

FDA's Role in Confronting the Opioid Epidemic

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

Alliance for Balanced Pain
Management

November 14, 2017



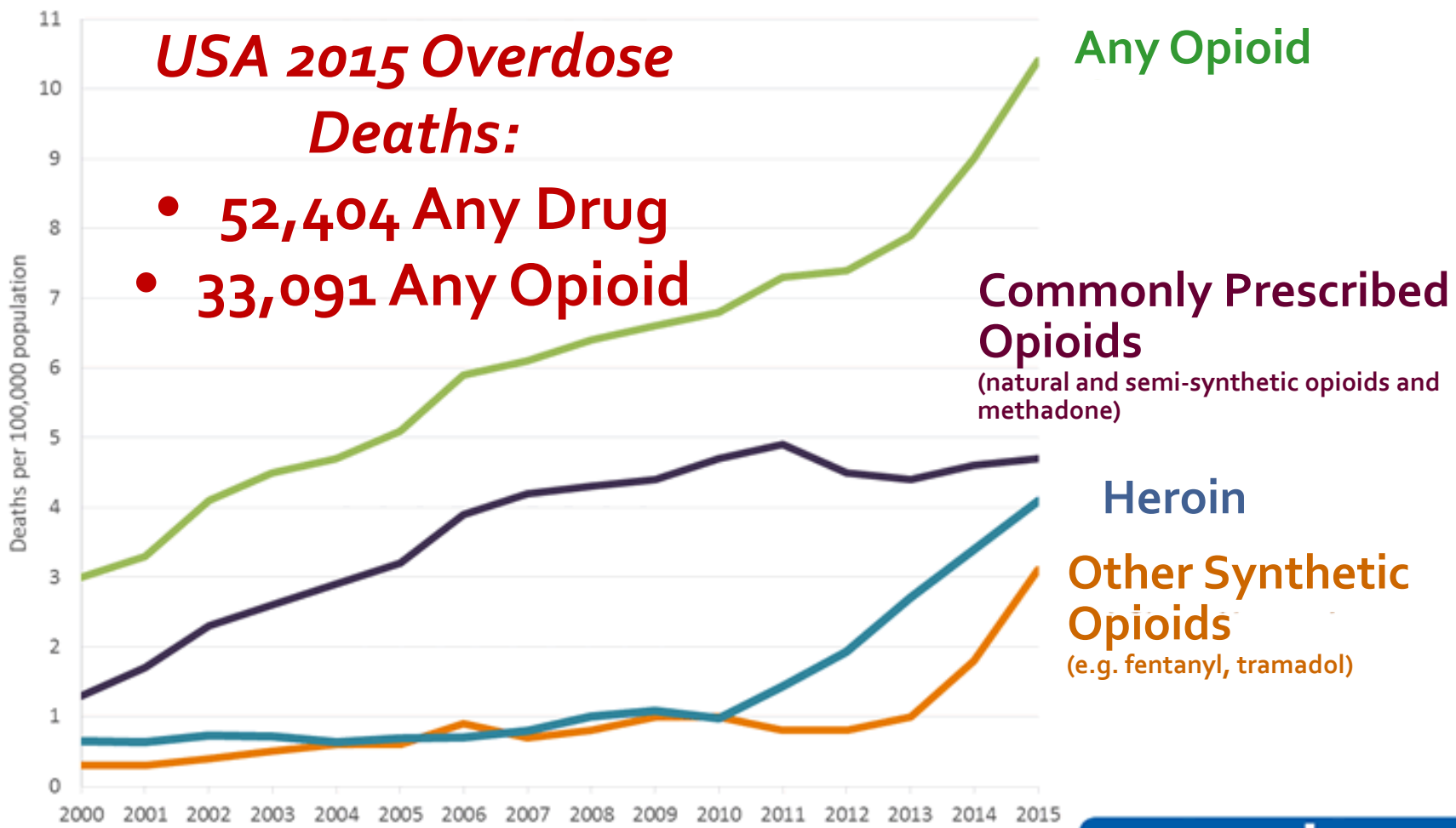
The opinions and information in this presentation are my own and do not necessarily reflect the views and policies of the FDA

Overall Messages

- 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 effective pain treatment
- Ongoing and planned activities reflect the commitment by FDA to use of all of our available tools to appropriately manage pain while also addressing the opioids crisis

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

Overdose Deaths Involving Opioids, United States, 2000-2015



USA 2015 Overdose Deaths:

- 52,404 Any Drug
- 33,091 Any Opioid

Any Opioid

Commonly Prescribed Opioids
(natural and semi-synthetic opioids and methadone)

Heroin

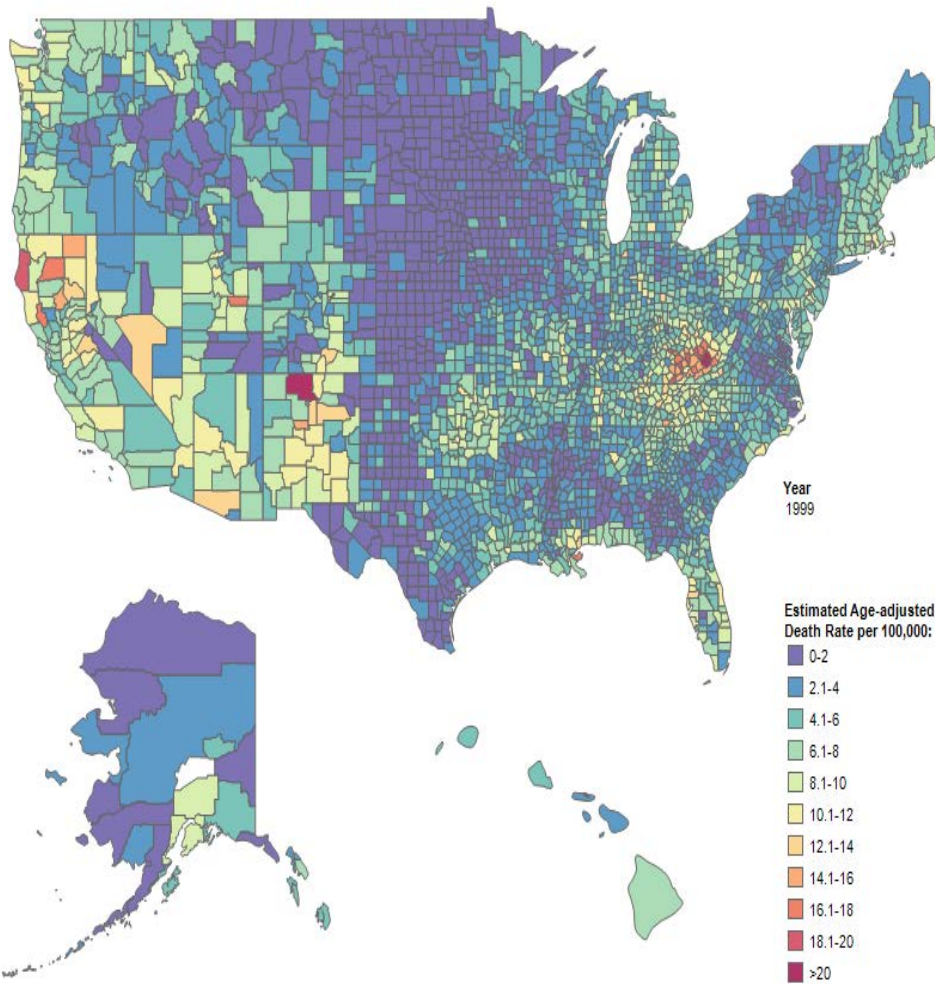
Other Synthetic Opioids
(e.g. fentanyl, tramadol)

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/>.

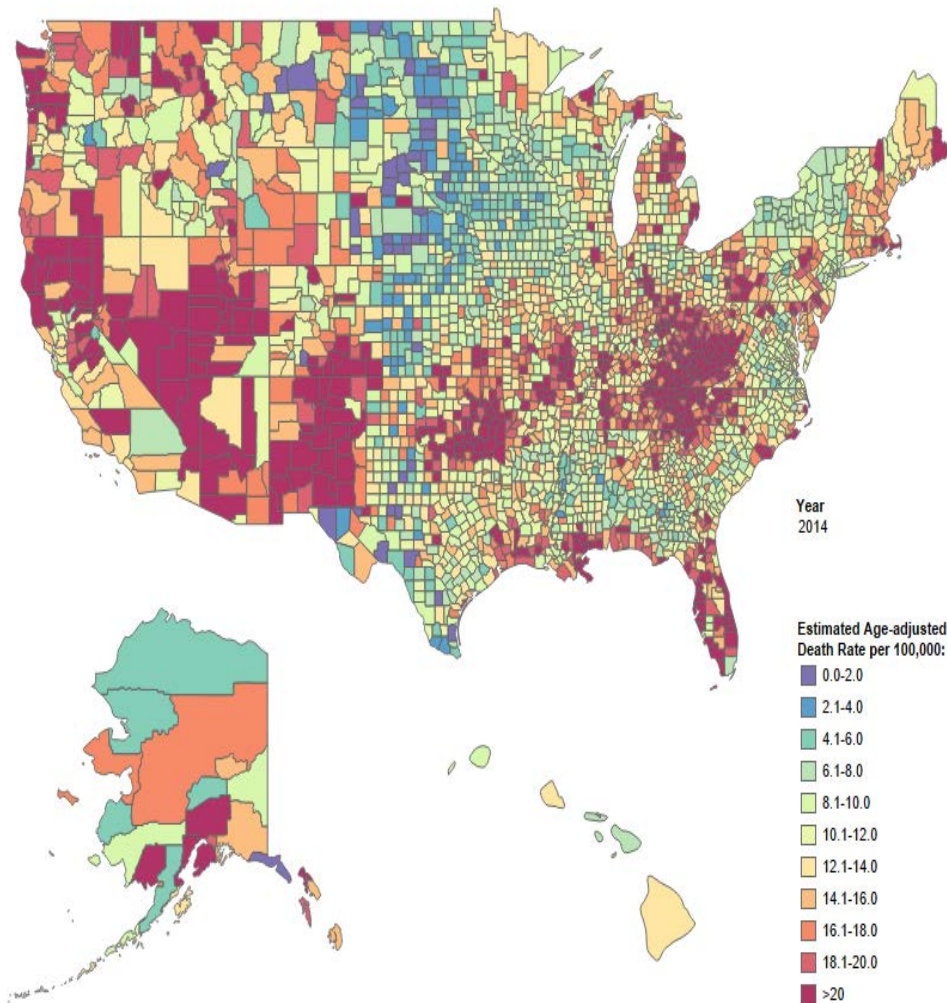


Overdose Death Rates

1999

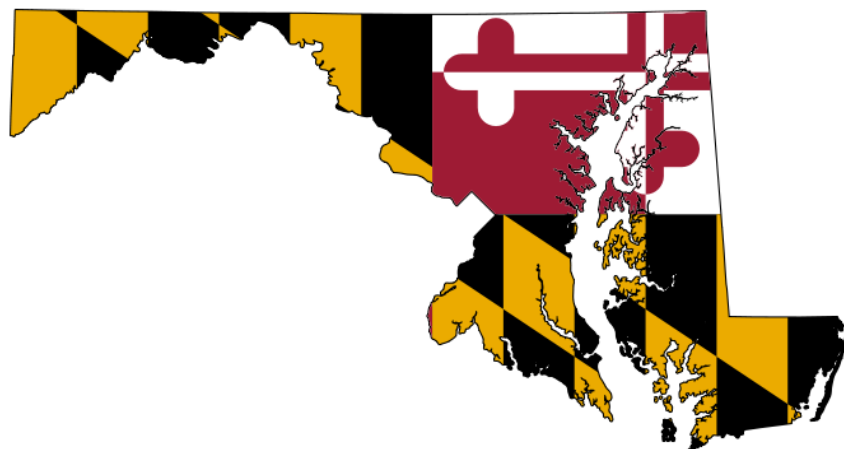


2014

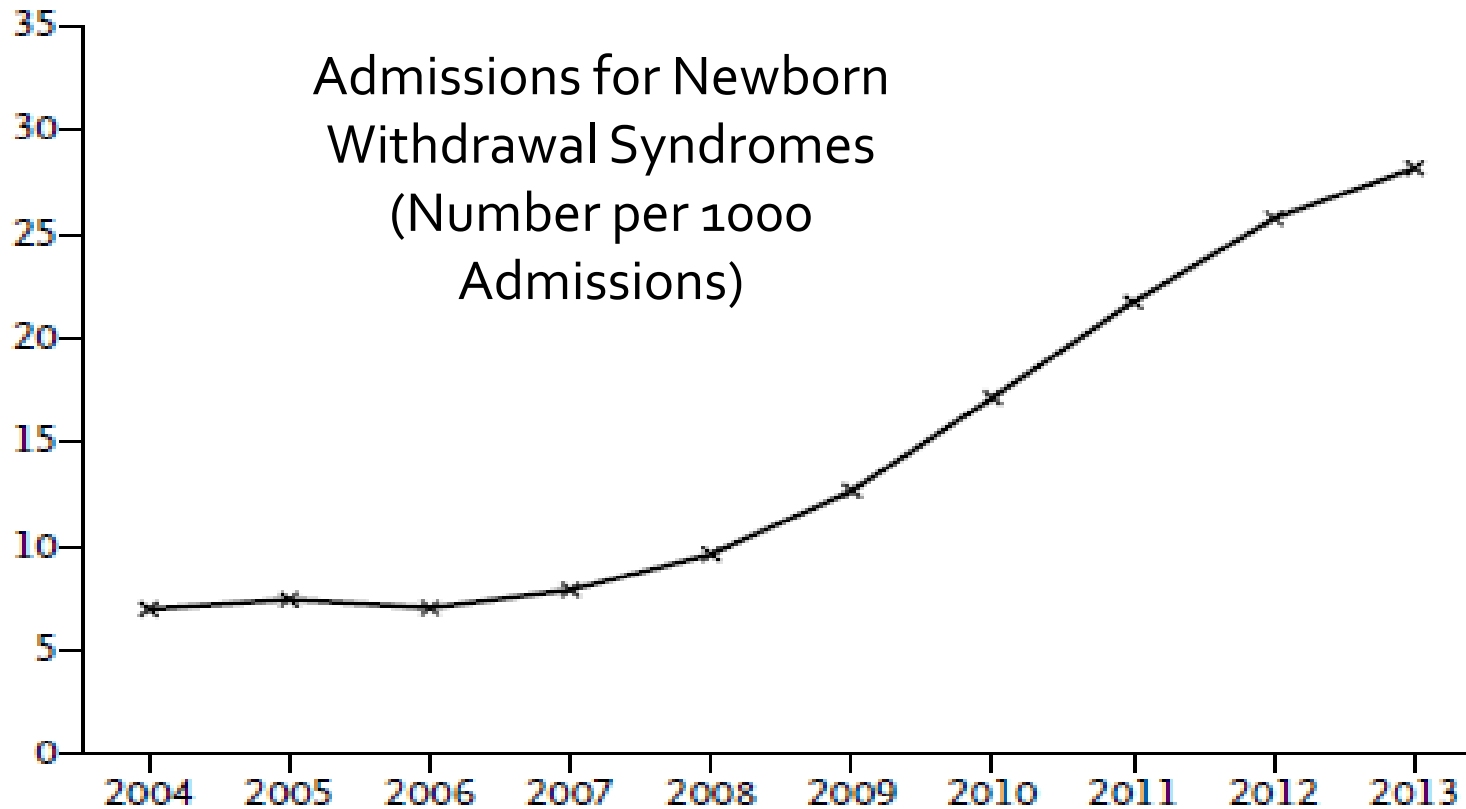


Opioid Epidemic in Maryland

- In 2015, 1259 overdose deaths state wide
- In first 9 months of 2016, 1468 overdose deaths
- Comparing the first 9 months of 2016 to 2015, overdose deaths increased 62%



Impact of Crisis: Increasing Prenatal Exposure



Impact of Crisis: Infectious Disease Transmission

HIV and Hepatitis C Outbreak Linked to Oxymorphone Injection Use in Indiana, 2015



Early Release / Vol. 64

Morbidity and Mortality Weekly Report

April 24, 2015

Peters et al.

The New England Journal of Medicine

2016;375:229-239

U.S. Prescribing Rates - Trends

- U.S. prescribing rates peaked in 2012 at 81.3 prescriptions per 100 persons¹¹
 - Total: 255 million prescriptions
- Opioid prescribing has been decreasing between 2012 and 2016.
- U.S. prescribing rate in 2016 was 66.5 prescriptions per 100 people
 - 214 million prescriptions
- Rates continue to vary widely
 - Some counties had rates 7 times the national average



Equally Critical Social and Medical Issue: Pain in America

- From the Functioning and Disability Supplement of the 2012 National Health Interview Survey
 - 126.1 million adults reported some pain in the previous 3 months
 - 25.3 million adults (11.2%) suffering from daily (chronic) pain
 - 23.4 million (10.3%) reporting a lot of pain.
 - Based on the persistence and bothersomeness of their pain, 14.4 million adults (6.4%) were classified as having the highest level of pain, category 4, with an additional 25.4 million adults (11.3%) experiencing category 3 pain.

Pain in America (cont)

- Treatment options for pain: pharmacologic, physical medicine, behavioral medicine, neuromodulation, interventional, and surgical
- Optimal patient outcomes often result from a comprehensive multidisciplinary approach where pharmacologic treatment is not the sole focus
- Patients experience ongoing barriers to adequate pain management
 - “many related to non-existent or insufficient insurance coverage and reimbursement for evidence- and consensus-based therapies”

-American Academy of Pain Medicine, 2014
- As a result, treatments have largely focused on prescription drugs, mainly opioids, and procedures, at least, in part, because of the reimbursement structure of our healthcare system

FDA Response to this Crisis

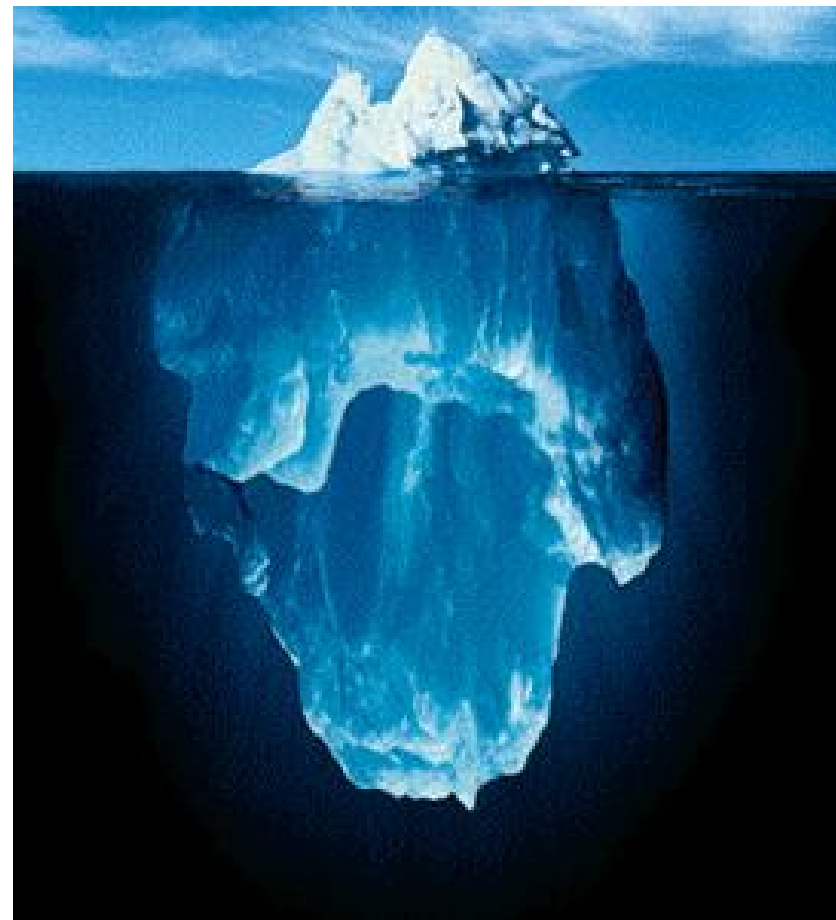
"Unquestionably, our greatest immediate challenge is the problem of opioid abuse. This is a public health crisis of staggering human and economic proportion ... we have an important role to play in reducing the rate of new abuse and in giving healthcare providers the tools to reduce exposure to opioids to only clearly appropriate patients, so we can also help reduce the new cases of addiction."

- Scott Gottlieb, FDA Commissioner
Address to FDA staff, May 15, 2017



Solutions Must Come from Many Sources

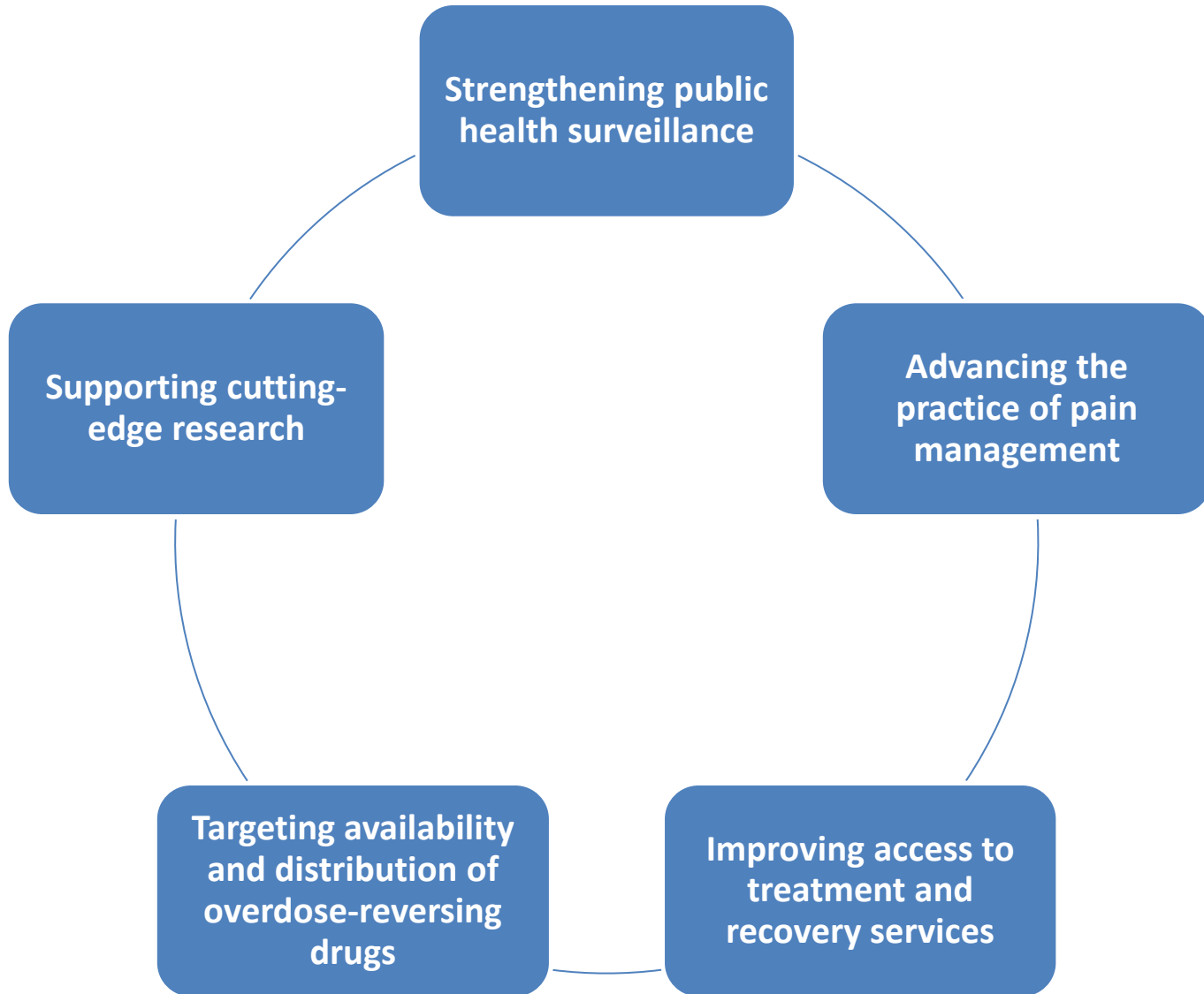
- FDA is one of many Federal agencies addressing issues involving opioids
- Many Federal Agencies working together on issue
- Each state has programs to address opioids
- Guidelines and educational programs are available from specialty societies and State Medical Boards
- Healthcare institutions
- Advocacy groups
- Individual providers (n = 800,000+)
- Patients (n = millions)



Take immediate steps to reduce the scope of the epidemic of opioid addiction

- **May 2017:** Established an FDA Opioid Policy Steering Committee (OPSC)
- **September 2017:** Soliciting public input on how **FDA authorities** can or should be **used to address the crisis**

Working Within HHS Opioid Strategy





Goals of HHS Opioid Strategy

- Empowering the public, patients and providers through education and awareness
- Preventing opioid abuse and overdose and related health consequences
- **Improving function and quality of life for individuals living with pain**
- **Ensuring patients who need opioid addiction treatment have access to it**
- Supporting people to achieve long-term recovery

The Opioid Crisis: FDA's Priorities

1. Decreasing Exposure & Preventing New Addiction

2. Supporting the Treatment of Those With Opioid Use Disorder

3. Fostering the Development of Novel Pain Treatment Therapies

4. Improving Enforcement & Assessing Benefit-Risk



FDA Priorities align to HHS Strategic Priorities and other National Activities



HHS STRATEGIC PRIORITIES

FDA PRIORITIES

OTHER ACTIVITIES

Strengthening public health surveillance

Targeting availability and distribution of overdose-reversing drugs

Supporting cutting-edge research

Improving access to treatment and recovery services

Advancing the practice of pain management

1. Decreasing Exposure & Preventing New Addiction

2. Supporting the Treatment of Those With Opioid Use Disorder

3. Fostering the Development of Novel Pain Treatment Therapies

4. Improving Enforcement & Assessing Benefit-Risk

President's Commission on Combatting Drug Addiction

Office of National Drug Control Policy Recommendations


Comprehensive Addiction and Recovery Act (CARA)

National Pain Strategy Recommendations

National Public Health Emergency

1. Decreasing Exposure and Preventing New Addiction



	HOW?	WHAT?
 <p>Appropriate Dose/Duration Labeling</p>	<ul style="list-style-type: none"> Facilitate appropriate prescribing of opioid analgesics. Evaluate indication specific doses. 	<ul style="list-style-type: none"> Ongoing research and ongoing discussions within FDA
 <p>Health Care Provider Education</p>	<ul style="list-style-type: none"> Consider appropriateness of mandatory education and how FDA would operationalize such a requirement. Ensure training is made available to non-physician prescribers, including nurses and pharmacists. 	<ul style="list-style-type: none"> May 9-10, 2017: FDA public workshop on pain management training. Issued revised Blueprint. Sept 28, 2017: FDA issued REMS letters that training be made available to health care providers who prescribe IR opioid analgesics.
 <p>Appropriate Packaging, Storage, and Disposal</p>	<ul style="list-style-type: none"> Explore how opioid analgesic drug products are packaged, stored, and discarded. Examine use of packaging strategies, such as unit-of-use packaging to improve opioid analgesic safety. 	<ul style="list-style-type: none"> Jun 1, 2017: FDA/Duke Margolis workshop and white paper on packaging, storage, and disposal solutions. Dec 11-12, 2017: FDA public workshop to gain input on packaging strategies.

Example: Improving Educational Tools for Healthcare Providers



- Opioid Risk Evaluation and Mitigation Strategy (REMS) program: requires drug companies making Extended-Release Long-Acting Opioids to fund continuing education programs on the use of these products
 - Content dictated by FDA Blueprint
- FDA held a public meeting regarding prescriber education on May 9 – 10, 2017
- FDA released a revised Blueprint with expanded topics to be included in the prescriber education program including education on pain management
- FDA has announced plans to expand the REMS:
 - to include the immediate-release (IR) opioids
 - to include pain management in the training , and
 - to expand training to include more members of the healthcare team

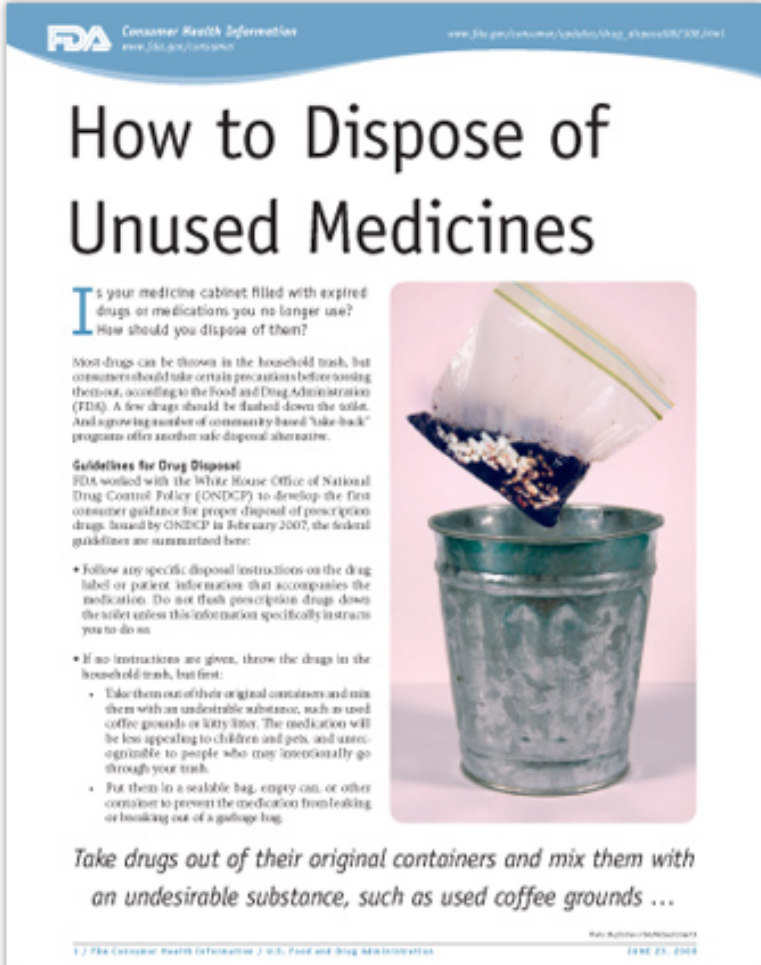
Example: Appropriate Packaging Storage & Disposal

Part of Federal efforts to educate consumers about appropriate disposal of unused medicines

FDA focus on disposal of selected high-potency drugs that can kill with a single dose to improve human safety

Example: lethal exposure to fentanyl patches

-- <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm101653.htm>



The image shows a poster from the FDA Consumer Health Information series. The title is 'How to Dispose of Unused Medicines'. The poster includes the FDA logo and the text 'Consumer Health Information' and 'www.fda.gov/consumers'. The main text explains that most drugs should not be thrown in household trash but should be disposed of properly. It provides guidelines for drug disposal, including following specific instructions on the drug label or patient information, and if no instructions are given, mixing the drugs with an undesirable substance like used coffee grounds in a sealable bag before disposal. A photograph shows a clear plastic bag being poured into a green glass jar. The footer of the poster includes the text 'FDA Consumer Health Information U.S. Food and Drug Administration' and 'JUNE 23, 2008'.

FDA Consumer Health Information
www.fda.gov/consumers

How to Dispose of Unused Medicines

Is your medicine cabinet filled with expired drugs or medications you no longer use? How should you dispose of them?

Most drugs can be thrown in the household trash, but consumers should take certain precautions before tossing them out, according to the Food and Drug Administration (FDA). A few drugs should be flushed down the toilet. And a growing number of community-based "take-back" programs offer another safe disposal alternative.

Guidelines for Drug Disposal
FDA worked with the White House Office of National Drug Control Policy (ONDCP) to develop the first consumer guidance for proper disposal of prescription drugs. Issued by ONDCP in February 2007, the federal guidelines are summarized here:

- Follow any specific disposal instructions on the drug label or patient information that accompanies the medication. Do not flush prescription drugs down the toilet unless this information specifically instructs you to do so.
- If no instructions are given, throw the drugs in the household trash, but first:
 - Take them out of their original container and mix them with an undesirable substance, such as used coffee grounds or kitty litter. The medication will be less appealing to children and pets, and unrecognizable to people who may intentionally go through your trash.
 - Put them in a sealable bag, empty can, or other container to prevent the medication from leaking or breaking out of a garbage bag.

Take drugs out of their original containers and mix them with an undesirable substance, such as used coffee grounds ...

FDA Consumer Health Information U.S. Food and Drug Administration
JUNE 23, 2008



Some Riskier Medications Should Be Flushed

A few prescription medicines, primarily controlled substances, are especially harmful or even fatal if taken accidentally by someone other than the patient. For this reason, they should be flushed down the sink or toilet to eliminate them from the home.

2. Supporting Treatment of Opioid Use Disorder

HOW?

WHAT?



Naloxone

- Exploring ways to **expand access** to naloxone and **facilitate the switch** to **OTC naloxone**.

- **Precedent setting: FDA-led labeling study** to facilitate the **switch** from prescription to **OTC naloxone**.



Medication Assisted Treatment (MAT)

- Facilitate the development of **new MAT options**.
- Take steps **promote the more widespread use** of existing, safe and effective, FDA approved therapies.
- Join efforts to **break the stigma** associated with medications used for treatment of addiction.

- Issue guidance for product developers to **facilitate the development of new treatments**.
- NIH **collaboration** to identify **new endpoints** in MAT drug development and **facilitate new formulations**.

Example: Development of Drugs for Overdose Intervention

Naloxone Distribution for opioid overdose victims. The potential for direct intervention to save lives.

➤ “Evzio” naloxone auto-injector APPROVED BY FDA, April 3, 2014



➤ “Narcan Nasal Spray” naloxone APPROVED BY FDA, November 18, 2015



Science = Solutions

3. Developing Novel Pain Treatment Therapies

HOW?

WHAT?



Partnerships & Meetings

- Expand use of partnerships with **non-profit organizations**, **public meetings**, and **Advisory Committee** meetings.
- **Collaborate** across HHS.

- **FDA grant** supported Drug-Free Kids campaign.
- **Public-private-partnership (PPP)** under the Critical Path initiative.
- **Jul 2017:** Commissioned NASEM **consensus report**.



Abuse Deterrent Formulations (ADFs)

- Support development of **innovative** ADFs, **data** to inform benefit-risk assessment, and **transition to an ADF-prominent market**.
- Ensure ADF **label nomenclature** enables providers to adequately distinguish between the risk of abuse and the risk of addiction.

- **Jul 2017: Public workshop** for postmarketing **ADF data and evaluation methods**.
- Issued **guidance** on **generic ADFs**.
- **Sep 2017:** Contracts to improve **data for ADF assessment** and understand **nomenclature**.



Pain Treatment Alternatives

- Explore use of Fast Track and Breakthrough Therapy Designations.
- Encourage novel therapies, including **medical devices**.

- **Summer 2017:** FDA/NIH **meeting series** on pain treatment alternatives.

Example: Supporting Abuse Deterrent Formulations (ADF) of opioids

- FDA has a goal of incentivizing the development of opioid medications with progressively better abuse-deterrent properties and support their widespread use
 - Abuse-deterrent is **not** *abuse proof*
- FDA requiring studies to understand the impact of ADFs in real-world settings
- In support of the goal, FDA has issued guidance for product development, including draft guidance on generic ADFs, reflecting importance of generic products in the US



4. Improving Enforcement & Assessing Benefit-Risk



HOW?

WHAT?



Improving Enforcement

- Consider how to fully **leverage** FDA's current **seizure authorities**.
- Increase oversight of **illicit** trade.

- **Collaboration** with Customs and Border Protection to **increase FDA staff** stationed at international mail facilities (IMFs) to increase **seizure of opioids** being smuggled into the United States through **international mail facilities (IMFs)**.



Assessing Benefit-Risk

- **Take action**, including product market **withdrawal recommendation**.
- **Improve robustness** of **benefit-risk assessment framework** for opioid analgesic formulations.

- **Jun 2017:** Requested market **withdrawal** of Opana ER due to **abuse risks**.
- **Sep 2017:** Pediatric **Advisory Committee** for hydrocodone or codeine containing cough treatment in **pediatric patients**.

Example: Ongoing Work by FDA on Benefit-Risk Assessment of Opioids



- Prescription opioids have impacts on both the patients when used as prescribed and on society when used inappropriately
- FDA considers both impacts in our regulatory decisions and is seeking to formalize that assessment
 - Opana decision
- FDA sought NASEM input on issue last year and is working to determine next steps and improve our processes
 - “...to ensure drug approval and removal decisions are made within a benefit-risk framework that evaluates not only the outcomes of opioids when used as prescribed, but also the public health effects of the inappropriate use of these drugs”



Summary and Conclusions

- FDA working to address opioid epidemic as a part of the larger HHS response
 - One of the FDA's very highest priorities
- Going forward, FDA is committed to taking decisive actions, grounded in the available science and appropriate public input to address this critical challenge to the US health and welfare
- Our focus is addressing opioid abuse while assuring appropriate access to effective pain treatment

Thank You



