

*Agenda:* To discuss the annual strategic plan updating process and services and supports activities.

*Place:*

*In Person:* National Institutes of Health, William H. Natcher Conference Center, 45 Center Drive/Building 45, Conference Rooms E1/E2, Bethesda Campus, Bethesda, MD 20892.

*Videocast:* <http://videocast.nih.gov>.

*Contact Person:* Ms. Lina Perez, Office of Autism Research Coordination, Office of the Director, National Institute of Mental Health, NIH, 6001 Executive Boulevard, Bethesda, MD 20892-9669, (301) 443-6040. [IACCpublicinquiries@mail.nih.gov](mailto:IACCpublicinquiries@mail.nih.gov).

Any member of the public interested in presenting oral comments to the Committee should notify the Contact Person listed on this notice at least 10 days in advance of the meeting. Interested individuals and representatives of organizations should submit a letter of intent, a brief description of the organization represented, and a written/electronic copy of the oral presentation in advance of the meeting. Only one representative of an organization will be allowed to present oral comments and presentations will be limited to a maximum of five minutes. Both printed and electronic copies are requested following the presentation for the public record. In addition, any interested person may submit written comments to the Committee by forwarding the statement to the Contact Person listed on this notice. The statement should include the name, address, telephone number and when applicable, the business or professional affiliation of the interested person.

NIH has instituted stringent security procedures for entrance onto the NIH campus. All visitors must enter through the NIH Gateway Center. This center combines visitor parking, non-commercial vehicle inspection and visitor ID processing, all in one location. The NIH will process all visitors in vehicles or as pedestrians. You will be asked to submit to a vehicle or personal inspection and will be asked to state the purpose of your visit. Visitors over 15 years of age must provide a form of government-issued ID such as a driver's license or passport. All visitors should be prepared to have their personal belongings inspected and to go through metal detection inspection.

When driving to NIH, plan some extra time to get through the security checkpoints. Be aware that visitor parking lots on the NIH campus can fill up quickly. The NIH campus is also accessible via the metro Red Line, Medical Center Station. The Natcher Conference Center is a 5-minute walk from the Medical Center Metro Station.

Additional NIH campus visitor information is available at: <http://www.nih.gov/about/visitor/index.htm>. Information about the IACC and a registration link for this meeting are available on the Web site: <http://www.iacc.hhs.gov>.

(Catalogue of Federal Domestic Assistance Program Nos. 93.242, Mental Health Research Grants; 93.281, Scientist Development Award, Scientist Development Award for Clinicians, and Research Scientist Award;

93.282, Mental Health National Research Service Awards for Research Training, National Institutes of Health, HHS)

*Dated:* April 13, 2009.

**Jennifer Spaeth,**

*Director, Office of Federal Advisory Committee Policy.*

[FR Doc. E9-9033 Filed 4-17-09; 8:45 am]

**BILLING CODE 4140-01-P**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Centers for Disease Control and Prevention**

**Disease, Disability, and Injury Prevention and Control**

Special Emphasis Panel: Pilot Lifestyle Interventions for Pregestational Diabetes or Gestational Diabetes, Potential Extramural Project, PEP 2009-R-02

*Correction:* This notice was published in the **Federal Register** on March 25, 2009, Volume 74, Number 56, page 12873. The original notice was published with an incorrect Potential Extramural Project number.

*Contact Person for More Information:* Linda Shelton, Public Health Analyst, Coordinating Center for Health and Information Service, Office of the Director, CDC, 1600 Clifton Road NE., Mailstop E21, Atlanta, GA 30333. Telephone (404) 498-1194.

The Director, Management Analysis and Services Office, has been delegated the authority to sign **Federal Register** notices pertaining to announcements of meetings and other committee management activities, for both CDC and the Agency for Toxic Substances and Disease Registry.

*Dated:* April 9, 2009.

**Elaine L. Baker,**

*Director, Management Analysis and Services Office, Centers for Disease Control and Prevention.*

[FR Doc. E9-8947 Filed 4-17-09; 8:45 am]

**BILLING CODE 4163-18-P**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. FDA-2009-N-0143]

**Risk Evaluation and Mitigation Strategies for Certain Opioid Drugs; Notice of Public Meeting**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice of public meeting; request for comments.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing a public meeting to obtain input on developing Risk Evaluation and Mitigation Strategies (REMS) for certain opioid drugs. The REMS would be intended to ensure that the benefits of these drugs continue to outweigh certain risks. The agency has long been concerned about adverse events associated with this class of drug and has taken steps in cooperation with drug manufacturers to address these risks. We intend to use the agency's REMS authority under the Food and Drug Administration Amendments Act of 2007 (FDAAA) to mitigate the risks of these drugs. The purpose of the public meeting is to receive information and comments on this topic.

**DATES:** The public meeting will be held on May 27 and 28, 2009, from 8 a.m. to 5 p.m. Register to attend the meeting by May 15, 2009. See section III of this document for information on how to register or make an oral presentation at the meeting. Written or electronic comments will be accepted until June 30, 2009.

**ADDRESSES:** The public meeting will be held at the Hilton Washington, DC North/Gaithersburg Hotel, 620 Perry Pkwy., Gaithersburg, MD 20877. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.regulations.gov>. All comments should be identified with the docket number found in brackets in the heading of this document. Transcripts of the meeting will be available for review at the Division of Dockets Management and on the Internet at <http://www.regulations.gov> approximately 30 days after the meeting.

**FOR FURTHER INFORMATION CONTACT:** Theresa (Terry) Martin, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6184, Silver Spring, MD 20993-0002, 301-796-3448, FAX: 301-847-8752, or Anne Henig, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg 51, rm. 6176, Silver Spring, MD 20993-0002, 301-796-3442, FAX: 301-847-8753, email: [OpioidREMS@fda.hhs.gov](mailto:OpioidREMS@fda.hhs.gov).

**SUPPLEMENTARY INFORMATION:**

**I. Background**

FDAAA (Public Law 110-85) created section 505-1 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355-1). Under section 505-1 of the act,

FDA may require a REMS when FDA determines that a REMS is necessary to ensure the benefits of a drug outweigh the risks associated with the drug. On February 6, 2009, FDA sent letters to manufacturers of certain opioid drug products, indicating that these drugs will be required to have a REMS to ensure that the benefits of the drugs continue to outweigh the risks. An example of the text of these letters is available on the agency's Web site at [http://www.fda.gov/cder/drug/infopage/opioids/meeting\\_template.pdf](http://www.fda.gov/cder/drug/infopage/opioids/meeting_template.pdf). A table of opioid products that may be required to have REMS is also available on the agency's Web site at [http://www.fda.gov/cder/drug/infopage/opioids/Opioid\\_Products\\_chart.htm](http://www.fda.gov/cder/drug/infopage/opioids/Opioid_Products_chart.htm). Copies of these documents may also be requested from Terry Martin or Anne Henig (see **FOR FURTHER INFORMATION CONTACT**).

The affected opioid drugs include brand name and generic products and are formulated with the following active ingredients: Fentanyl, hydromorphone, methadone, morphine, oxycodone, and oxymorphone. The REMS would be intended to ensure that the benefits of these drugs continue to outweigh 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. REMS for opioids would likely 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. The purpose of this meeting is to examine specific features of REMS for these drugs and provide interested persons an opportunity to comment. The meeting will also address issues associated with creating and implementing the REMS and evaluating its effectiveness.

#### A. Opioids

Opioid drugs have effects similar or identical to those of opiates produced naturally in the opium poppy. On the molecular level, they act at protein sites called opioid receptors, which are found in the brain, spinal cord, gastrointestinal tract, peripheral nerve terminals, and other peripheral sites. The actions of these drugs at certain opioid receptors in the brain, spinal cord, and other sites can effectively block the transmission of pain messages to the brain. Opioid drugs currently marketed in the United States for pain relief include products formulated with active ingredients such as fentanyl, hydromorphone, methadone, morphine, oxycodone, and

oxymorphone. Individual patients respond differently to different opioid drug substances, and some patients develop tolerance to the effects of a particular opioid after chronic exposure. Physicians use a technique known as "opioid rotation" whereby they switch a patient from one opioid to another if the patient develops tolerance to the drug's analgesic effects and cannot get adequate pain relief from any single drug.

Some opioids are naturally long acting; others are incorporated into extended release formulations. Long acting opioids and extended release opioid formulations are often useful for the management of persistent, moderate to severe pain in patients requiring continuous, around-the-clock pain relief for an extended period of time. Long acting products allow these patients to have their pain controlled for long periods of time without the need for another dose and to significantly reduce the number of tablets the patient must take each day. Therefore, having long acting opioids and extended release opioid formulations available provides important pain relief options for patients who require management of persistent, moderate to severe pain.

The expected duration of treatment with long acting opioids and extended release opioid formulations ranges from a few weeks to months or longer. In some cases, moderate to severe pain requiring continuous, around-the-clock opioid therapy is associated with a serious condition that is unlikely to improve.

These types of opioids are widely prescribed, posing challenges for the development of REMS for these products. Long acting and extended release opioid formulations were used by nearly 4 million patients in the United States in 2007. Physicians who prescribe and administer long acting and extended release opioid drugs practice in a wide variety of areas including family practice, anesthesiology, internal medicine, orthopedic surgery, psychiatry, neurology, rheumatology, oncology, and other areas. A REMS, to adequately manage the risks of these products without unduly burdening the health care system or reducing patient access to these medications, must be carefully designed.

#### B. Adverse Events Associated With Opioids

The most serious of the known adverse events associated with opioid pain relievers are: Respiratory depression, central nervous system depression, addiction, and death.

Adverse events are associated with improper dosing, indication, and patient selection, as well as with abuse and addiction. For example, some products and doses are indicated only for the management of persistent moderate to severe pain in patients who have demonstrated opioid tolerance. Use of these products in non-opioid-tolerant patients may result in fatal respiratory depression. In other cases, when extended release products are intentionally crushed or dissolved, the controlled-release mechanism may be defeated, allowing a large dose to be taken at once. This presents a risk of fatal overdose, particularly in individuals who are not tolerant to opioids.

#### C. Efforts to Address the Risks of Opioid Use

FDA and drug manufacturers have taken steps to decrease abuse and misuse of long acting opioids and extended release opioids while seeking to ensure that they remain available for patients who suffer daily from chronic pain. Since 2001, FDA has required boxed warnings, the agency's strongest warning, on the labeling of long acting opioid drugs to educate physicians and patients on the risks and proper uses of these products. The agency has also required risk management plans for many of these products. These plans have incorporated educational programs for prescribers, pharmacists, and patients, and surveillance systems to monitor for signals of increasing abuse, misuse, and diversion, as well as plans for intervention when these signals are noted. In addition, drug manufacturers have sought to incorporate features into their products intended to deter abuse. For example, the active ingredient may be incorporated into a matrix from which it cannot easily be extracted or that is not easily ground into powder. In other cases, an opioid antagonist is sequestered in the inner core of an extended release tablet, designed to be released if the tablet is crushed or dissolved.

#### D. REMS for Long Acting and Extended Release Opioids

Despite existing efforts to address the risks associated with opioid drugs, misuse and abuse are increasing. Data from multiple sources, including the Centers for Disease Control (CDC) and the Substance Abuse and Mental Health Services Administration (SAMHSA), indicate increasing misuse and abuse of prescription opioid analgesic medications over the past decade. For example, SAMHSA's National Survey on Drug Use and Health estimates that

11 million Americans over the age of 12, or 4.7 percent of that population, took pain relievers for nonmedical use in 2002. That number increased to 12.5 million, or 5.0 percent of the population over 12, in 2007. Likewise, data compiled by SAMHSA show a significant increase from 2000 to 2006 in admissions to substance abuse treatment services for individuals abusing opioid analgesics. Much of this misuse has involved the extended release opioid analgesics and methadone. To address this public health problem, the agency has indicated it will require REMS for certain opioid products.

Section 505-1 of the act authorizes FDA to require persons submitting certain drug approval applications to submit a proposed REMS as part of the application. FDA may require a REMS when FDA determines that a REMS is necessary to ensure the benefits of the drug outweigh the risks associated with the drug. Section 505-1 of the act also authorizes FDA to require holders of certain drug applications approved without a REMS to submit a proposed REMS if the agency becomes aware of new safety information and makes a determination that a REMS is necessary to ensure the benefits of the drug outweigh the risks. Once FDA notifies the holder of an approved covered application that a REMS is necessary, the holder must submit a proposed REMS within 120 days, or within such other reasonable time as FDA requires.

Every REMS must include a timetable for the submission of assessments of the REMS. A REMS may also include a Medication Guide (as provided in 21 CFR part 208), a patient package insert, a communication plan, and certain "elements to assure safe use." The elements to assure safe use must include one or more goals to mitigate a specific serious risk listed in the labeling of the drug. These elements may include the following requirements:

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

The elements to assure safe use may also include an implementation plan, whereby the applicant monitors,

evaluates, and works to improve the implementation of certain of these elements. FDAAA states that when elements to assure safe use are required for a drug that is also marketed in one or more generic forms, the pioneer drug and the generic(s) shall use a single, shared system unless the generic applicant obtains a waiver in accordance with statutory criteria. A waiver may be granted if the burden of creating a single, shared system outweighs the benefits of a single, shared system or if an aspect of the elements to assure safe use is entitled to protection as a trade secret or is protected by a patent for which the generic applicant has unsuccessfully sought a license (section 505-1(i)(1) of the act).

We are mindful of the provisions in FDAAA that state the elements to assure safe use must be, among other things, commensurate with the specific serious risk listed in the labeling of the drug, not be unduly burdensome on patient access to the drug, and be designed to be compatible with established distribution, procurement, and dispensing systems (section 505-1(f)(2) of the act). Marketed opioid products include both innovator and generic drugs. FDAAA requires, with limited exception, that innovator and generic drugs use a single, shared system for a REMS that contains elements to assure safe use. Putting together a workable system will involve innovator and generic sponsors working together to develop a single, shared system.

## II. Scope of Meeting

FDA is holding this public meeting to allow affected sponsors and other interested persons to present comments and information on what a REMS should look like for these products, how to minimize the burden on the health care community and patients while achieving the objective of ensuring that the benefits of these drugs continue to outweigh the risks, and how FDA should evaluate the REMS to determine whether it is achieving these objectives.

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

### A. Elements of the REMS

1. FDA believes that one key element to assure safe use for these products will be prescriber certifications to ensure prescribers are educated about the risks of these products and proper patient selection, and the importance of counseling patients on the safe and appropriate use of their prescription medication. Please comment on what type of education should be provided to

prescribers and how this certification should be administered (e.g., through state Medical Boards, DEA (Drug Enforcement Agency), other Federal or state systems, or privately, through a contractor established to administer the REMS). Some combination of administration could also be considered.

2. FDA believes that another key element to assure safe use for these products will be certifications of pharmacists, prescribers, and other health care providers or institutions that dispense or directly administer covered opioid products to ensure these representatives of the health care system also are educated about the risks of these products and the importance of counseling patients on the safe and appropriate use of their prescription medication. These representatives of the health care system could be asked to check that the prescriber has obtained the certification necessary to prescribe these products. Please comment on what type of education should be provided to pharmacists and other health care providers who dispense or directly administer covered products and how this certification should be administered (e.g., through state Boards of Pharmacy, DEA, other Federal or state systems, or privately, through a contractor established to administer the REMS). Some combination of administration could also be considered.

3. FDA believes patient education, in conjunction with a prescriber-patient agreement, is another key element of the REMS. What education should be provided to patients, and should the system be designed to ensure such education is provided? For example, other REMS programs require prescriber-patient agreements that patients sign before receiving a prescription to acknowledge that they have been advised about the risks and appropriate use of the products and received a Medication Guide or other appropriate patient information. Is such a system necessary for opioid products?

4. Are other REMS elements necessary to support the safe use of approved opioids? A list of possible REMS elements is provided in section I.D of this document.

### B. System Issues

1. How restrictive a system should be designed? For example, in some previously approved risk management systems, covered drugs are provided only when prescribers, pharmacists, and patients are all enrolled in a program designed to ensure that all understand the risks and appropriate use of the

products. Such systems have been put in place for drugs that are or are suspected to be teratogenic, and the programs are designed to ensure patients are not pregnant and will not become pregnant while taking the drug. Such systems create burdens on patients and the health care system. Is such a system necessary for opioids? How would such a program be implemented given the number of patients, prescribers, and other health care providers involved in their use?

2. Should the REMS include controls on distributors who distribute products to pharmacies and other health care providers? What controls are necessary, and how can they be efficiently provided without being unduly burdensome on the health care system?

3. What existing systems (for example, in pharmacies) already exist that could be used to implement a REMS? For example, could patient information be provided through existing pharmacy systems to patients? Are there systems for providing education to prescribers that could be used to provide the educational component of a REMS?

4. FDAAA requires that innovator and generic application holders use a single, shared system to provide a REMS with elements to assure safe use. What obstacles need to be addressed before such a system could be developed?

5. What metrics should be used to assess the success of the REMS? Please comment on the metrics that should be applied to measure the success of each of the components of the REMS (e.g., educational requirements) as well as metrics to assess the impact of the overall REMS on decreasing abuse and misuse of long acting opioids and extended release opioids while seeking to ensure that they remain available for patients who suffer daily from chronic pain.

### III. Attendance and Registration

Register via email to [OpioidREMS@fda.hhs.gov](mailto:OpioidREMS@fda.hhs.gov) by providing complete contact information for each attendee (including name, title, affiliation, address, email address, and phone number(s)) by May 15, 2009. Registration is free and will be on a first-come, first-served basis. Early registration is recommended because seating is limited. Please send no more than two individuals from your organization. Registration on the first day of the meeting will be provided on a space available basis beginning at 8 a.m.

If you wish to make an oral presentation at the meeting, you must indicate this at the time of registration. FDA has included questions for

comment in section II of this document. You should also identify by number each question you wish to address in your presentation. FDA will do its best to accommodate requests to speak. Individuals and organizations with common interests are urged to consolidate or coordinate their presentations, and to request time for a joint presentation. FDA will determine the amount of time allotted to each presenter and the approximate time that each oral presentation is scheduled to begin. If you need special accommodations because of disability, please e-mail [OpioidREMS@fda.hhs.gov](mailto:OpioidREMS@fda.hhs.gov) at least 7 days before the meeting.

### IV. Comments

Regardless of attendance at the public meeting, interested persons may submit written or electronic comments to the Division of Dockets Management (see **ADDRESSES**). Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. To ensure consideration, submit comments by June 30, 2009. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

### V. Transcripts

Transcripts of the meeting will be available for review at the Division of Dockets Management and on the Internet at <http://www.regulations.gov> approximately 30 days after the meeting. A transcript will also be made available in either hard copy or on CD-ROM, upon submission of a Freedom of Information request. Written requests are to be sent to Division of Freedom of Information (HFI-35), Office of Management Programs, Food and Drug Administration, 5600 Fishers Lane, rm. 6-30, Rockville, MD 20857.

Dated: April 14, 2009.

**Jeffrey Shuren,**

*Associate Commissioner for Policy and Planning.*

[FR Doc. E9-8992 Filed 4-17-09; 8:45 am]

**BILLING CODE 4160-01-S**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

#### Amended Notice

The purpose of this notice is to inform the public that the National Institutes of

Health (NIH) is cancelling the May 5, 2009 meeting of the NIH Blue Ribbon Panel to Advise on the Risk Assessment of the National Emerging Infectious Diseases Laboratories at Boston University Medical Center. The announcement for the May 5, 2009 meeting was previously published in the **Federal Register** on April 3, 2009 (74 FR 15296).

The meeting will be rescheduled and the new date for the meeting will be announced and published in the **Federal Register**.

Dated: April 14, 2009.

**Kelly Fennington,**

*Special Assistant to the Acting Director, Office of Science Policy, National Institutes of Health.*

[FR Doc. E9-9037 Filed 4-17-09; 8:45 am]

**BILLING CODE 4140-01-P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

#### National Heart, Lung, and Blood Institute; Notice of Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of a meeting of the National Heart, Lung, and Blood Advisory Council.

The meeting will be open to the public as indicated below, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

*Name of Committee:* National Heart, Lung, and Blood Advisory Council.

*Date:* June 10, 2009.

*Open:* 8 a.m. to 12 p.m.

*Agenda:* To discuss program policies and issues.

*Place:* National Institutes of Health, Building 31, 31 Center Drive, C-Wing, Room 10, Bethesda, MD 20892.

*Closed:* 1 p.m. to 5 p.m.