DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
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STATEMENT

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"EXAMINING THE FEDERAL GOVERNMENT'S RESPONSE TO THE PRESCRIPTION DRUG ABUSE CRISIS"

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INTRODUCTION

Mr. Chairman, Ranking Member Pallone, and Members of the Subcommittee, I am Dr. Douglas Throckmorton, Deputy Director for Regulatory Programs in the Center for Drug Evaluation and Research at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to be here today to discuss the epidemic of misuse, abuse, and diversion of prescription drugs, especially prescription opioids, in the United States.

This is a problem that has cast a terrible shadow across our nation and led to a public health crisis of devastating proportions. It is a crisis that has affected us all, and meaningful and enduring solutions will require all of our collective efforts.

Many of us are all too familiar with the numbers associated with this epidemic. According to the latest estimates from the Centers for Disease Control and Prevention (CDC), in 2010, prescription opioid drugs were involved in 16,650 overdose deaths, a 313 percent increase over the past decade. And the Substance Abuse and Mental Health Services Administration (SAMHSA) reports that for each death, there are an additional nine treatment admissions,[1] 32 emergency department visits, [2] and 734 non-medical users of these drugs. [3] Although the problem partly is attributable to inappropriate or illicit use, such as sharing

[1] Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. *Treatment Episode Data Set (TEDS): 2000-2010. National Admissions to Substance Abuse Treatment Services.* DASIS Series S-61, HHS Publication No. (SMA) 12-4701. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2012.

[2] Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality, SAMHSA, Drug Abuse Warning Network, 2010 available at *http://www.samhsa.gov/data/dawn/nations/Nation_2011_AllMA.xls*.

[3] Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. *Results from the 2011 National Survey on Drug Use and Health:* detailed table 1.1A (HHS Publication No. SMA 12-4713, NSDUH Series H-44). Rockville, MD: Substance Abuse and Mental Health Services Administration, 2012.

medication with family and friends or theft of the drug from home medicine cabinets, legitimate use of medications for pain may also lead to unnecessary adverse events, addiction, and death for some patients. Beyond these grim statistics, we find individuals and their families whose lives have been shattered by prescription opioid abuse, misuse, and addiction.

We play a critical role in the development, review, and approval of drugs. FDA reviews applications for opioid medical products, requires accurate drug prescribing information, and monitors how these products are used once they go to market—and a balance must be struck between their benefit in treating patients and the risks associated with misuse, abuse, and addiction to those patients and to others.

Combating opioid misuse, abuse, and addiction has long been a priority for the Agency, and FDA has taken many steps to address this problem over the last few decades. We have taken action to build upon existing initiatives and develop new ones, including establishing a task force to focus on this critical issue.

Over the last decade or so, FDA has worked to pursue a targeted, science-based, multi-pronged approach that addresses misuse, abuse, and addiction at critical points in the development of an opioid product and in its use throughout the health care system. This comprehensive approach includes five broad areas:

- Encouraging scientific work into the development of safe and effective treatments for pain and into the most appropriate uses of pain medicines;
- Encouraging the development of abuse-deterrent drug formulations for opioids;
- Working to improve the appropriate use of opioids to treat pain through prescriber and patient education;

- Evaluating opioid labeling, and
- Improving the availability of products that treat abuse and overdose.

Research, Scientific, and Development Needs

As a scientific and public health regulatory agency, FDA's approach to regulation of prescription opioids must be grounded in science; specifically, we must bring to bear the best available knowledge and understanding concerning both the treatment of pain and potential adverse consequences of opioid use. FDA has long been committed to obtaining the best information possible about the appropriate and safe use of opioid drugs in pain management. For example, we held a joint meeting with the National Institutes of Health last May on what is known scientifically about the efficacy of opioids in treating chronic non-cancer pain. And we are continuing to work with academics and other scientists to ensure that we have reliable data to guide FDA's decision-making on these complex and challenging issues.

The Food and Drug Administration Safety and Innovation Act (FDASIA, Pub. Law 112-144) required FDA to "hold a public meeting to solicit advice and recommendations to assist in conducting a scientific and medical evaluation in connection with a scheduling recommendation to the Drug Enforcement Administration (DEA) regarding drug products containing hydrocodone, combined with other analgesics or as an antitussive." That meeting took place on January 24-25, 2013. The Advisory Committee was provided data and heard presentations from various experts, and then the majority of the Committee voted to recommend rescheduling hydrocodone combination products from Schedule III to Schedule II.

FDA also received and is in the process of reviewing 768 comments from the public—patients, parents, and health care professionals such as dentists, nurse practitioners, ophthalmologists and physicians—expressing their views on rescheduling. The data provided at the meeting, public comments, and the Committee's recommendation will help inform FDA's scheduling recommendation.

Abuse-deterrent Formulations

The continued development of opioids that are specifically formulated to deter abuse is an important component of our twin goals of minimizing abuse and misuse of prescription opioids while maintaining and improving access to these medications for patients who need them. Abuse-deterrent formulations target known or expected routes of abuse, such as crushing the product or extracting the active ingredient from the product to facilitate rapid release of the opioid following swallowing, snorting, or injection.

FDA is working to encourage the development of abuse-deterrent forms of opioid medicines. First, in January of this year, FDA issued a draft guidance document on the development of abuse-deterrent opioid drug products, as required by FDASIA. The draft guidance sets forth FDA's current thinking regarding the studies that should be conducted to demonstrate that a given formulation has abuse-deterrent properties, how those studies will be evaluated by FDA, and what labeling claims may be approved based on the results of those studies. FDA will participate in an upcoming public meeting to discuss the issues addressed in the draft guidance on September 30 and October 1, 2013.

FDA has also recently taken regulatory actions regarding two opioid products—OxyContin and Opana ER—that were reformulated with the intention of making the products

more difficult to manipulate for purposes of abuse. The regulatory implications have been the subject of independent, extensive consideration by FDA experts over the course of many months. Our decisions took into account the totality of the evidence for the particular drug at issue and were made on a case-by-case basis.

First, on April 16, 2013, FDA approved updated labeling for Purdue Pharma L.P.'s reformulated OxyContin that describes its abuse-deterrent properties; specifically, the new labeling indicates that the product has physical and chemical properties that are expected to make abuse via injection difficult and reduce abuse via the intranasal route (snorting). The Agency also decided that the company's original formulation had been withdrawn for safety or effectiveness reasons, because it posed an increased potential for abuse by snorting and injecting, compared to reformulated OxyContin. As a result, FDA will not approve any generic versions of the original formulation of OxyContin.

Second, on May 10, 2013, FDA determined that the original formulation of Opana ER was *not* removed from the market for safety or effectiveness reasons, because the available evidence was insufficient to conclude that the original formulation had an increased potential for abuse compared to reformulated Opana ER. While there is an increased ability of the reformulated Opana ER to resist crushing relative to the original formulation, study data show that the reformulated version's extended-release features can be compromised when subjected to other forms of manipulation, such as cutting, grinding, or chewing, followed by swallowing. As a result, FDA will not take steps to remove existing generic versions of the original formulation from the market and will continue to approve such generics, so long as they meet all applicable requirements.

Although these actions had different outcomes based on the science presented, they demonstrate that FDA can and will act in this area to exercise our regulatory authority to protect the public health. While we intend to take a flexible, adaptive approach to the evaluation and labeling of potentially abuse-deterrent products, we will be driven by science and the data presented to us for each product to ensure that products that claim to be abuse-deterrent actually deter abuse.

While we recognize that abuse-deterrent formulations are not a panacea, they are an important part of a multi-faceted approach to the epidemic of prescription drug abuse.

Prescriber and Patient Education

Prescribers and patients both play a critical role in preventing the abuse and misuse of opioids, and FDA has taken a number of steps to educate these groups. On March 1, 2013, FDA issued an open letter asking all prescribers of opioids to ensure that they have a thorough knowledge of the FDA-approved product labeling for the opioids they prescribe and to ensure that they have adequate training in opioid therapy. The letter was supported by the American Medical Association, American Academy of Family Physicians, and other leading health professional groups.

The Federal Food, Drug, and Cosmetic Act, as amended by the Food and Drug Administration Amendments Act of 2007, authorizes FDA to require sponsors to develop and comply with risk evaluation and mitigation strategies (REMS) when necessary to ensure that the benefits of a drug outweigh the risks. In July 2012, after a three-year effort, FDA approved a REMS for manufacturers of over 20 extended-release and long-acting (ER/LA)

opioids. This REMS acknowledges that our nation's front-line health care professionals play an important role in efforts to reduce the abuse and misuse of opioids.

It is also critically important to improve prescribers' knowledge about the best uses of opioids, including knowing when these products should be used and by which patients. Thus prescriber education is an important element of this REMS for ER/LA opioids. Under the ER/LA opioid REMS, manufacturers are required to ensure that prescriber training programs—offered by accredited continuing education providers—are made available for all U.S.-licensed prescribers, using a syllabus developed by FDA with input from many stakeholders. As a part of our assessment of this REMS, these courses will be audited to ensure that they are unbiased and accurate.

The first of these voluntary prescriber training programs was rolled out on March 1, 2013, and others will soon follow. Training is an important public health measure, and the Administration continues to support mandatory education for prescribers, as called for in the 2013 National Drug Control Strategy.

Finally, FDA tries to use its platform as a public health agency to educate patients and prescribers about the appropriate use and potential risks of drugs. In addition to training for prescribers, patients also need access to educational materials to help guide the use of opioid medicines. Under the REMS for ER/LA opioids, manufacturers have developed a patient-friendly counseling tool for prescribers to give to every patient, when they write a prescription for an ER/LA opioid. The REMS also includes a product-specific Medication Guide to be provided to the patient when they pick up their prescription. Included in these materials is information on how to safely store medications, while it is still in use, and what to do with the leftover supply, when it is no longer needed. Given the importance of educating patients, we

are also partnering with other groups. For instance, FDA and SAMHSA are working with the National Council on Patient Information and Education in a patient education campaign aimed at teenagers and college students.

Opioid Labeling

The primary tool that FDA uses to inform prescribers about the approved uses of medications is the approved product labeling (or package insert). The approved information is based on scientific and clinical information gathered about the drug, including clinical pharmacology studies, animal studies, clinical studies and post-market experience. It is important to note that FDA does not regulate the practice of medicine, and how an opioid product is prescribed is dependent on the prescriber's assessment of the benefits and risks to a particular patient based on factors, including the patient's pain management needs.

Over the past several years, FDA has made many changes to opioid product labeling in an effort to improve their proper use and to reduce their misuse and abuse. Today these labels have some of the most restrictive language that can be found in drug labeling, including a boxed warning about their potential for abuse, which calls attention to serious or life-threatening risks. In response to calls to further restrict the indications for these products and make changes to the labeling, we have held public meetings as recently as February of this year to get input on opioid labeling and identify what data exist that could inform further review of the labeling. We are currently reviewing that information and comments from stakeholders to determine whether additional changes are appropriate.

Finally, with regard to improving the labeling for opioids, FDA agrees that opioid exposure from misuse or abuse can create significant problems for mothers and infants and

that the labeling needs to be accurate. Current FDA-approved labeling for opioid medications addresses the effects of *in utero* exposure on neonates and advises against the use of opioids in women during and immediately prior to labor and delivery. Labeling also addresses the effects of opioid exposure to newborns of mothers who continue to use opioids while nursing. Recently, the dangers of opioid withdrawal in infants born to mothers who were using opioids have been raised, and FDA is reviewing the labeling of opioids to ensure that it accurately reflects the available data on the effects of opioid exposure in pregnant and nursing women and their infants.

Products to Treat Overdose and Abuse

Finally, FDA has been working with many other stakeholders to explore the best ways to treat overdoses of opioids, including overdoses of FDA-approved opioid medications. In 2009 and 2010, over 15,000 people died from an overdose involving opioid medications. Naloxone is an injectable medication that is the standard treatment to rapidly reverse the overdose of either prescription (e.g., oxycodone) or illicit (e.g., heroin) opioids. Naloxone is most commonly used by trained medical personnel in emergency departments and on ambulances. There is a growing interest by prescribers and patients in exploring the broader uses of naloxone, including its use in non-medical settings such as nursing homes.

FDA, working with other parts of the Federal Government, is looking at how naloxone may be delivered safely in ways that are potentially easier to use and do not require needles or syringes. Any such product would be subject to FDA review. FDA is providing priority regulatory assistance to manufacturers who are working on new ways of giving naloxone,

using autoinjectors or intra-nasally, that would be easier to use in non-medical settings. FDA approval would be contingent on the safety and effectiveness of the new product.

CONCLUSION

In summary, we face an ongoing challenge and a dual responsibility—we must balance efforts to address misuse, abuse, and addiction that harm our families and communities against the need for appropriate access and the pain management needs of patients who rely on these important medications. There can be no doubt that there is much to be done—and we must act now. In my testimony I have discussed some of the many activities that FDA is working on in this area. These are not simple issues and there are no easy answers. Given the complexity of the issues surrounding the abuse, misuse, and addiction to prescription painkillers, real and enduring progress will require a multi-faceted approach combined with the dedication, persistence, and full engagement of all parties. We welcome the opportunity to work with Congress, our Federal partners, the medical community, advocacy organizations, and the multitude of interested communities and families to turn the tide on this devastating epidemic.

Thank you for your continued interest in this important topic and for the opportunity to testify regarding FDA's contributions to progress on this issue. I am happy to answer any questions you may have.