



FDA Perspective on Abuse-Deterrent Opioid Development

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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

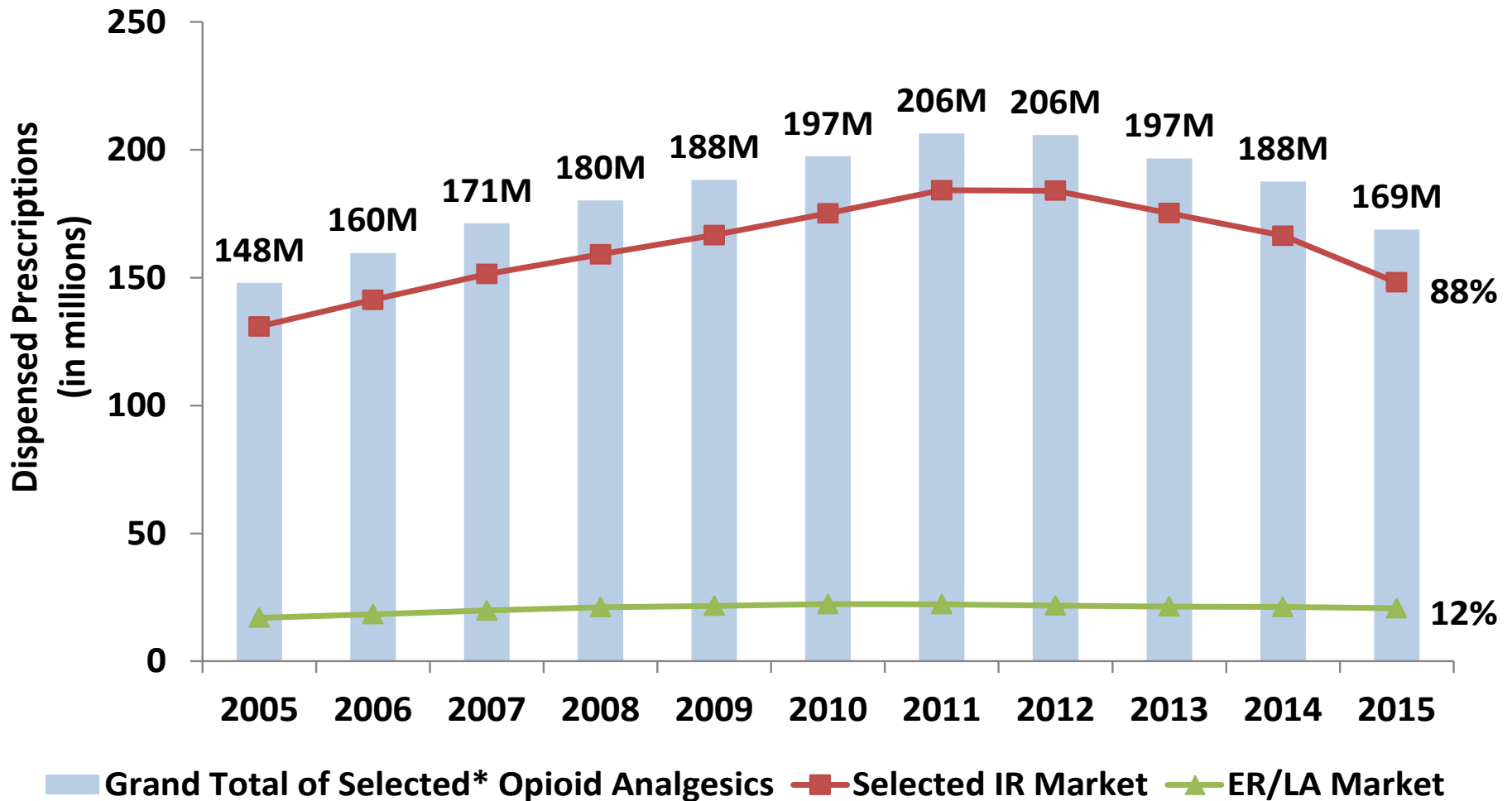
Outline

- Background on Epidemic
- Federal Context for FDA Efforts to Address Prescription Opioid Abuse
 - Other Federal Efforts
- FDA Action Plan
- FDA Focus on Abuse-Deterrent Formulations of Opioids

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
- Abuse Deterrent Opioids are one important part of FDA work to address opioid epidemic
- 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

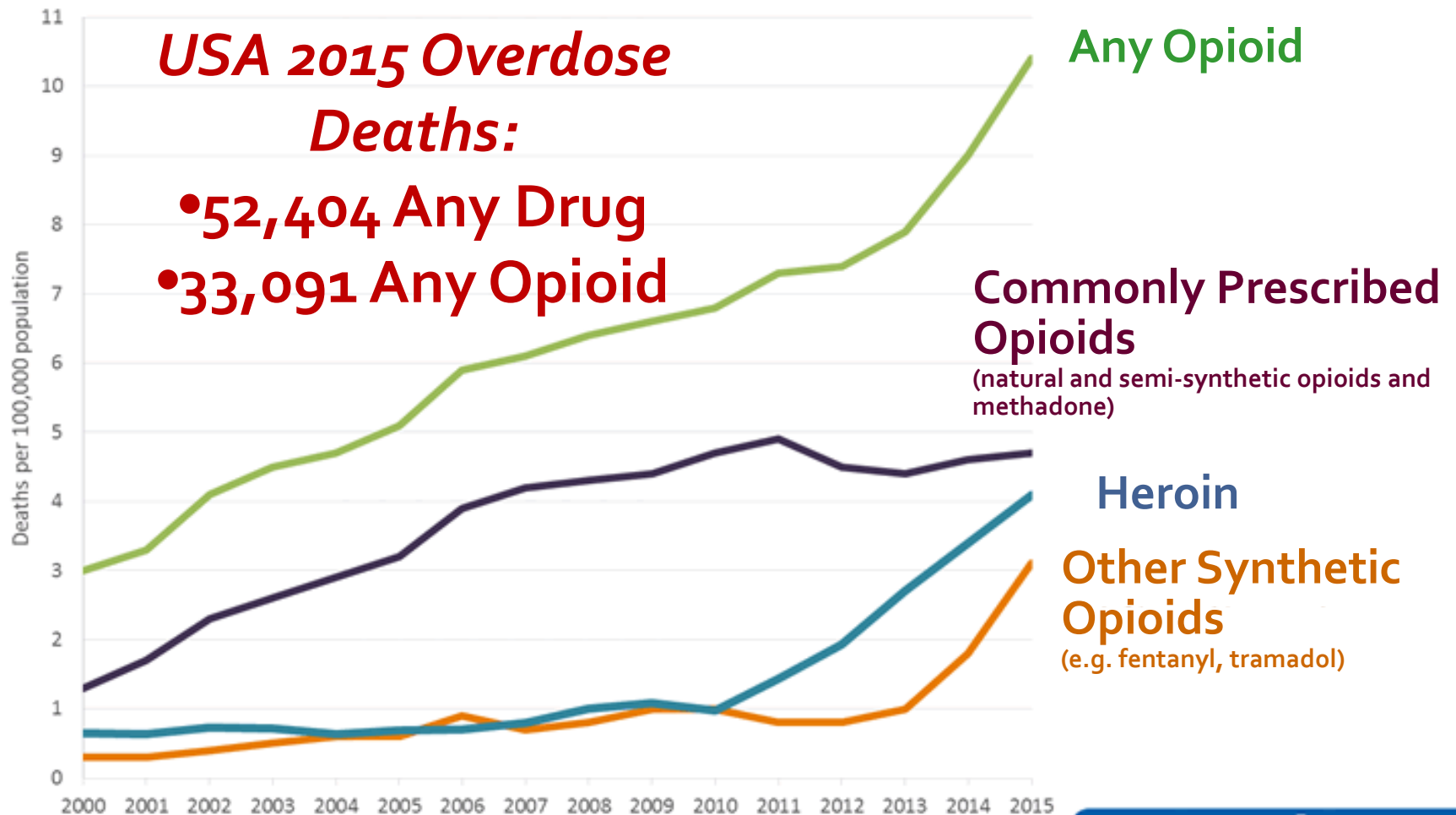
Nationally Estimated Number of Prescriptions Dispensed for Selected* Opioid Analgesics Oral Solids and Transdermal products from U.S. Outpatient Retail Pharmacies



Source: National Prescription Audit (NPA). Extracted May 2015 (For 2005-2014 data) and November 2016 (For 2015 data).

Marked *Increases in Prescription Opioid and Heroin Overdose Deaths* in the USA 2000 to 2015

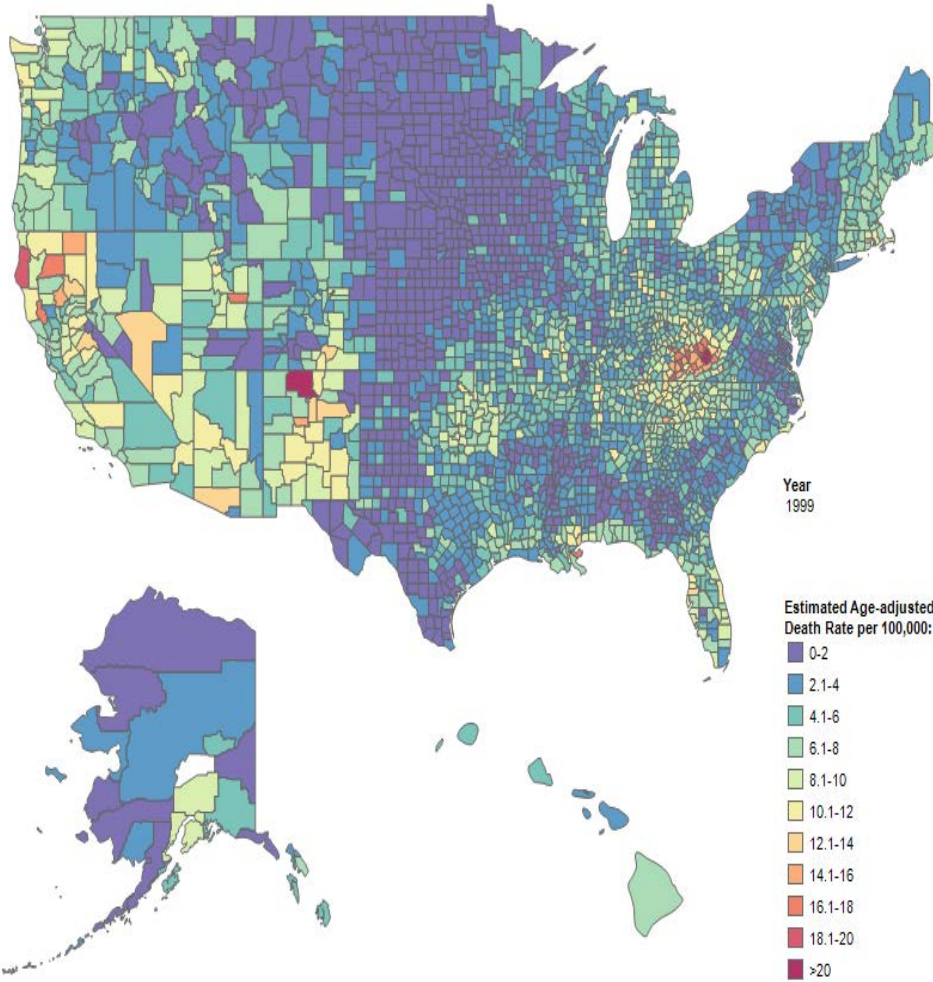
Overdose Deaths Involving Opioids, United States, 2000-2015



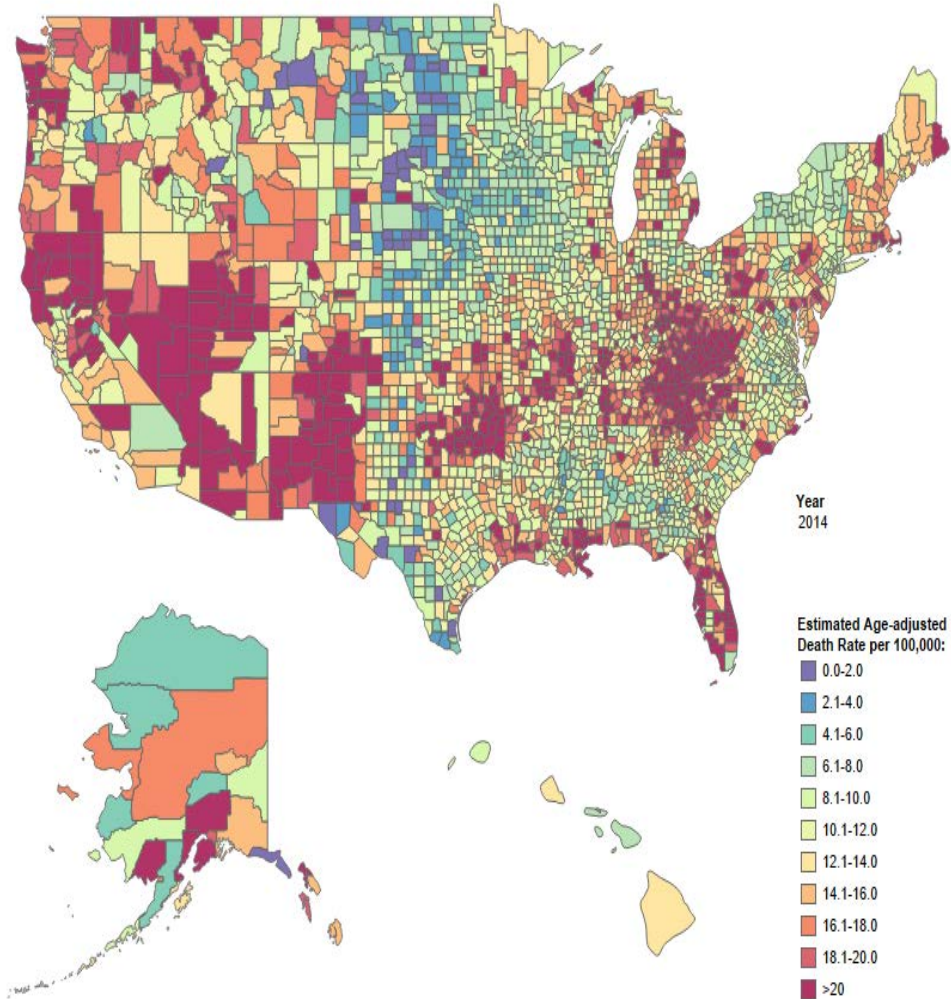
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2016. <https://wonder.cdc.gov/>.

Overdose Death Rates

1999

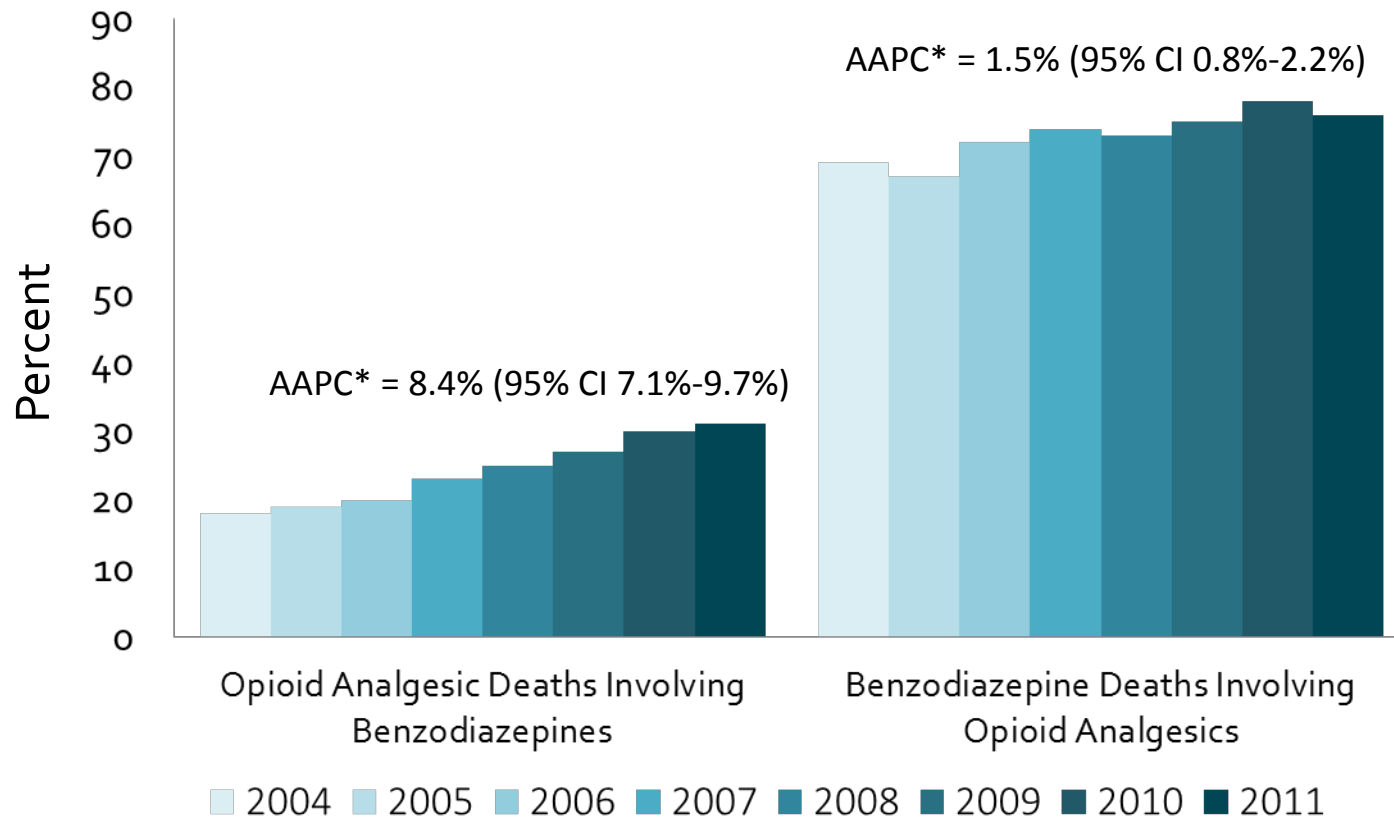


2014



Overlap of *Benzodiazepines and Opioids*

Opioid OD Deaths Involving Benzodiazepines & Benzodiazepine OD Deaths Involving Opioids



*AAPC = Average annual percent change

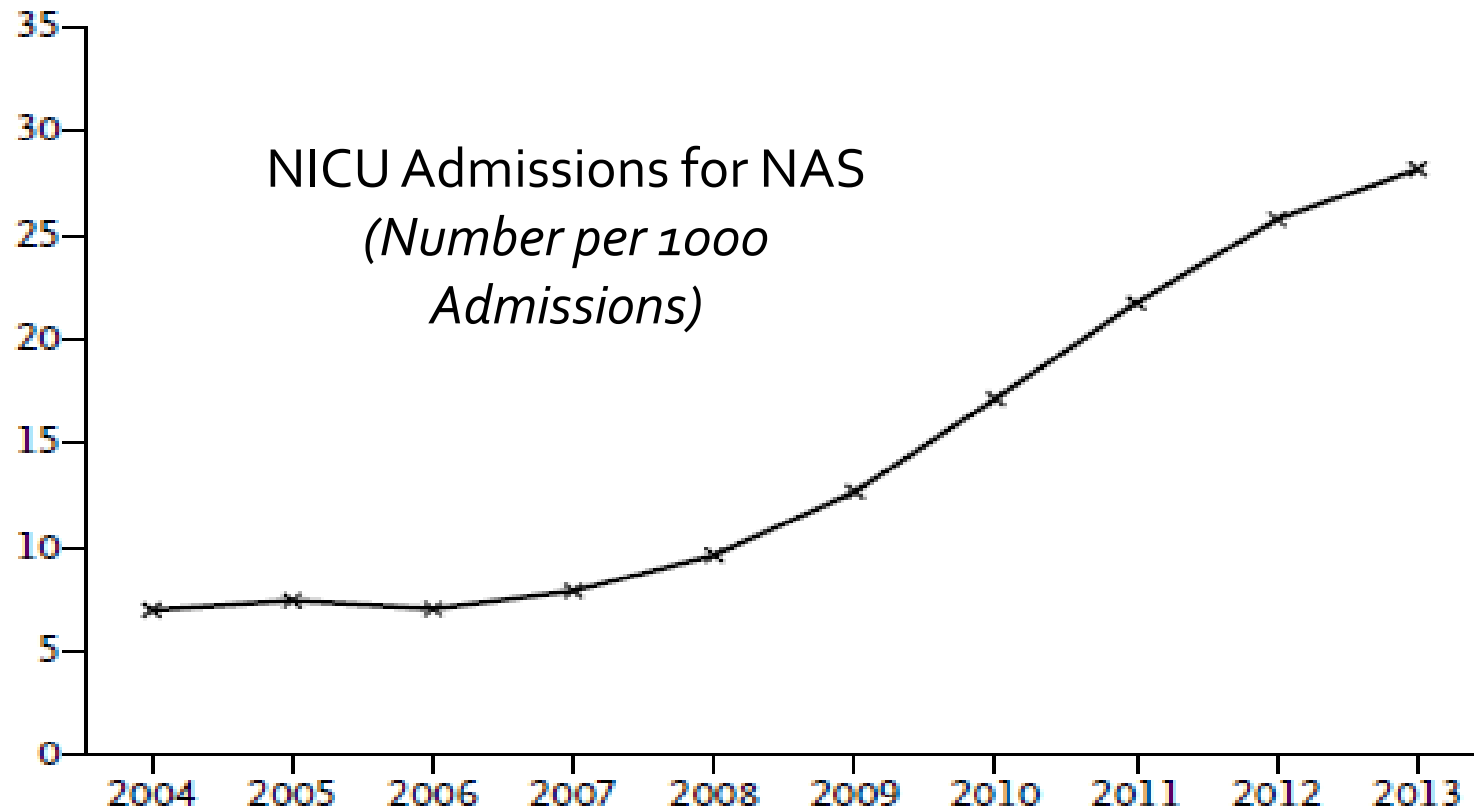
Science = Solutions



Outbreak of **HIV** Linked to IDU of Oxymorphone in Indiana, 2014-2015

- Through November 2015, **181 cases of HIV** identified in county of ~15,000
- 96% reported injection drug use
- Of these, **92% reported injecting prescription oxymorphone in past 12 months**
 - Frequently described preparing and injecting extended-release oxymorphone (Opana ER, Endo Pharmaceuticals)
- Public health emergency declared—syringe exchange program established

Increasing *Neonatal Abstinence Syndrome*



Source: Tolia VN, Patrick SW, et al. *NEJM* 2015;372:2118-2126

Science = Solutions

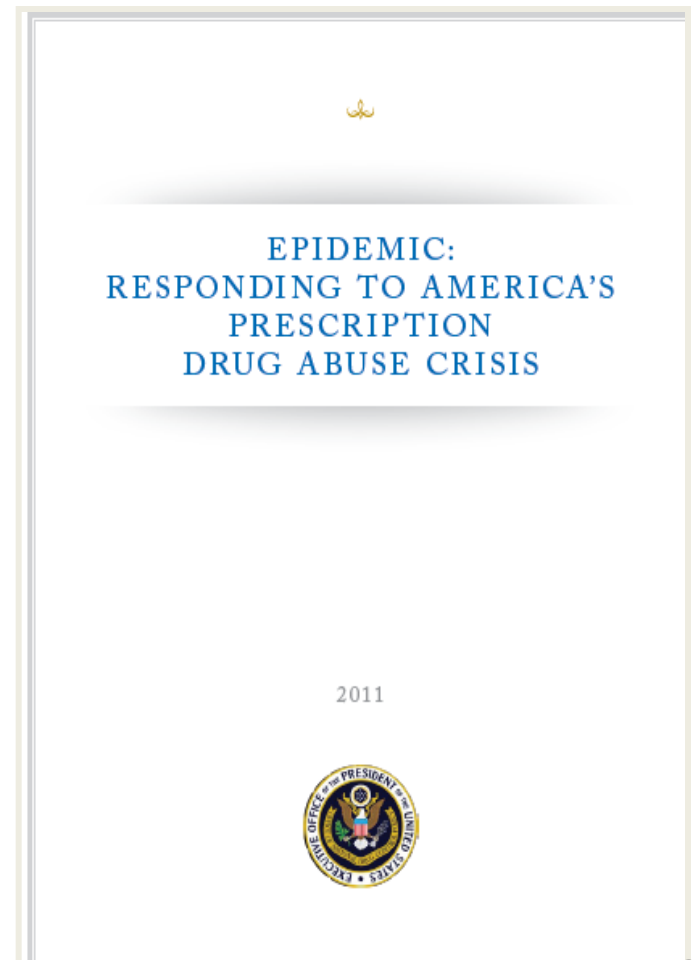
FDA is a Part of a Larger Governmental Response to Opioids Abuse

Office of the National Drug Control
Policy (ONDCP) Plan

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 U.S. 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
- **Surgeon General's Call to End the Opioid Crisis**
 - Launched a new prescriber education campaign, Turn the Tide
 - Issued the first-ever Surgeon General's Report on Alcohol, Drugs and Health: Facing Addiction in America
- **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, FDA called for a far-reaching action plan to reassess the agency's approach to opioid medications. The plan focused on policies aimed at reversing the epidemic, while still providing patients in pain access to effective relief.



FDA Opioids Action Plan

- Expand the 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 for Prescription Opioids
- **Expand access to abuse-deterrent formulations (ADFs) to discourage abuse**
- Support better treatment for prescription opioid abuse and overdose
- Reassess the risk-benefit approval framework for opioid use

FDA and Abuse-Deterrent Formulations of Opioids

Part of Larger FDA/HHS Efforts to
Improve Tools for Pain Management

Development of New Pain Treatments

Abuse-deterrent Opioid formulations



Pro-drugs



Crush/extraction resistant formulation



Drug combinations with adverse effects if injected

Non-Opioid based analgesics
Cannabinoids;
Inflammatory mediators;
Ion channel blockers

Non-pharmacological treatments

Surgical interventions;
Neural stimulation;
Spinal cord stimulation

Transcranial Magnetic Stimulation





Spurring Development of Abuse-Deterrent (AD) Opioids: FDA Goals

- 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 U.S. healthcare
 - Generic drugs play a critical role in U.S. healthcare, including important role in controlling costs and expanding access



FDA Tools to Support AD Formulation Development

- **Scientific Research**
- **Regulatory Activities**
 - Decisions on applications
 - Sponsor discussions as a part of individual product development
- **Guidances**
 - Final guidance on developing AD formulations of opioids issued April 2015
 - Draft guidance on generics development and testing issued March 2016
- **Public Discussion and Comment**
 - Public meetings, including meeting held October 2014 and 2016
 - Comments on draft guidance
 - Citizen petitions

Policy Development: Generic AD Opioids

- Generic drugs play a critical role in U.S. healthcare, including important role in controlling costs and expanding access
- March, 2016: FDA released draft guidance: “General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products”
- October, 2016: FDA held a 2-day meeting to discuss draft guidance and standardization of in vitro testing for AD opioids
- FDA plans to publish a final guidance to the March 2016 draft in 2017 in accordance with the requirements of the Comprehensive Addiction and Recovery Act of 2016.

Regulatory Activity: Supporting AD Opioid Development

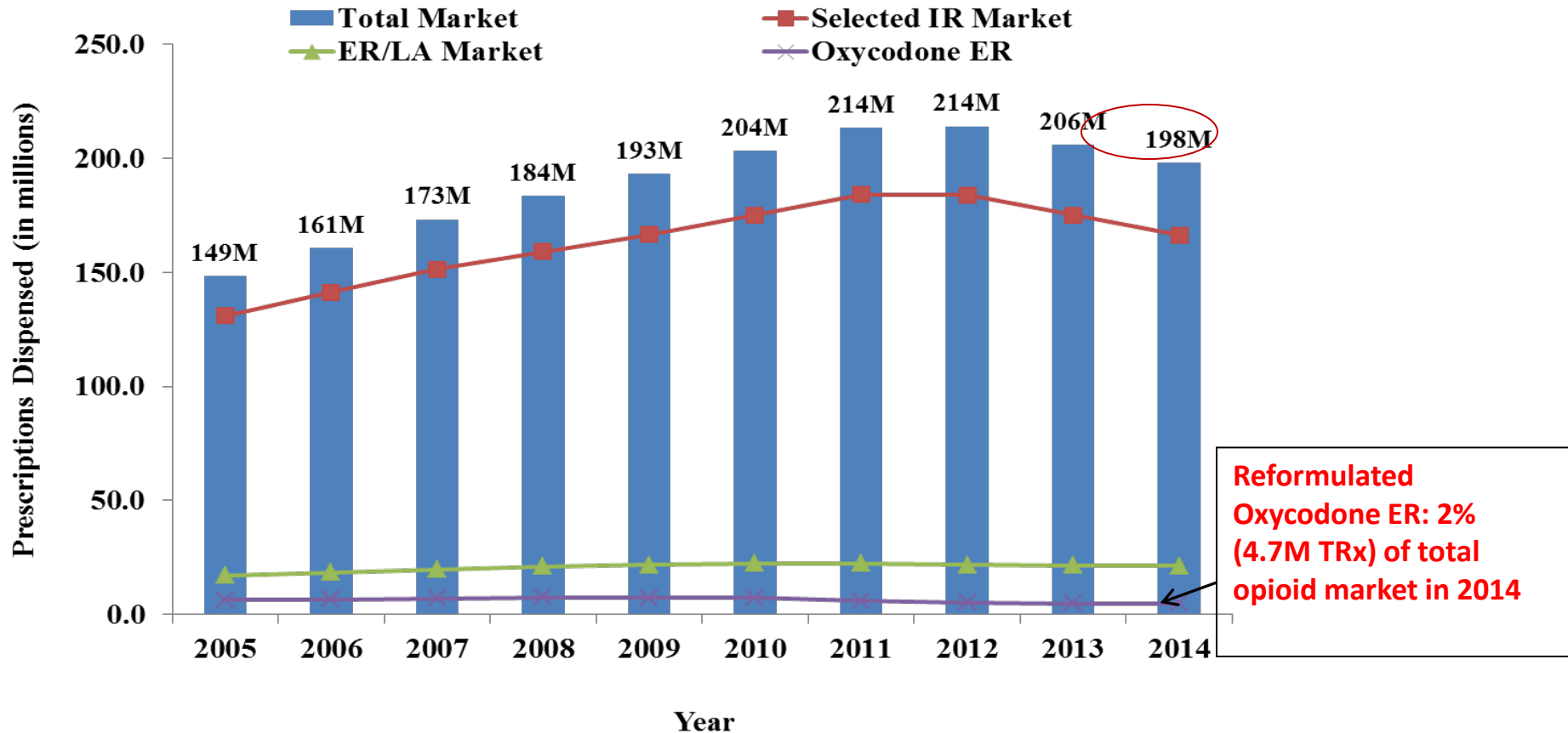


- **9** new opioids approved with abuse-deterrent formulations (latest January, 2017)
(OxyContin, Targiniq ER, Embeda, Hysingla ER, MorphaBond, Xtampza ER, Troxyca ER, Arymo ER, Vantrela ER)
- Work to date has often focused on use of crush/extraction-resistant and agonist/antagonist technologies, but many new approaches being explored
- More than 30 active investigational new drug applications (INDs) being discussed for AD formulations
 - New technologies being explored by industry (e.g., pro-drugs that require activation to prevent IV abuse and snorting)

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

IR and ER/LA Opioid Prescriptions



Nationally estimated number of prescriptions dispensed for selected IR and ER/LA opioid analgesics from U.S. outpatient retail pharmacies

- No prescriptions captured for Hysingla ER or Embeda in 2014

Challenges in Getting to the Future for AD Opioids

- Incentivizing innovation: Current FDA incentives include product labeling and Hatch-Waxman exclusivity
- Encouraging iterative development and use 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 opioid--
 - Are part of larger effort on opioids
 - Will not ‘prevent’ abuse, and are not ‘silver bullets’

Summary and Conclusions

- FDA working to address opioids epidemic as a part of the larger HHS response
 - One of the FDA's highest priorities
- FDA Opioids Action Plan provides framework for FDA response to the challenge of opioids abuse epidemic
- Supporting development and use of progressively better abuse deterrent opioids one important FDA goal within the Action Plan
 - FDA looks forward to the day, not far in the future, when the majority of opioids on the market are known to be abuse deterrent

Thank you



