



FDA Policies and Actions Related to the Development and Use of Opioids to Treat Pain

**Douglas C. Throckmorton MD
Deputy Director for Regulatory
Programs
CDER, FDA**

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The opinions and information in this presentation are my own and do not necessarily reflect the views and policies of the FDA

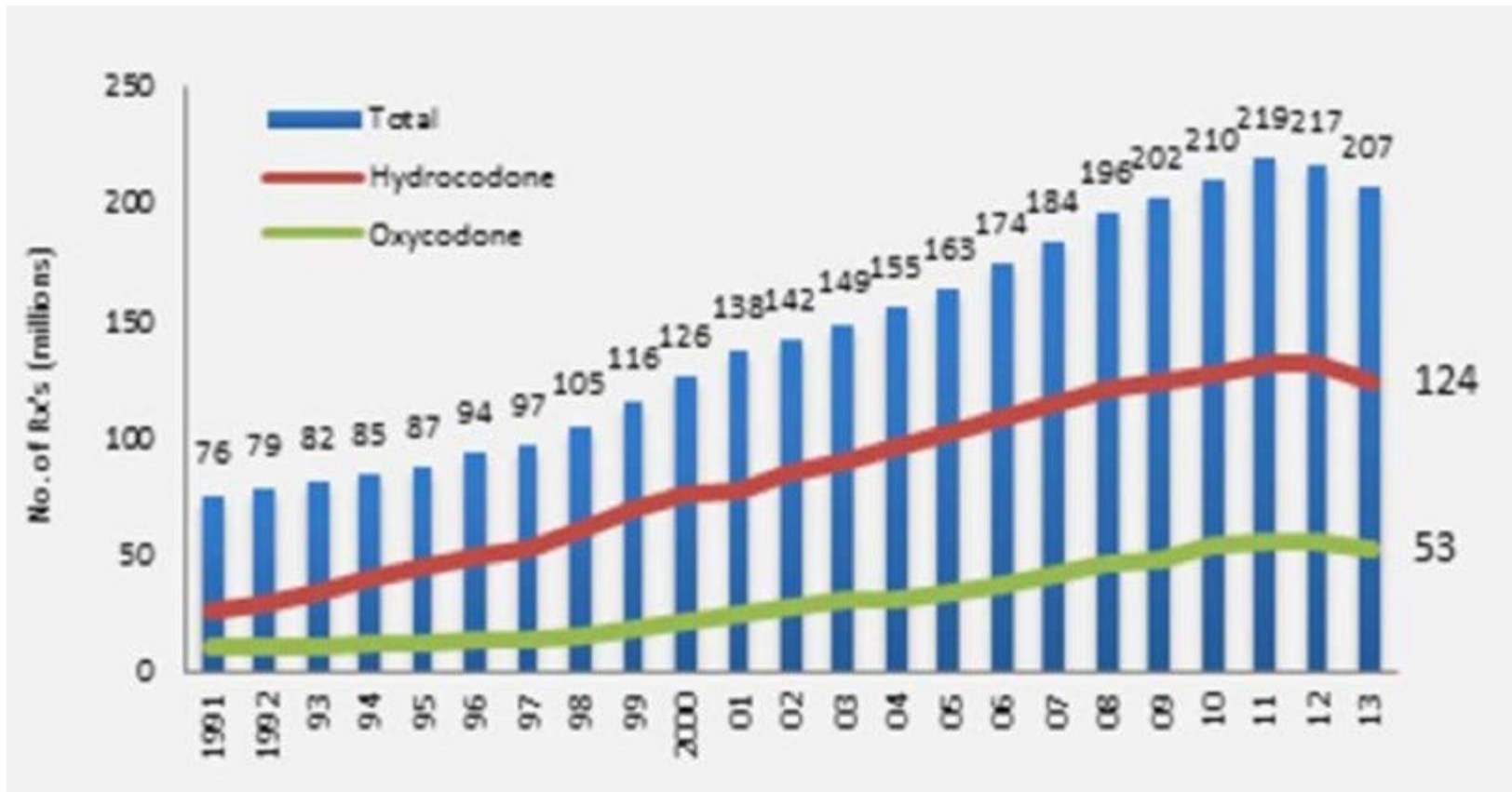
Outline

- Context for FDA Efforts to Address Prescription Opioid Abuse
 - Other Federal Efforts
- FDA Action Plan and Goals
- Types of Activities FDA is Undertaking
 - Selected examples

Overall Message

- The FDA work to improve the safe use of opioids is taking place within a larger policy framework aimed at addressing opioid abuse while assuring appropriate access to pain treatment
- Ongoing and planned activities reflect the commitment by FDA to integrate the use of all of our available tools to achieve our goals related to the safe use of prescription opioids

Prescriptions for Opioid Analgesics Dispensed by US Retail Pharmacies



From: <https://www.drugabuse.gov/about-nida/legislative-activities/testimony-to-congress/2016/americas-addiction-to-opioids-heroin-prescription-drug-abuse>

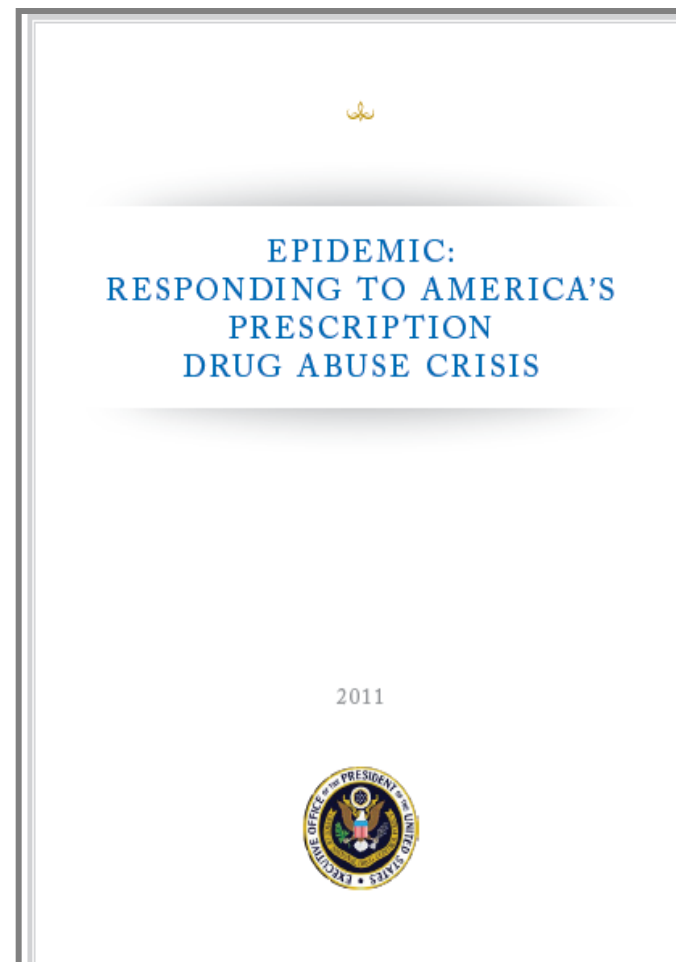


FDA is a Part of Larger Governmental Response to Opioids Abuse

Office of the National Drug Control
Policy Plan and
Health and Human Services
(HHS) Secretary's Plan

ONDCP National Drug Abuse Prevention Plan

- Issued April 2011
- Four major areas of focus to reduce prescription drug abuse and other harm from drugs
 - Education
 - Monitoring
 - Proper medication disposal
 - Enforcement



HHS Secretary's Initiative to Combat Opioid Abuse

- Improving opioid prescribing practices to reduce opioid use disorders and overdose
- Expanding use and distribution of naloxone
- Expanding Medication-assisted Treatment (MAT) to reduce opioid use disorders and overdose

Other Critical US Governmental Efforts FDA is Supporting

- **National Pain Strategy**

- Focuses on key areas of pain and pain care, including professional education and training, public education and communication, service delivery and reimbursement

- <http://iprcc.nih.gov/docs/DraftHHSNationalPainStrategy.pdf>

- **National Pain Research Strategy**

- Strategic plan under development for pain research across federal agencies

- **CDC Guidelines for Prescribing Opioids for Chronic Pain**

- Provides recommendations for the prescribing of opioid pain medication focused on the use of opioids in treating chronic pain

- <http://www.cdc.gov/drugoverdose/prescribing/guideline.html>



FDA Response to Opioids Abuse



FDA Action Plan (February 4, 2016)

- In response to the opioid abuse epidemic, today Dr. Robert Califf, the FDA's Deputy Commissioner for Medical Products and Tobacco, along with other FDA leaders, called for a far-reaching action plan to reassess the agency's approach to opioid medications. The plan will focus on policies aimed at reversing the epidemic, while still providing patients in pain access to effective relief.

FDA Opioids Action Plan

- Expand use of advisory committees
- Develop warnings and safety information for immediate-release (IR) opioid labeling
- Strengthen postmarket requirements to get needed data
- Update Risk Evaluation and Mitigation Strategy (REMS) Program
- Expand access to abuse-deterrent formulations (ADFs) to discourage abuse
- Support better treatment
- Reassess the risk-benefit approval framework for opioid use

Center for Drug Evaluation (CDER) Activities Reflect the Action Plan

- Provide patients in pain access to effective relief
- Reduce the misuse and abuse of prescription opioids through:
 - Preventing prescription drug abuse
 - Treating opioid addiction
 - Saving lives from opioid overdose



CDER Will Accomplish These Goals Through the Use of All Available Tools

- Improving the use of opioids through careful and appropriate regulatory activities
- Improving the use of opioids through careful and appropriate policy development
- Improving the treatment of pain through improved science
- Improving the safe use of opioids through communication, partnership and collaboration



Improving the Safe Use of Opioids Through Regulatory Activities:

ER/LA REMS Education

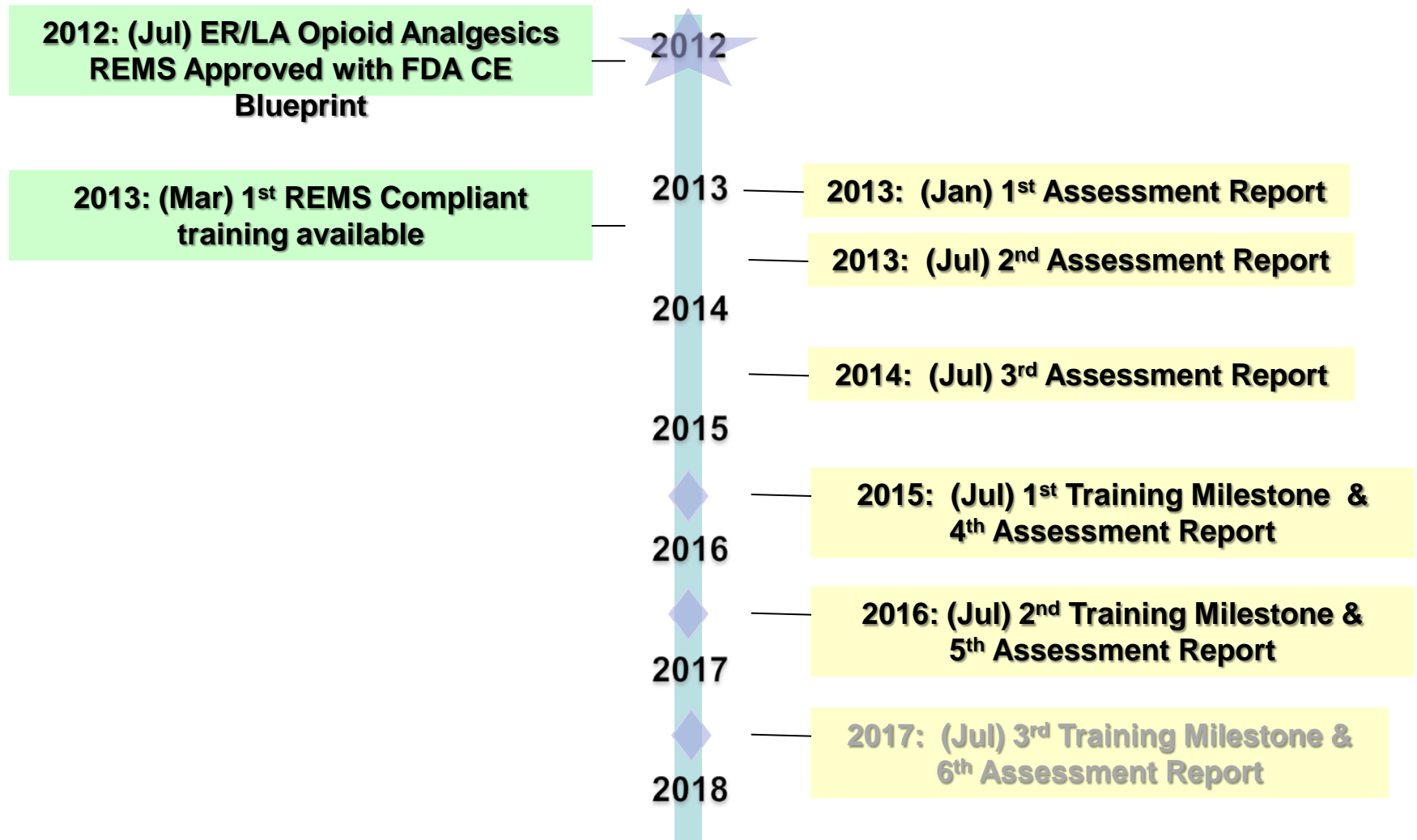


Regulatory Activity: ER/LA REMS and Prescriber Education

- In 2012, FDA required makers of extended-release, long-acting (ER/LA) opioids to make balanced and scientifically accurate Continuing Education (CE) materials available to prescribers
- Created by independent CE providers using their national standards
- Required content “Blueprint ”created by FDA



History of ER/LA REMS



Goals of ERLA REMS

- to reduce serious adverse outcomes resulting from inappropriate prescribing, misuse, and abuse of ER/LA opioid analgesics while maintaining patient access to pain medications. Adverse outcomes of concern include addiction, unintentional overdose, and death.



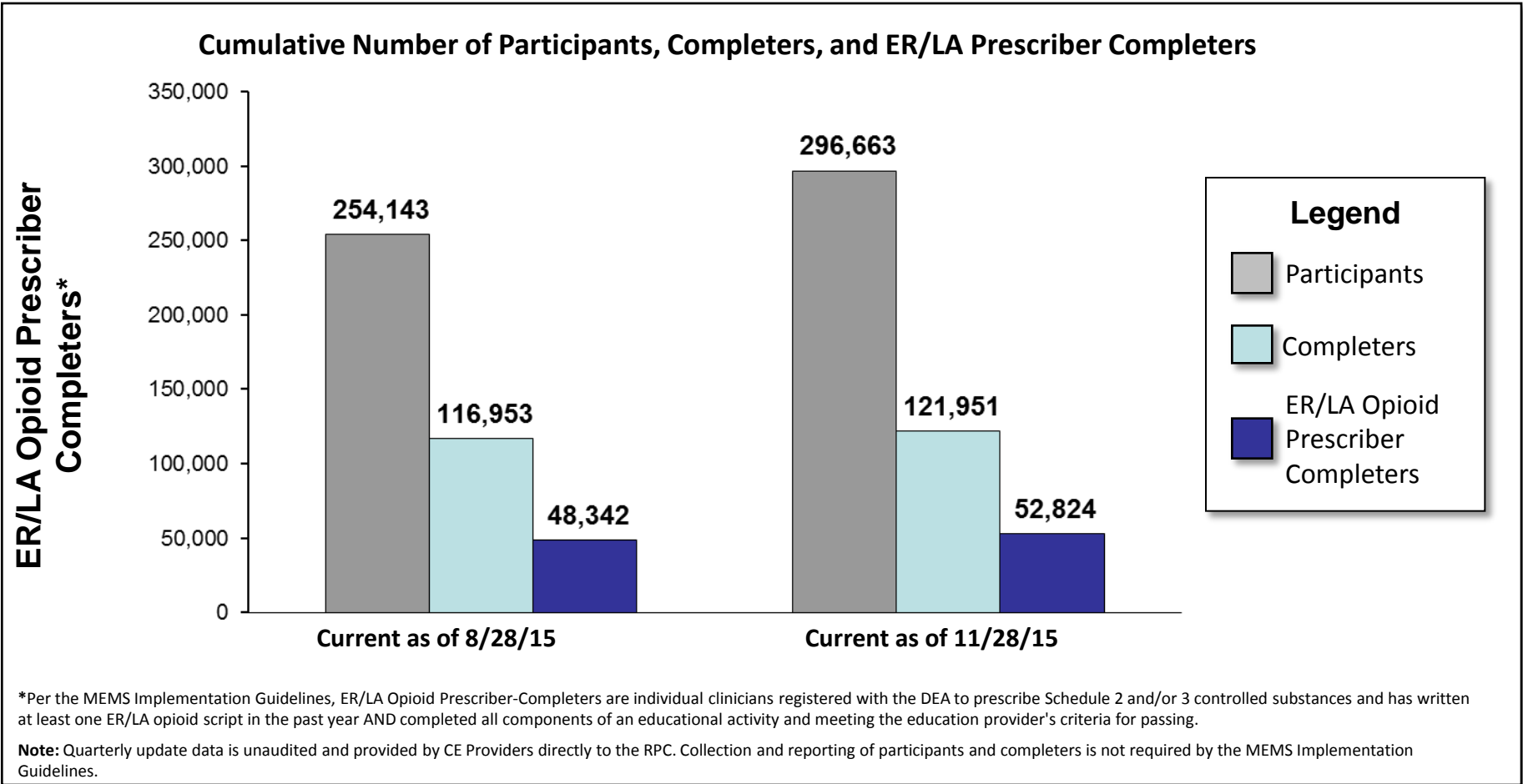
ERLA REMS Assessment After 36 Months

- Results submitted to FDA July 9, 2015
- Discussion at public Advisory Committee May 3-4
 - Impact of REMS on variety of metrics, including:
 - prescriber education, outcomes of public health interest, patient access
 - Discussion about any changes that need to be made to the REMS

Some Metrics for ERLA REMS Assessment

- Prescriber CE Training
- CE Auditing Compared with FDA Blueprint
- Drug Utilization
- Patient Understanding
- Changes in prescriber behavior
- Changes in trends for misuse, abuse, overdose and death
- Patient Access

Participants, Completers, ER/LA Opioid Prescriber Completers



REMS AC Meeting

- Extensive discussion of the challenge in assessing impact of REMS in the context of many other efforts
- Strong support by Committee members for modifying REMS
 - Focus on what members believe needs to happen (broadened education, mandatory education for prescribers)
- Next steps: FDA to complete assessment and determine next steps



Improving the Safe Use of Opioids Through Policy Development

Abuse-Deterrent (AD)
Formulations of Opioids

Twin FDA Policy Goals for Abuse Deterrent (AD) Formulations of Opioids

- Incentivize the development of opioid medications with progressively better AD properties and support their widespread use
- Assure appropriate development and availability of generics, reflecting their importance in US healthcare

Regulatory Activity: Innovator Guidance on AD Opioid Formulations

- Promised as part of Office of National Control Policy (ONDCP) Rx Drug Abuse Plan (2011)
 - Draft guidance release for comment: January 9, 2013
 - Final Guidance released April, 2015
 - <http://www.fda.gov/downloads/drugs/guidancecompliance/regulatoryinformation/guidances/ucm334743.pdf>

Regulatory Activity: Draft Guidance on Development of Generic AD Opioid Formulations

- Generic products represent a significant fraction (>80%) of all prescriptions in the US today
- March 24, 2016: General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products
 - <http://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm492116.htm>

Results of Policy: Development

- 6 products given abuse-deterrent claims in label
 - OxyContin (oxycodone, crush/extraction resistant): April, 2013
 - Targeniq (oxycodone hydrochloride and naloxone, naloxone aversive): July, 2014
 - Embeda (morphine/naltrexone, naltrexone is aversive/precipitates withdrawal when abused): October, 2014
 - Hysingla (hydrocodone, crush/extraction resistant): November, 2014
 - MorphaBond (morphine sulfate, crush/extraction resistant): October, 2015
 - Xtampza (oxycodone, crush/extraction resistant): May, 2016²⁷

Development Activity Related to AD Opioids: Development (Cont)

- Manufacturers working on new technologies
- >30 active INDs being discussed with CDER
 - New technologies being explored
 - Example: recent Advisory Committee on Apadaz ‘pro-drug’ form of hydrocodone with APAP

Next Steps: Need for Assessment of Impact on Real-world Abuse

- Current labels based on clinical and in vitro data to predict the formulation will reduce abuse
- Real-world assessment needed (and ongoing) as we know AD formulations are not silver bullets and can be defeated
- DECIDE WHAT WORKS AND WHAT DOESN'T

Future for AD Opioids

How Will We Get There?

- **Progressively Series of Regulatory Actions**
 - Giving a labeling claim for specific products
 - Also blocking the approval of other drugs that lack the same (or better) abuse-deterrent properties
 - Also, taking action against existing products with the same opioid
 - Also, taking action against existing products, including those with different opioids

Challenges in Getting to the Future for AD Opioids

- Incentivizing innovation: Primary incentive FDA has available is labeling
- Encouraging iterative development of effective abuse-deterrent formulations
 - Challenge to assess impact of individual formulations
 - Challenge to encourage uptake of effective products by payers
- Managing expectations: abuse-deterrent opioids will not ‘prevent’ abuse, and are not ‘silver bullets’

Improving the Safe Use of Opioids Through Scientific Work

Advancing Development and
Assessment of Abuse-Deterrent
(AD) Formulations of Opioids

Understanding Formulation Science of AD Opioids

- Scientific need: how to test AD formulations as new technologies are developed to support FDA policies related to AD opioids
 - Aid in regulatory review of new products
 - Give advice to manufacturers to speed development of effective products

Understanding Formulation Science of AD Opioids (cont.)

- FDA laboratory response: Creation and testing of formulations in FDA labs
 - 30+ formulations manufactured
 - Working to identify the process conditions that are critical for AD formulation performance and product stability
 - Validations of the AD performance tests to be done using these formulations
- Goal: development and publication of a standardized *in vitro* ADF performance evaluation matrix



Improving the Safe Use of Opioids Through Collaboration

Educational Partnerships

Partnerships on Prescription Drug
Monitoring Programs (PDMPs)

Importance of Collaboration with Non-governmental Partners

- Collaborations with non-governmental groups expands FDA's capacity to achieve our public policy goals
- Examples
 - Partnership with Partnership for Drugfree, NCPIE, & National Consumers League to help educate consumers and patients about the
 - Partnership with Brandeis University in support of broadened data sharing between Prescription Drug Monitoring Programs (PDMPs)

Many Other FDA Activities

- Additional input from outside groups, including additional Advisory Committees, National Academy of Science
- Changes to immediate-release opioids labeling to improve information for prescribers
- Required post-market studies to better understand the use of opioids
- Work on the use of novel packaging technologies to address abuse and misuse
- Work to support non-opioid pain medicines, new treatments for opioid overdose, and new treatments for substance use disorder
- Re-examine the risk-benefit paradigm for opioids and ensure that the agency considers the wider public health impacts of our decisions

Shared Responsibility

- FDA is one part of complex set of stakeholders needed to address opioid abuse and appropriate pain management

Summary

- FDA is using all of our available tools to address prescription opioid abuse, incorporating the broader public health impact of opioid abuse both to the patient and to others who may obtain them inappropriately into our regulatory decision-making
- Within our broad range of activities in this area, our regulatory mission remains at the heart of FDA role in opioids
 - FDA will act within its authorities, based on science, in support of our public health mission
 - Change will require work by many stakeholders