE SAFE USE**

Undoubtedly the most dramatic change in regulation established by the new REMS provisions is the creation of a category of restrictions on inappropriate access known as "Elements to Assure Safe Use" (ETASU).<sup>5</sup> ETASUs are intended to continue to provide availability of drugs that are associated with a serious risk but would otherwise be removed from the market were it not for the REMS program, or would not be approved if the drug has yet been approved. Mandatory ETASUs are established to mitigate a specific risk listed in the labeling of a drug. Certain specific determinations must be made by the FDA prior to the implementation of an ETASU. These determinations include:

- That the drug, which has been shown to be effective but is associated with a serious adverse drug experience, can be approved only if such elements are required, or would be withdrawn unless the elements are required.
- That for a drug initially approved without an ETASU, other possible elements of a REMS are not sufficient to mitigate the serious risk.

The types of ETASUs that may be required under a REMS are varied. Some are quite onerous, while others are relatively benign. These types of ETASUs include, but are not limited to:

- Health care providers who prescribe the drug must have particular training or experience, or are specially certified.
- Pharmacies, practitioners, or health care settings that dispense the drug must be specially certified.
- The drug must be dispensed only in particular health care settings, such as hospitals.
- The drug must be dispensed only to patients with evidence or other documentation of safe-use conditions such as laboratory tests.
- Each patient using the drug is required to undergo certain monitoring.
- Each patient using the drug must be enrolled in a registry.

These restrictions pose significant barriers to product access and the FDA has recognized that for classes of drugs such as opioid analgesics there are already a number of regulatory barriers imposed both by the FDA and DEA. The agency has also said that it would be inappropriate to fully implement all of these restrictions for opioid analgesics, as the restrictions on access for legitimate pain patients would not be justified by the mitigation of risks.

Drug sponsors are required to submit to the FDA the materials they propose to use in support of an ETASU. These materials may include health care provider attestations that a drug is being used consistently with product labeling; pharmacy, practitioner, health care setting, and patient enrollment forms; training materials for prescribers and pharmacists; specified procedures that must be undertaken in the use of the drug; patient/physician agreements or other informed consent processes that assure a meaningful dialogue between patients and health care professionals; patient educational materials; safety protocols; medical monitoring procedures; and data collection forms.

### **HEALTH CARE PROVIDER CERTIFICATION**

The REMS provisions allow for an ETASU that could require certification of training, or attestation of specific experience or knowledge, before the health care provider can be enrolled in a program that allows the provider to prescribe the product.<sup>6</sup> This requirement is understandably controversial among physicians and other prescribers, who resent being required by a government agency to undergo training on appropriate professional practice prior to being qualified to prescribe a drug that is subject to a REMS.

As an example, in order to be certified, the health care provider may be required to show the ability to do the following things:

- Diagnose the condition for which the product is indicated.
- Understand the risks and benefits of the product, having read the educational materials for prescribers.
- Diagnose and treat potential adverse reactions associated with the product.

The REMS program may require periodic recertification and reenrollment of prescribers. The opportunity to obtain this training or certification must be available to any willing provider, for example through an online or mail course, at a reasonable cost to the provider.

It appears likely that prescriber education will be a cornerstone of any opioid analgesic REMS. The restriction of opioid prescribing to those who have demonstrated that they possess the knowledge necessary to prescribe opioids safely will challenge pharmacists to assure that prescribers whose prescriptions are presented for filling are qualified under REMS to issue the prescription.

#### **RESTRICTION TO CERTIFIED DISPENSERS**

A very controversial provision of the REMS program is the potential for restriction of access to particular medications only from pharmacies that have been certified as able to manage the use of a drug that is subject to a REMS.<sup>7</sup> This would mean that licensure by a state board of pharmacy would not be sufficient to allow a pharmacy to dispense the drug. Rather, the ETASU could impose expanded requirements for the pharmacy. ETASUs under this category might require certification of training or attestation of specific experience or knowledge before a pharmacy is enrolled in a program that allows the pharmacy to dispense the product. For example, to be certified, pharmacy personnel could be required to demonstrate that they:

- Understand the risks and benefits of the product and have read the educational materials before the drug is dispensed.
- Agree to fill a prescription and dispense the drug only after receiving authorization.
- Agree to check laboratory values, or check for the presence of stickers that providers affix to prescriptions for specified products to indicate that the patient has met all criteria for receiving the product ("qualification stickers"), before dispensing the drug.
- Agree to fill a prescription and dispense the drug only within a specified period of time after the prescription is written.
- Agree to fill prescriptions only from enrolled prescribers.

This ETASU may require periodic recertification and reenrollment, and it must be made available to any willing provider. The restriction of opioid analgesic availability to only specific pharmacies appears highly unlikely under the current FDA view of REMS. This approach, while technically permitted under the legislation, would restrict access to needed pain medications to an extent far greater than the risks warrant.

#### **DISPENSING LIMITED TO CERTAIN PRACTICE SITES**

Under this provision, the party who holds the approval of the drug would be required to limit distribution in such a way as to assure that the recipient of the drug is within a health care setting that is able to monitor the drug's use and can restrict access to those patients who are likely to derive benefit from the drug without unnecessary exposure to risk.<sup>8</sup> This ETASU provision has the potential to exclude traditional community pharmacies from the distribution chain, in favor of locations that demonstrate the ability to monitor drug therapy. For example, the drug distributor could be required to:

- Ensure that the drug is dispensed only in hospitals that have met certain conditions.
- Ensure that the drug is dispensed only to physicians' offices equipped to treat the potential risks associated with the drug following administration of the drug (e.g., access to medication and equipment necessary to treat a serious allergic reaction).

#### **LIMITING ACCESS TO PATIENTS WITH EVIDENCE OF SAFE-USE CONDITIONS**

This provision specifies that there are certain criteria that can be associated with behaviors of patients that are linked to qualifying the patient for access to the drug.<sup>9</sup> For example, evidence or other documentation of safe use conditions may include:

- Patients have been counseled about the risks and benefits of the product and have signed an acknowledgement that they understand the risks and benefits of the product.
- Patients have been provided a copy of patient educational materials and demonstrated that they understand the risks and benefits of the product.
- Patients receive the drug only after specified authorization is obtained and verified by the pharmacy. Examples of authorizations include checking laboratory values and checking for physician qualifications (stickers) on the prescription.

#### **PATIENTS SUBJECT TO MONITORING**

An ETASU could require that patients be monitored or that specific follow-up would occur at specified time points during the use of the drug.<sup>10</sup> Here are several examples of how that could be done:

Patients' laboratory tests are monitored on a specified periodic basis to prevent identified serious risks.

Patients are required to contact the prescriber within a specified period of time after beginning treatment with the drug to ensure that they are still appropriate candidates for treatment.

Patients are required to contact their prescriber periodically during and following treatment to ensure that they did not experience serious risks associated with the use of the drug.

### PATIENT REGISTRY

An ETASU could require that patients be enrolled in a registry to mitigate a specific serious risk listed in the labeling of the drug.<sup>11</sup> The use of a registry could be combined with another ETASU to assure that dispensing is limited to patients with documentation of safe-use conditions, or to document that each patient using the drug is subject to certain monitoring requirements. Drug access would be contingent on patient enrollment. The types of information collected on enrolled patients could include:

- Information on clinical outcomes.
- Clinical and laboratory data.
- Safety information.
- Data on compliance with prescribed management and prescribing protocols.
- Data on the impact of tools to assure compliance and good outcomes.

The primary purpose of a registry would be to enroll patients to mitigate a serious risk associated with a drug under a REMS. Registries could also serve as a repository for clinical data, and allow for case finding and follow-up. As such, registries could serve a useful secondary purpose in post-marketing surveillance. However, the primary purpose of a registry is risk mitigation for specific patients who are identified as being at high risk.

### THE REGULATION OF OPIOID ANALGESICS

Pharmacists know well that most opioid analgesics are classified as Schedule II or Schedule III controlled substances, and as such they are subject to stringent regulation. The DEA imposes requirements throughout the distribution chain for these drugs, requiring that formal requisites of prescribing and dispensing be observed, and that records be made to document the acquisition and dissemination of all such drugs. Yet, the DEA is focused primarily on preventing the diversion of controlled substances from legitimate medical use to non-medical use.<sup>12</sup> Under DEA regulations, a controlled substance has been diverted if it has been prescribed for other than a legitimate medical purpose or outside the usual course of professional practice. A pharmacist, who knows that an order for a controlled substance medication has been issued outside medical practice, and who dispenses medication pursuant to such a purported prescription, has violated DEA regulation. The DEA is not concerned with the appropriateness of use by a legitimate patient within a clearly medical context. That area of concern comes under the auspices of the FDA. When a controlled substance is diverted to non-medical use, it is a DEA issue. When an opioid analgesic is used unsafely by a legitimate patient who has been prescribed the drug to treat pain, it is an FDA issue. The FDA's opioid REMS project addresses the mitigation of risks by implementing programs that will improve the quality of prescribing, and will thus improve the quality of medication use by patients.

### VARYING APPROACHES FOR DIFFERENT OPIOID RELEASE MECHANISMS

The FDA has indicated that it would prefer to have REMS programs applied across a class of drugs. A class wide REMS would replace multiple programs created for individual drugs within a class where all drugs share essentially the same risks and could use essentially the same risk mitigation strategies. This approach could create efficiencies within REMS programs, avoiding the multiplicative use of resources to achieve the same goal. Of course, the creating of a class wide REMS would require cooperation among competitors, and this is a challenge for the agency.

Within opioid analgesics, the agency has identified what could be considered three broad classes of drugs, and has taken a different approach for each class. Perhaps the most challenging and controversial class is comprised of the extended-release, long-acting (ER/LA) products. A second class is the immediate release products, for which little discussion has been held thus far. The third class contains the rapid onset opioids, in which the transmucosal immediate-release fentanyl (TIRF) products are currently placed.

### REMS FOR TRANSMUCOSAL IMMEDIATE-RELEASE FENTANYL (TIRF) PRODUCTS

The rapid onset fentanyl products are often prescribed for breakthrough pain in chronic pain patients who are also using extended release products such as a fentanyl patch.<sup>13</sup> These products are often restricted in their labeling to use by cancer patients, and are not intended to be used as around-the-clock therapies. One goal of the TIRF REMS is to limit the prescribing and dispensing of these products to appropriate patients, which includes use ONLY in opioid-tolerant patients. Other goals include preventing inappropriate conversion between fentanyl products, preventing accidental exposure to children and others for whom the product has not been prescribed, and educating prescribers, pharmacists, and patients on the potential for misuse, abuse, addiction, and overdose. While the final structure of the TIRF REMS is yet to be determined, it is likely that pharmacy will play a critical role in the risk mitigation strategies for these products.

Key elements of the TIRF REMS are likely to include these requirements:

- Prescribers will not be eligible to prescribe TIRF products for outpatient use unless the prescribers are enrolled in the TIRF REMS after having reviewed prescriber education materials and having completed a knowledge assessment and enrollment form.

- Patients will be required to complete a patient-prescriber agreement before they can receive the drug on an outpatient basis.
- Outpatient pharmacies must assure that an authorized pharmacist has reviewed a TIRF REMS educational program, and has successfully completed a knowledge assessment and enrollment form. Enrolled pharmacies will be permitted to dispense TIRF products only if the prescriber and the pharmacy are enrolled and active, and if the patient has not been inactivated from the program.
- Inpatient pharmacies will be required to have an authorized pharmacist review the educational program and successfully complete the knowledge assessment and enrollment form. For inpatient use, the enrollment of prescriber and patient in the REMS program is not required, but inpatient pharmacies may not dispense TIRF products for outpatient use.

### **REMS FOR EXTENDED-RELEASE, LONG-ACTING (ER/LA) OPIOID PRODUCTS**

Although the future for risk mitigation of the ER/LA opioids is undetermined, it appears that for the present there will be only a limited role for pharmacists. The focus of current REMS activities is on prescribers, and the specific strategy is to better educate them about the mitigation of risks of using ER/LA opioids. In an unprecedented step, the FDA has provided a detailed blueprint for continuing medical education (CME).<sup>14</sup> Traditionally, CME has been regulated by the states as a means to assure the continuing competency of health professionals who are state licensed. The creation of federal standards for CME program content is noteworthy, because it could signal a step in the direction of similar standards for pharmacists and other health care professionals. The blueprint for these standards is of interest to pharmacists, both because it provides guidance on the appropriate monitoring of drug therapy by those whose primary role is to dispense opioids, and because the failure of this approach to mitigate ER/LA opioid risks could lead to requirements directly affecting pharmacists.

### **FDA CME BLUEPRINT FOR ASSESSMENT OF PATIENTS FOR TREATMENT OF ER/LA OPIOID THERAPY**

- Prescribers should consider risks involved with ER/LA opioids and balance these against potential benefits. Risks include:
  - Risk of overdose due to the high dosage of opioid available as an ER/LA formulation.
  - Intentional abuse by patient or household contacts.
  - Addiction.
  - Interactions with other medications and substances.
  - Inadvertent exposure to household contacts, especially children.
- Prescribers should assess each patient's risk of abuse, including history of substance abuse and serious mental illness. Prescribers should:
  - Be knowledgeable about risk factors for opioid abuse and risk-assessment methods.
  - Complete a comprehensive history and physical examination, including assessment of psychosocial factors and family history of substance abuse, as well as special considerations for the elderly, women, children, and cultural/ethnic groups. Identify appropriate referrals when the conditions warrant.
  - Understand and appropriately utilize screening tools for addiction or abuse, such as Prescription Drug Monitoring Programs (PDMPs), to help assess potential risks associated with chronic opioid therapy and to help manage patients using opioid products.
  - Adequately document all evaluations and treatment plans.
- Prescribers should be able to determine if a patient is opioid-tolerant and should know which products are safe for use only in opioid-tolerant patients.

### **FDA CME BLUEPRINT FOR INITIATING THERAPY, MODIFYING DOSING, AND DISCONTINUING USE OF ER/LA OPIOIDS**

- Prescribers should have awareness of federal & state regulations on opioid prescribing.
- When initiating therapy with an ER/LA opioid, prescribers should be aware that:
  - Dose selection is critical, particularly when initiating therapy with an ER/LA opioid as the first opioid.
  - Titration should be based on efficacy and tolerability.
- When modifying the dose of an ER/LA opioid, prescribers should understand equianalgesic dosing concepts and follow patients closely during all periods of dose adjustments.
- Prescribers should also:
  - Be knowledgeable about converting patients from immediate-release to ER/LA products and from one ER/LA opioid product to another ER/LA opioid product.
  - Be aware of the concept of incomplete cross-tolerance in order to safely convert patients from one opioid to another.

- Understand that tapering the opioid dose is necessary to safely discontinue treatment with ER/LA opioids when therapy is no longer needed.

#### **FDA CME BLUEPRINT FOR MANAGING THERAPY WITH ER/LA OPIOIDS**

- Prescribers should establish goals for therapy and continuously evaluate pain as well as functioning level and quality of life.
- Prescribers should also be aware of the existence of Patient Provider Agreements (PPAs), although FDA is not requiring their use.
  - PPAs are documents signed by both prescriber and patient at the time an opioid is prescribed. PPAs can help ensure patients understand the goals of treatment, the risks, and how to use the medications safely.
  - PPAs can include commitments to return for follow-up visits, to comply with appropriate monitoring (such as random drug screens) and to safeguard the medication.
- Prescribers should ensure that patients adhere to a treatment plan and monitor patients for misuse and abuse by:
  - Recognizing aberrant behavior.
  - Utilizing PDMPs to identify potential abuse where available.
  - Understanding the role of drug testing and performing drug screens as indicated.
  - Screening and referring for substance abuse treatment when indicated.
  - Performing medication reconciliation at each visit.
- Prescribers maintaining patients on ER/LA opioids should over time reassess whether opioids continue to be necessary for management of the patient’s pain. Prescribers should also:
  - Understand how to manage adverse events associated with ER/LA opioid products.
  - Understand the need for reevaluation of patients’ underlying medical condition if symptoms change over time.

#### **FDA CME BLUEPRINT FOR COUNSELING PATIENTS AND CAREGIVERS ABOUT THE SAFE USE OF ER/LA OPIOIDS**

Prescribers should:

- Give product-specific information about the prescribed opioid.
- Explain how to take the opioid as prescribed.
- Explain adherence to dosing regimen and how to handle missed doses.
- Warn that under no circumstances should an oral ER/LA opioid be broken, chewed or crushed, and patches should not be cut or torn prior to use, as this may lead to rapid release of the ER/LA opioid causing overdose and death.
- Caution that the use of other CNS depressants, alcohol, or illegal drugs with ER/LA opioids can cause overdose and death. Patients should only use other CNS depressants under the instruction of their prescriber.
- Discuss that withdrawal symptoms can occur if an ER/LA opioid is discontinued suddenly. Patients should discuss plans to stop the ER/LA opioid with their prescriber. Patients should discuss a tapering regimen with their prescriber.
- Explain that sharing ER/LA opioids with others may cause serious side effects including death, and that selling or giving away ER/LA opioids is against the law.
- Counsel patients to store their ER/LA opioid in a safe and secure place away from children and pets and to read the product-specific disposal information included with the ER/LA opioid product.
- Caution patients that ER/LA opioids can cause serious side effects that can lead to death. Patients should call their prescriber or get emergency medical help if they have symptoms of overdose or respiratory depression; symptoms of stomach or intestinal blockage; or allergic reactions. Patients should also be counseled on the most common side effects of ER/LA opioids and be cautioned about the risk of falls, working with heavy machinery, and driving.

#### **THE PRESCRIPTION DRUG USER FEE ACT (PDUFA V) AND REMS IMPROVEMENTS**

All legislation is subject to modification through amendments that can be passed in any legislative session. For FDA laws, one of the most common vehicles for statutory amendments is the law that allows the agency to charge fees for those who use the agency to approve their products prior to marketing. This law, known as the Prescription Drug User Fee Act (PDUFA) must be renewed periodically, and September, 2012 is the next opportunity for its renewal. This will be the fifth iteration of PDUFA, thus it is referred to as PDUFA V. The American Pharmacists Association has already offered suggestions for modification of the REMS program as a possible component of the PDUFA V legislation.<sup>15</sup> These suggestions are:

- Outline the strategy and time frame for FDA to continue to discuss and gather public input on improving REMS programs.

- Improve REMS standardization and the use of existing and evolving medical and pharmacy practice technologies and processes.
- Consider, communicate, and discuss REMS programs earlier in the drug review process.
- Develop guidance on the assessment of REMS program effectiveness, the impact on patient access, and the burden on the health care system.
- Develop guidance on how to apply the statutory criteria for when a REMS is required.

**CONCLUSION**

Pharmacists have opportunities within the REMS program, and these opportunities carry with them specific responsibilities for risk mitigation. This is especially the case with drugs such as opioid analgesics that pharmacists already monitor closely. As the REMS program evolves, pharmacy will be well positioned to expand practice opportunities that mitigate the risks of drug use.

**REFERENCES**

21 U.S.C. §355-1.  
<http://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm163647.htm>  
 21 U.S.C. §355-1(e).  
 21 U.S.C. §355-1(f)(2).  
 21 U.S.C. §355-1(f)(3).  
 21 U.S.C. §355-1(f)(3)(A).  
 21 U.S.C. §355-1(f)(3)(B).  
 21 U.S.C. §355-1(f)(3)(C).  
 21 U.S.C. §355-1(f)(3)(D).  
 21 U.S.C. §355-1(f)(3)(E).  
 21 U.S.C. §355-1(f)(3)(F).  
 21 C.F.R. §1306.04.  
<http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm268824.htm>  
<http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM277916.pdf>  
<http://www.pharmacist.com/AM/Template.cfm?Section=Home2&TEMPLATE=/CM/HTMLDisplay.cfm&CONTENTID=27204>

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**Anticipated Topics for 2012**

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Update: nuclear pharmacy	Prevalence of skin cancers	Healthcare impact on pharmacy

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**LESSON EVALUATION**

Please fill out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?

- |  |     |    |
|--|-----|----|
| List principles of risk mitigation established under FDA guidelines        | Yes | No |
| Describe options for using REMS to assure safe drug use (ETASUs)           | Yes | No |
| Discuss steps that have been taken to implement REMS for opioid analgesics | Yes | No |
| Discuss improvements to REMS that may take place pursuant to PDUFA 2012    | Yes | No |

2. Was the program independent & non-commercial Yes No

	Poor			Average		Excellent
	1	2	3	4	5	6 7

3. Relevance of topic

4. What did you like most about this lesson? \_\_\_\_\_

5. What did you like least about this lesson? \_\_\_\_\_

**Please Select the Most Correct Answer(s)**

- |   |  |
|---|--|
| <p>1. Through what legislation will the REMS Program likely be modified?</p> <p>A. FDAMA<br/>                 B. PDUFA<br/>                 C. FDAAA<br/>                 D. FDCA</p> <p>2. What legislation authorized the FDA to implement the REMS Program?</p> <p>A. Durham-Humphrey Amendments-1951<br/>                 B. Kefauver-Harris Amendments 1962<br/>                 C. FDA Amendments Act-2007<br/>                 D. PDUFA-2012</p> <p>3. Although the future for risk mitigation of the ER/LA opioids is undetermined, it appears that for the present there will be only a limited role for pharmacists.</p> <p>A. True<br/>                 B. False</p> <p>4. Prior to REMS, the FDA had a voluntary program on which REMS is based. What was that program called?</p> <p>A. The Safety Initiative<br/>                 B. RiskMaps<br/>                 C. OBRA-90<br/>                 D. NDA</p> <p>5. What government agency is concerned with the appropriateness of drug use by a legitimate patient for a real use?</p> <p>A. APhA<br/>                 B. FDA<br/>                 C. DEA<br/>                 D. FBI</p> | <p>6. On what documents do most REMS Programs currently rely?</p> <p>A. MedGuide or a PPI<br/>                 B. Product label &amp; product labeling<br/>                 C. The NDA &amp; the ANDA<br/>                 D. PDR &amp; Facts &amp; Comparisons</p> <p>7. Recognizing the principle of balance in regulation, the REMS Program requires that restrictions on drug use not be unduly burdensome on patient access.</p> <p>A. True      B. False</p> <p>8. A REMS may require that a patient contact the prescriber within a specified period of time after beginning treatment with a drug to ensure that the patient is still an appropriate candidate for treatment.</p> <p>A. True      B. False</p> <p>9. Why are mandatory ETASUs established?</p> <p>A. To facilitate the promotion of a drug by its manufacturer<br/>                 B. To establish standards for counseling by pharmacists<br/>                 C. To coordinate care between healthcare professionals<br/>                 D. To mitigate a specific risk listed in the labeling of a drug</p> <p>10. The primary purpose of a REMS patient registry is to assist law enforcement in the identification of those persons who are diverting controlled substances from legitimate to non-medical uses.</p> <p>A. True      B. False</p> |
|---|--|

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