

On July 22- 23, 2010 the Food and Drug Administration (FDA) will be holding meetings to discuss the Risk Evaluation and Mitigation Strategy (REMS). The public has 1 hour to comment during this meeting. ASPMN has requested time to provide oral comments during the meeting and hopefully we will be able to do so as we did in May of 2009. Even if we are not one of the few able to speak (and even if we are) we will be submitting written testimony as we also did back in June 2010 that will be included in the public record. Interested stakeholders can submit written comments/testimony. We encourage our members to do this. If you do (and we hope you will) submit comments/testimony please send a copy of them to Wade Delk at [wade@aspmn.org](mailto:wade@aspmn.org) . If you have additional questions please contact Wade as well. Below is the link to the Federal Register notice for the July two day meeting followed by a summary of the issue. [http://www.federalregister.gov/OFRUpload/OFRDData/2010-13535\\_PI.pdf](http://www.federalregister.gov/OFRUpload/OFRDData/2010-13535_PI.pdf).

### **Summary of the issue:**

In February 2009, FDA sent letters to manufacturers of certain opioid drug products, indicating that these drugs will be required to have a Risk Evaluation and Mitigation Strategy (REMS) to ensure that the benefits of the drugs continue to outweigh the risks. Specifically, the Agency stated that the REMS is to target the risks associated with: (1) use of high doses of long-acting opioids and extended-release opioid products in non-opioid-tolerant and inappropriately selected individuals; (2) abuse; (3) misuse; and (4) overdose, both accidental and intentional. FDA has further indicated that the REMS for these opioids should include elements to assure safe use to ensure that prescribers, dispensers, and patients are aware of, and understand the risks and how these products should be used. Finally, the Agency has indicated that the REMS should seek to manage the identified risks while also minimizing burdens to the health care system.

Following its February 2009 notice to sponsors, the Agency solicited input through meetings with sponsors and other stakeholders, a public hearing, and a docket for receipt of written comments. In these forums, stakeholders have expressed significant concerns about the design and implementation of a class-wide REMS. Given the large number of patients and prescribers potentially impacted by the REMS – estimated at 4 million patients, 1 million prescribers, and 28 million prescriptions per year – it is critical that the Agency carefully consider stakeholder concerns and suggestions to help ensure that the REMS achieves the stated goals without compromising patient care.

### **Our Concerns:**

#### ***REMS elements should be proven to reduce risk of abuse, misuse, or diversion***

One important means of minimizing the burdens associated with the REMS is to incorporate only those elements proven effective in modifying prescriber, dispenser, and patient behavior. While reducing the risks associated with opioid medicines is critically important, a kitchen sink approach where the REMS incorporates all elements theorized to be effective is completely unworkable. Unlike other REMS programs, FDA has asked manufacturers to address many non patient risks. To our knowledge, this is unprecedented and therefore there is no evidence that it can be done successfully without restricting the delivery of health care and impacting access by legitimate patients.

#### ***The REMS Should Not Include A Patient Registry***

A requirement that patients be registered in order to receive medicines covered by the REMS, such as that required in the iPLEDGE program for isotretinoin, should not be included in the opioid class REMS. Experience with iPLEDGE and other similar programs demonstrates that patient registries increase the complexity of providing and receiving care, and are extremely burdensome on prescribers, patients, and dispensers.

#### ***Existing DEA Registration Procedures Should Be Used To Track And Confirm Prescriber Education***

The Agency has indicated that one component of the REMS will be education intended to encourage prescribing and dispensing practices that would minimize the potential abuse and misuse of opioid drugs. In order to optimize risk mitigation, and to prevent prescribers from opting-out, the educational component of the REMS must eventually be mandatory or tied to incentives for all prescribers of controlled substances.

### ***Short-Acting Opioids Should Also Be Subject To The Class-Wide REMS***

In considering an opioid class-wide REMS, one critical determination is the scope of the class. In its discussions about a potential opioid class REMS, FDA statements indicate an intent to require the REMS only for extended-release oral, transdermal, and inherently long-acting opioids. However, drug abuse surveillance data, presentations at the May 2009 Public Hearing, and subsequent submissions to the opioid class REMS docket identify several compelling reasons to include short-acting opioid analgesics, including combination products, in the class as well. A broad-based approach would be impossible to achieve if REMS requirements were applied only to long-acting products. Indeed, rather than helping to discourage and potentially decrease abuse of all types of opioid-containing products, limiting REMS requirements only to long-acting products would inevitably lead to increased abuse of short-acting single-entity and combination opioid products exempted from the REMS.

### ***Implementing a Narrow REMS Covering Only Extended-release Oral, Transdermal, and Inherently Long-acting Opioids May Result in Substitution Prescribing***

Information presented at the May 2009 Public Hearing indicated that, if the REMS were restricted to extended-release oral, transdermal, and inherently long-acting opioids, prescribers would, for many reasons, become more likely to prescribe short-acting opioids in lieu of products covered by the REMS. Long-acting opioid medications have specific clinical uses and advantages within those uses that would be lost with substitution with other types of opioid medications. .

### ***Access To Appropriate Medicines Should Not Be Disrupted***

*The REMS should not interfere with the ability of prescribers to develop the most appropriate pain-care management regimen for patients, or discourage them from doing so. Any class REMS should recognize the importance of opioids in the management of pain and should not introduce new barriers to their appropriate and legitimate use.*

### **Summary and Recommendations:**

1. The problems FDA is seeking to solve with a class-wide opioid REMS, as well as obvious potential consequences (such as, fewer prescribers and reduced access to care) need to have clear definitions and baseline measurements to adequately assess the effectiveness of any REMS.
2. The REMS elements should be proven to reduce the defined problems before finalizing them as regulations, including the use of phased-in testing if no such evidence exists.
3. Any opioid REMS should include ALL classes of opioids, not just extended release opioids.
4. The REMS should not include a patient registry.
5. The REMS should include comprehensive, interoperable State Prescription Drug Monitoring Programs and FDA should appeal to Congress and the Administration for expansion of these programs, through greater funding of the NASPER law or other means.
6. Appropriate opioid education, developed by professional associations, should be voluntary for all prescribers of controlled substances until a system can be put in place that can verify education without disrupting the access to these important medicines and without disrupting the delivery of care. Any system should have minimal administrative burdens on both prescribers and dispensers
7. A strong, public campaign should be employed to educate the public about the risks of opioid misuse and diversion, the importance of securing their medication and proper disposal of unused opioids.