DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
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STATEMENT

OF

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BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

COMMITTEE ON ENERGY AND COMMERCE

U.S. HOUSE OF REPRESENTATIVES

"What is the Federal Government Doing to Combat the Opioid Abuse Epidemic?"

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INTRODUCTION

Mr. Chairman, Ranking Member DeGette, and Members of the Subcommittee, I am Dr. Douglas Throckmorton, Deputy Director for Regulatory Programs, within the Center for Drug Evaluation and Research (CDER) 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 important role that FDA plays in combating opioid abuse and encouraging the safe use of these drugs by patients, as part of FDA's mission to protect and promote the public health by ensuring the safety, efficacy, and quality of medical products.

Opioid analgesics (e.g., hydrocodone, oxycodone, morphine, and fentanyl) play a vital role in the treatment of pain and the availability of multiple effective pain medicines, including opioids, for patients with pain is an important component of proper pain management. Because individual patients respond differently to pain medications, having a variety of pain drugs available is important to meet the needs of patients. Unfortunately, in addition to this important role in the management of pain, the abuse and misuse of opioid medications has become a public health crisis. Recognizing this, combating opioid misuse, abuse, addiction, and overdose is a priority for the Agency, and FDA has taken many steps to address this problem. As a science-based Agency, our work is guided by all of the available information, including basic science, clinical trials, and studies looking at the epidemiology of opioid use and abuse. In my remarks, I'd like to discuss just a few of the important FDA activities we believe are making a difference in this

crisis; activities we believe will help ensure the continued availability of these important medications for patients who genuinely need them, while also reducing the risks of their abuse and misuse. I will do this by discussing these examples within a context of the larger role FDA plays in regulating medicines in the United States.

I would like to note at the outset, however, that while FDA plays an important role, we cannot fix the opioid misuse and abuse epidemic alone. A successful and sustainable response will require the action of many stakeholders. This hearing helps to highlight the broad range of work going on in many parts of the Federal government aimed at reducing opioid abuse and improving the safe use of opioid medicines, and you will hear today from our other Federal partners about the various complementary efforts they are undertaking to address this complex issue. To succeed, this comprehensive approach must include Federal and state governments, public health, opioid prescribers, addiction experts, researchers, industry, patient organizations, and others. Working together, we can and must address opioid abuse and misuse now.

FDA's Role

When FDA reviews a drug product application to determine whether the drug is safe and effective, we also approve labeling that describes approved uses for the medicine, potential safety risks, and other information to support safe use of the medicine—information that health care providers can then use to make the decision about what is best for their patients.

As with other drugs, the Agency carefully reviews the evidence to determine whether a new opioid product's expected benefits outweigh its potential risks. In addition, we also consider the risk that could occur if opioid drugs are misused or abused.

FDA also carefully follows opioid medicines after they are on the market so that we can understand how they are being used in clinical practice and measure their impact on the public health. Where necessary, this enables us to make changes to the labeling of these drugs to improve their safe use.

Next, I'd like to discuss a few of the initiatives FDA is taking to facilitate the development of safer pain medicines, as well as actions we have taken to support the appropriate use of opioid analgesics.

Abuse-deterrent Formulations of Opioids

One area of great promise to reduce the abuse of opioids is to develop formulations that are specifically designed to deter abuse. 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, with a goal of reducing the abuse of the product.

While not a silver bullet that will prevent all abuse, FDA sees the development of these abuse-deterrent opioids as an important step toward balancing appropriate access to opioids for patients with pain with the critical need to reduce opioid misuse and abuse.

Given the importance of this balance, the essential features of successful abuse-deterrent formulations are: (1) the product must deliver a consistent and effective dose of opioid when used as intended for pain management, and (2) based on the science, the product's potentially abuse-deterrent properties can be expected to, or actually do, result in a significant reduction in that product's abuse potential. In addition, the labeling that describes the abuse-deterrent features of the product must be based on scientific data, and any labeling based on premarket studies must be confirmed using post-market data to assess abuse deterrence in everyday clinical practice.

To incentivize the development and broad use of these new opioid drug products with abuse-deterrent features, FDA first created a draft guidance in 2013 that lays out a roadmap for developers to follow. Since then, we have carefully reviewed comments from scientists, academics, and manufacturers to refine and improve that draft. On April 1, 2015, FDA issued the final guidance on abuse-deterrent formulations of opioids. In addition to laying out the pathway for drug makers to follow in developing these products, it sets forth how we intend to review data submitted regarding the products' potentially abuse-deterrent properties and how we will evaluate proposed labeling describing those properties.

In addition, we are actively meeting with manufacturers about developing these products and to date, we have approved four opioid formulations with abuse-deterrent claims in their labeling. Importantly, the sponsors of these products—and the sponsor of any future products so labeled—are required to study the impact of their products' abuse-deterrent properties on actual abuse in the community, and FDA will revisit the labeling of these products as necessary, based in part on the results of these studies. We hope this labeling will encourage practitioners to integrate these products into their practices.

With FDA's focus on abuse-deterrent opioid products, including the labeling guidance and last October's public meeting, which discussed a range of regulatory issues related to these products, interest in producing these products has increased dramatically: FDA has already received some 30 investigational new drug (IND) applications from manufacturers seeking to conduct clinical trials on potential abuse-deterrent products. Many of these manufacturers are exploring promising alternatives to the currently marketed abuse-deterrent formulations, which are primarily designed to resist crushing and extraction. The INDs that we have received present a fascinating array of scientific techniques and approaches to abuse-deterrent formulation. And it helps FDA envision a day, not so far in the future, when the majority of opioids in the marketplace are in effective, abuse-deterrent forms; forms that substantially reduce all forms of abuse, including abuse by the oral, intranasal, and intravenous routes.

Labeling Changes for Opioids

The second activity I would like to discuss relates to work FDA is doing to improve the information available to prescribers about how best to use opioid medications and to help prescribers determine if an opioid is the right choice for their patient. The primary tool that FDA uses to inform prescribers about the approved uses of medications is the product labeling. The approved information, which includes scientific and clinical information gathered about the drug, including clinical pharmacology studies, animal studies, clinical studies, and post-market experience, is used by prescribers to make the decisions about what is best for their patients.

As mentioned before, FDA continuously monitors the use of drugs in the marketplace. Using what we have learned, over the past several years, FDA has made significant changes to opioid product labeling in an effort to improve their safe use and to reduce their misuse and abuse. For example, based on our analysis of the serious risks of abuse, addiction, overdose, and death associated with the currently marketed extended-release, long-acting (ER/LA) opioids, we determined that changes needed to be made to their labeling to help provide additional information to prescribers.

Last year we changed the indication for these products to inform practitioners that these drugs should only be used for pain severe enough to require daily, around-the-clock treatment, when alternative treatment options, including non-opioid analgesics, were ineffective, not tolerated, or would be otherwise inadequate to provide sufficient pain relief.

FDA has also significantly augmented the safety warnings for these opioids, and today the labels for ER/LA opioid medicines have some of the most restrictive language that can be found in drug labeling, including a boxed warning about their potential for abuse and clear language that calls attention to potential serious or life-threatening risks of opioids, including the risk of fatal overdose. We also added a warning that maternal use of these products during pregnancy can result in neonatal opioid withdrawal syndrome (NOWS), which may be life-threatening and require careful management, according to protocols developed by neonatology experts. NOWS can occur in a newborn exposed to opioid drugs while in the mother's womb. With these changes, FDA is working to support the safest possible uses of these powerful medicines in appropriately selected and monitored patients.

Prescriber and Patient Education

FDA also is working in other ways to improve the information available to prescribers of opioid medications. It is critically important to ensure that prescribers have adequate, high-quality education in appropriate pain management, including the use of opioids. It is also important that prescribers know the content of the most current drug labels to help them determine whether these products are appropriate for their patients and to help them educate their patients about the appropriate use of opioids, their potential risks, and proper storage and disposal techniques.

Under appropriate circumstances, FDA can require manufacturers to develop risk evaluation and mitigation strategies (REMS) to ensure that the benefits of a drug outweigh the risks. In July 2012, after an extensive review, FDA approved a REMS for manufacturers of ER/LA opioids.

This REMS acknowledges the critical role that our nation's front-line health care professionals play in efforts to reduce the abuse and misuse of opioids. To assist prescribers, as an important element of this REMS, manufacturers are required to fund the development of continuing education programs on proper opioid-prescribing practices for prescribers. These programs are provided by accredited continuing education providers, using a syllabus developed by FDA, with input from many stakeholders, and are audited to ensure the content is accurate and unbiased. Using these voluntary prescriber training programs will assist prescribers in their efforts to treat appropriately selected patients with opioids and minimize the risks of abuse and misuse.

The first of these voluntary prescriber training programs was rolled out on March 1, 2013. Although this training is an important public health measure, FDA continues to support mandatory education for prescribers, as called for by the Administration in the 2011 Prescription Drug Abuse Prevention Plan, and re-emphasized in the 2014 National Drug Control Strategy.

FDA also recognizes the importance of providing educational materials for patients. 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 prescriptions. Included in these materials is information on how to safely store medications, while still in use, and what to do with the leftover supply, when it is no longer needed. These educational programs for both providers and patients are an important part of the comprehensive approach to reducing opioid misuse and abuse. In addition, these programs serve as a part of the Secretary's Opioid Initiative, which focuses on improving prescribing practices, expanding the use of naloxone to reverse opioid overdose, and enhancing access to medication-assisted treatment for opioid use disorders.

Rescheduling of Hydrocodone Combination Products

FDA also plays a role in limiting inappropriate access to opioids, as demonstrated by our role in recommending additional restrictions on the use of hydrocodone-containing, fixed-combination drugs. For the hydrocodone combination products, after our analysis, HHS recommended that the Drug Enforcement Administration (DEA) move these products from Schedule III to the more restrictive Schedule II. We based our recommendation on factors including the products' actual or relative potential for abuse, their liability to cause dependence, and dangers they might pose to public health. Rescheduling took effect in October of last year.

Increasing Access to Naloxone

Finally, FDA understands the critical importance of preventing overdose deaths—the most devastating consequence of this public health crisis. We have been working with many other stakeholders to explore the best ways to treat overdoses of opioids, including overdoses of FDA-approved 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's ability to reverse opioid overdose has long been recognized. But for many years, the available products were primarily used by medical personnel and not always well-suited for use by others. That is why FDA, in collaboration with other agencies across the Federal government, has sought to facilitate the development of naloxone formulations that would be easier to use by anyone responding to an opioid overdose in the community.

To make progress on this goal, we used our expedited review programs, including fast-track designation and priority review, to approve the first auto-injector formulation of naloxone, which is intended to be administered by patients and their families and caregivers. An auto-injector has the advantage of being easier and quicker to use in an emergency situation than vial and/or syringe formulations that are currently approved. As an example of the priority that the Agency places on our role in helping address the abuse and overdose crisis, we completed our review and approved this product in just 15 weeks so that auto-injectors could be made available as quickly as possible.

Recognizing the pressing need for additional formulations and routes of delivery of naloxone, we continue to use our expedited review programs to speed the progress of new formulations of naloxone. Having an approved product is a major step forward, but it's also crucial to get it into the hands of people so they can use it when and where it's needed. That's why FDA, in partnership with other HHS agencies, is planning a public meeting in July to bring together key stakeholders to deal with questions of access, co-prescribing of naloxone along with opioids, and state and local best practices.

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 access to appropriate pain management. 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 this issue, 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.