

# Addressing Opioids: The FDA Response to Challenges in Public Health

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# Central Message

- FDA is responding to the public health challenges of opioids using all of our available tools to:
  - Address the ongoing crisis of opioid abuse and misuse
  - Address the ongoing shortages of injectable prescription opioids

# The Opioid Challenges:

**Opioid Abuse and Misuse**

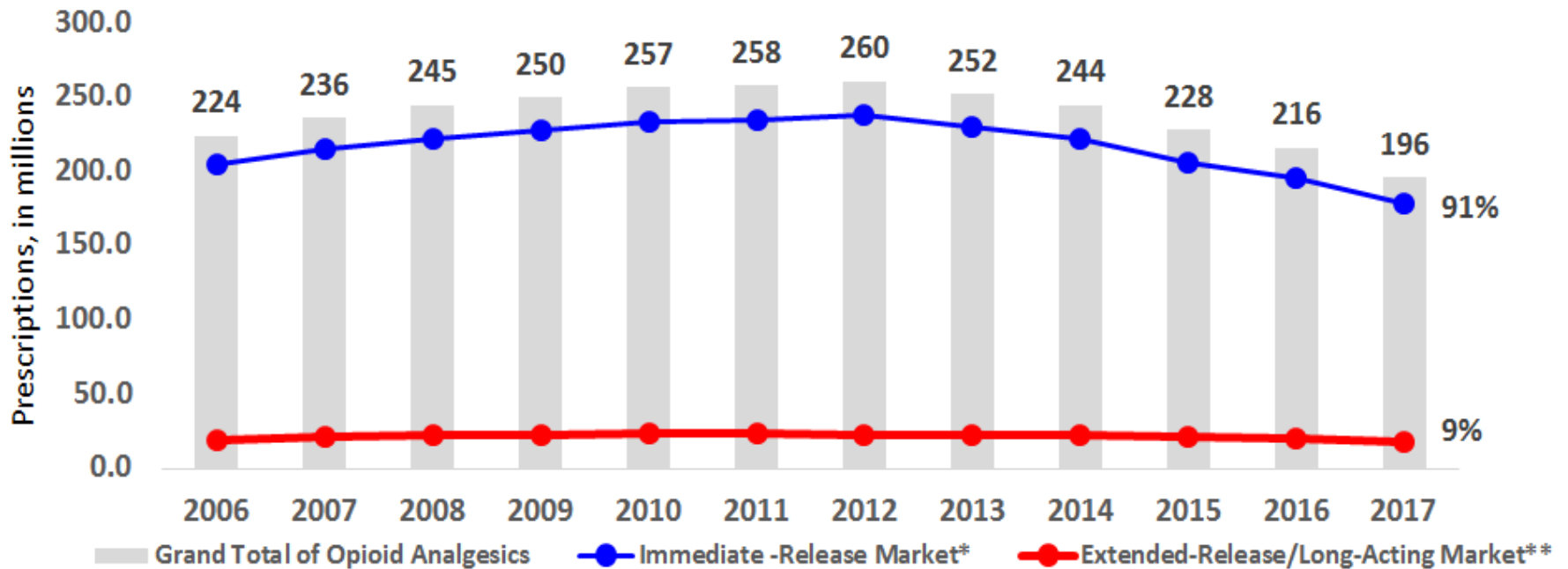
Injectable Opioid Shortages

# Misuse and Abuse of Prescription Opioid Analgesics Remains an Important Public Health Problem

- In 2017, prescription opioids were the largest category of pharmaceutical products misused and abused in US
  - 11.1 million people estimated to have past-year misuse/abuse
  - 1.7 million people estimated with DSM IV criteria for substance use disorder involving prescription opioid analgesics
- In comparison, 886,000 estimated to have past-year heroin use

**Source:** Substance Abuse and Mental Health Services Administration. (2018). Key substance use and mental health indicators in the United States: Results from the 2017 National Survey on Drug Use and Health (HHS Publication No. SMA 18-5068, NSDUH Series H-53). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from <https://www.samhsa.gov/data/>.

# Crisis Ongoing Despite Falling # of Prescriptions for Opioid Analgesics



Source: IQVIA, National Prescription Audit (NPA) and static data 2006-2011. January 2006-December 2017. Static data extracted March 2017 and 2012-2017 data extracted February 2018.

\*Immediate-Release formulations include oral solids, oral liquids, rectal, nasal, and transmucosal

\*\*Extended-Release/Long-Acting formulations include oral solids and transdermal patches

Note: Include opioid analgesics only, excluding injectable formulations as well as opioid-containing cough-cold products and opioid-containing medication-assisted treatment (MAT) products

# Consequences: Prescription Opioids and Overdose Death in the US



## Drugs Involved in U.S. Overdose Deaths, 1999 to 2017

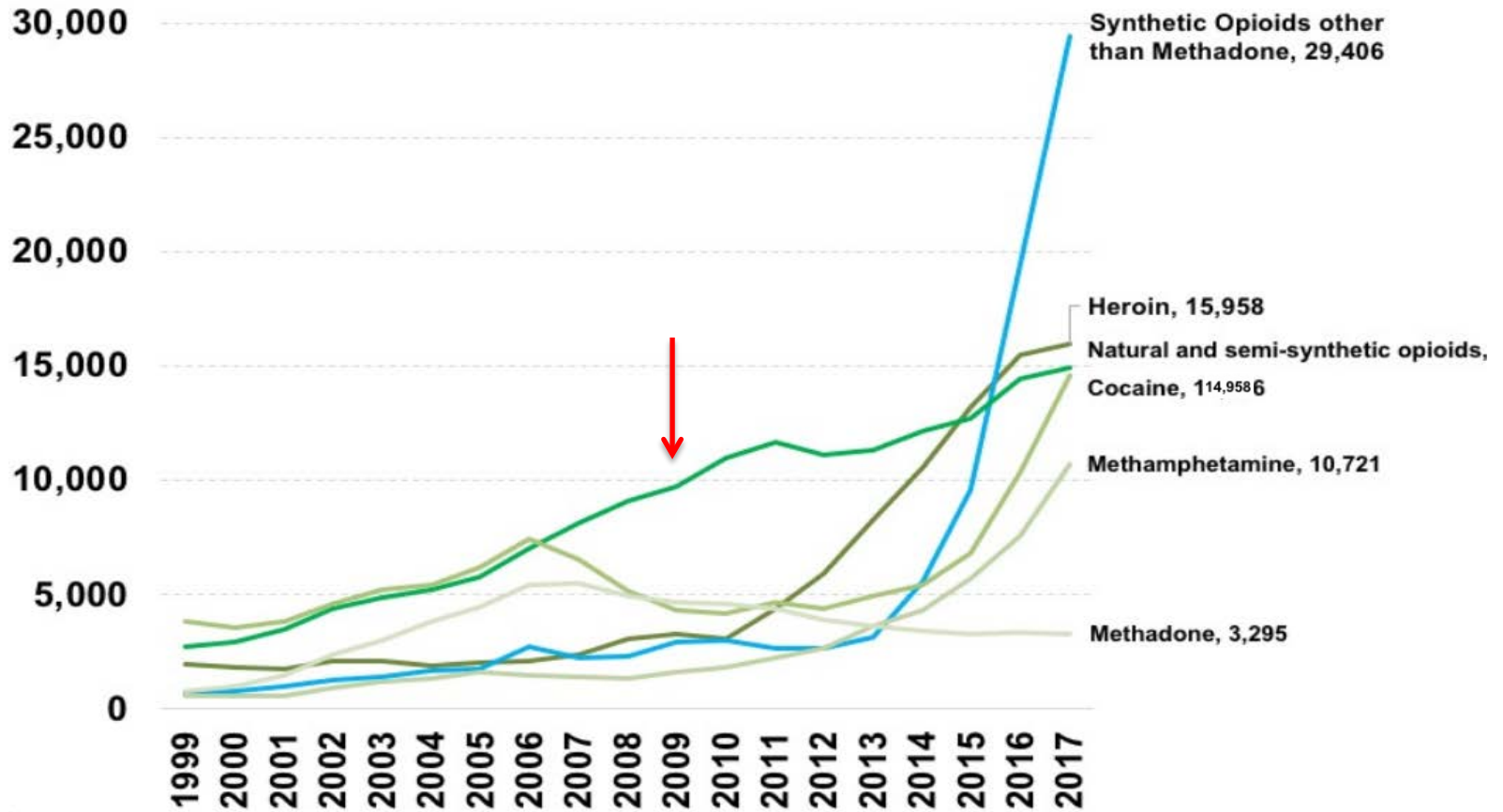


Figure Source: National Institute on Drug Abuse Data Source: CDC Wonder

Available from: <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>

# The FDA and Opioid Abuse/Misuse

"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

1. Decreasing Exposure & Prevent 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



## 1. Decreasing Exposure & Prevent New Addiction



Appropriate Dose/Duration Labeling



Appropriate Packaging, Storage, and Disposal



Health Care Provider Education

## 2. Supporting the Treatment of Those With Opioid Use Disorder



Naloxone



Medication Assisted Treatment (MAT)

## 3. Fostering the Development of Novel Pain Treatment Therapies



Partnerships & Meetings



Abuse Deterrent Formulations (ADFs)



Pain Treatment Alternatives

## 4. Improving Enforcement & Assessing Benefit-Risk



Improving Enforcement



Assessing Benefit-Risk

# FDA Priorities align to HHS Strategic Priorities and other National Activities



## HHS STRATEGIC PRIORITIES      FDA PRIORITIES      OTHER ACTIVITIES

Better data

Better targeting of overdose-reversing drugs

Better research

Better addiction prevention, treatment, and recovery services

Better pain management

1. Decreasing Exposure & Prevent 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 Opioid Initiative

Office of National Drug Control Policy Recommendations

Comprehensive Addiction and Recovery Act (CARA)

National Pain Strategy Recommendations

National Public Health Emergency

# FDA Priorities Align with Recently Passed SUPPORT Act

- Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT)
- Many new provisions affecting FDA including tools to:
  - more efficiently stop illegal, illicit, unapproved, counterfeit and potentially dangerous drugs from entering the U.S. through the IMFs
  - reduce exposure to opioids as a way to lower the rate of new addiction
  - require certain packaging, such as unit dose blister packs, for opioids and other drugs that pose a risk of abuse or overdose
  - require that opioids be dispensed with a mail-back pouch or other safe disposal option
- Implementation ongoing

<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm624268.htm>

# Example: Decreasing Exposure & Preventing New Addiction



## HOW?

## WHAT?

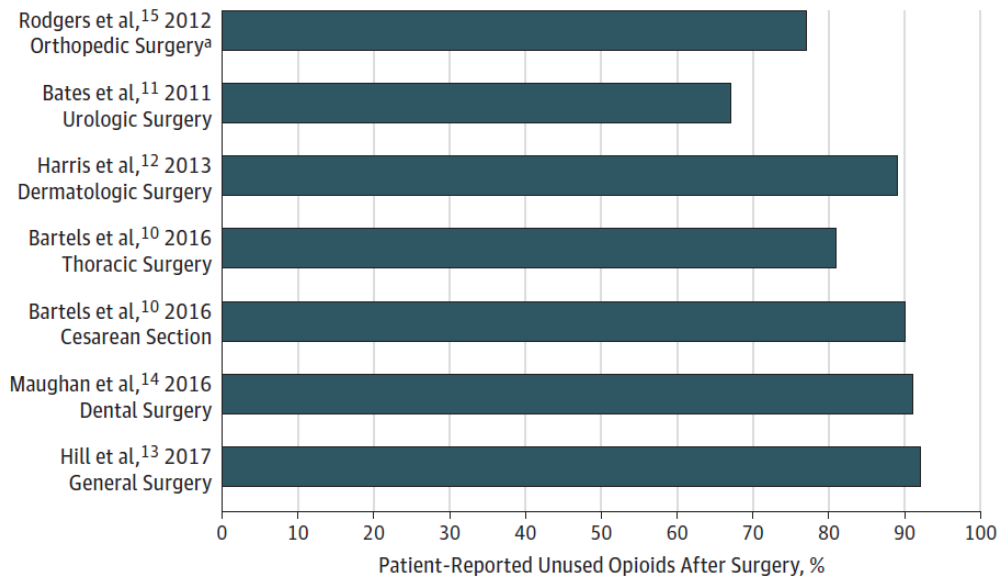


### Appropriate Packaging, Storage, and Disposal

- 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.
- **Jun 1, 2017:** FDA/Duke Margolis **workshop and white paper** on packaging, storage, and disposal solutions.
- **Dec 11-12, 2017: Public workshop** to gain input on **packaging strategies**. Public docket closed March 2018 with 44 comments.
- **Jan 2018:** Requested **packaging in limited amounts** of over-the-counter anti-diarrheal medicine **loperamide** to **curb intentional misuse and abuse**.

# Target: Leftover Opioid Analgesics Reported in Post-surgical Populations

Figure. Prevalence of Unused Opioids Prescribed After Surgery



<sup>a</sup>percentage of patients reporting use of 15 tablets or fewer

- Across many surgical procedures,
  - >50% of patients reported excess supply of opioid analgesics after treatment of acute pain
  - Most patients kept excess supply and stored supply in unsecured locations

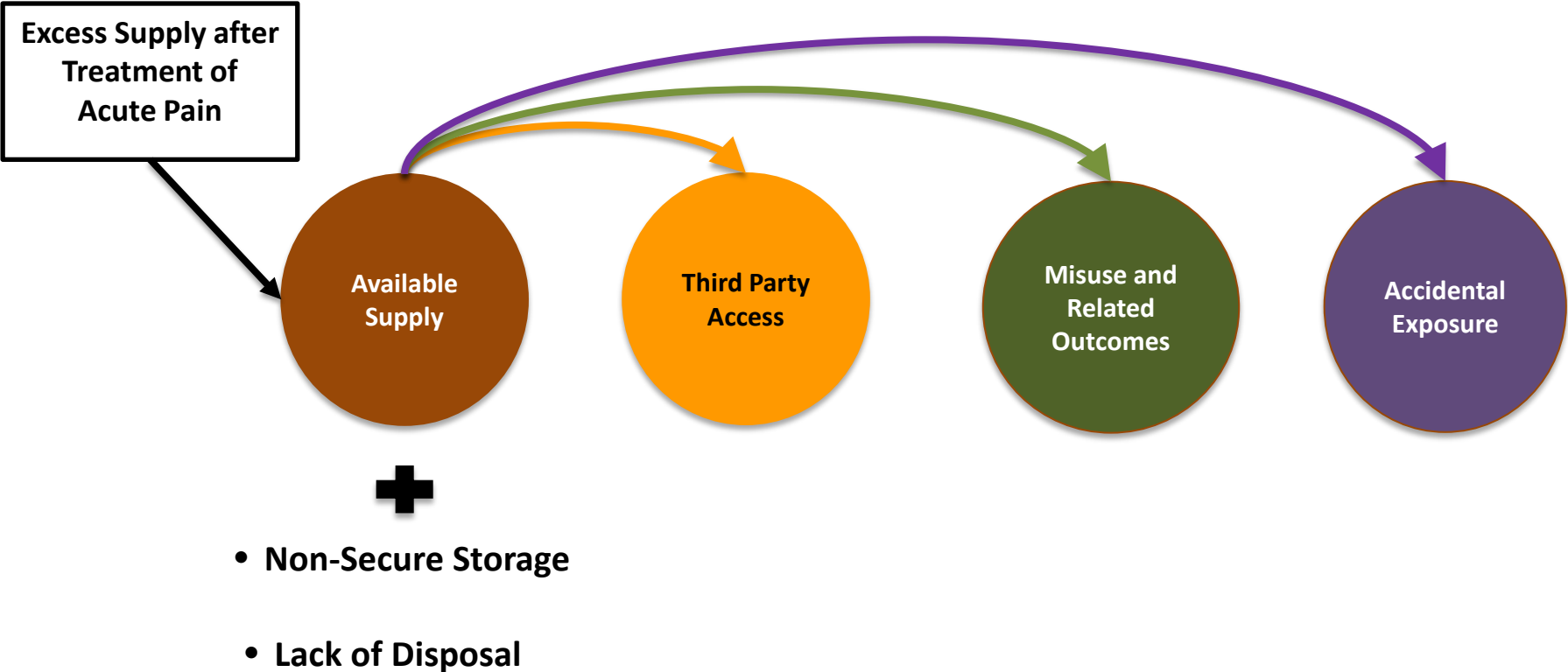
Figure Source: Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription Opioid Analgesics Common, ... After Surgery: A Systematic Review. JAMA Surg. 2017 Nov 1;152(11):1066-1071.

# Opioid Analgesic Needs Vary by Condition/Procedure

Procedure	Mean/ (range) tablets filled	Mean/Median tablets consumed	~Days Used	~Leftover tablets
Outpatient Shoulder Surgery	60 (n.d.)*	37 (n.d.)*	9-10	23
Cesarean Delivery	40 (5-80)*	20*	4-5	20
Tooth Extraction	28 (n.d.)	13	2-3	15
Upper Extremity Surgery	30 (n.d.)	14 (Bone); 9 (Soft Tissue)	2-3	15
Laparoscopic Cholecystectomy	30 (0-100)	10-12	2-3	20
Laparoscopic Appendectomy	30 (n.d.)*	12*	2-3	18
Partial Mastectomy with Node Biopsy	23 (0-60)	6	1-2	17
Laparoscopic Inguinal Hernia Repair	33 (15-70)	9	1-2	24
Open Inguinal Hernia Repair	30 (15-120)	9	1-2	21
Partial Mastectomy	21 (0-50)	3	1	18
Dermatologic Surgery	9 (3-20)	4	1	5

1. Hill, et al., *Ann Surg*, 2017; 2. Bateman, et al., *Obstet Gyn*, 2017; 3. Maughan, et al., *Drug Alc Dep*, 2016; 4. Harris, et al., *JAMA Dermatol*. 2013; 5. Bockman, et al. *J Pain*, 2017 (Abstract); 6. Kumar, et al. *AJSM*, 2017

# Issue: Opioid Analgesic in the Home Can Feed Other Problems if Misused



## FDA Response: Potential Work on Packaging

- Exploring whether a defined, short-term supply of medication could be packaged in a manner that limits the number of pills dispensed (e.g., blister packs)
- Exploring packaging that could make it easier to track the number of doses that have been taken or reduce the risk for third-party access, such as teens ingesting pills they found in a medicine cabinet
- Work to improve storage and encourage prompt disposal to reduce the available supply of unused opioids



# The Opioid Challenges:

Opioid Abuse and Misuse

**Injectable Opioid Shortages**

# Shortages of Injectable Opioids

## Opioid shortages leave US hospitals scrambling

By Pauline Bartolone, California Healthline  
Updated 5:45 AM ET, Mon March 19, 2018



More from CNN

- California te... charges after a...
- Utah teen ge... life for helpi... herself

HEALTH CARE

## In the midst of a massive opioid crisis, hospitals are experiencing an opioid shortage

By Aaron Schachter  
May 14, 2018 | 5:22 PM



HOME / CIVIC / HEALTHCARE OF TOMORROW

## Hospitals Face Prolonged Injected Opioid Shortage

The other opioid crisis: Hospitals are frequently running out of widely used injected painkillers, and some patients are feeling the pain.

June 27, 2016, at 8:54 a.m.



### HEALTHCARE OF TOMORROW

The health care industry is evolving, thanks to changes, societal shifts and technological advances. Healthcare of Tomorrow from U.S. News & World Report examines the challenges facing health care, and how it must change to face the future. See more of our special reports.

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# Origins of the IV Opioids Shortage

- Critical need for use in post-op settings
- One large manufacturer reported shortages of multiple critical drugs including injectable hydromorphone and morphine due to manufacturing, distribution, third party supplier delays, as well as remediation efforts at one of their facilities, beginning in July of 2017
- Lack of alternative sources for needed products with sufficient capacity to meet added demand

# FDA Work to Address IV Opioids Shortage



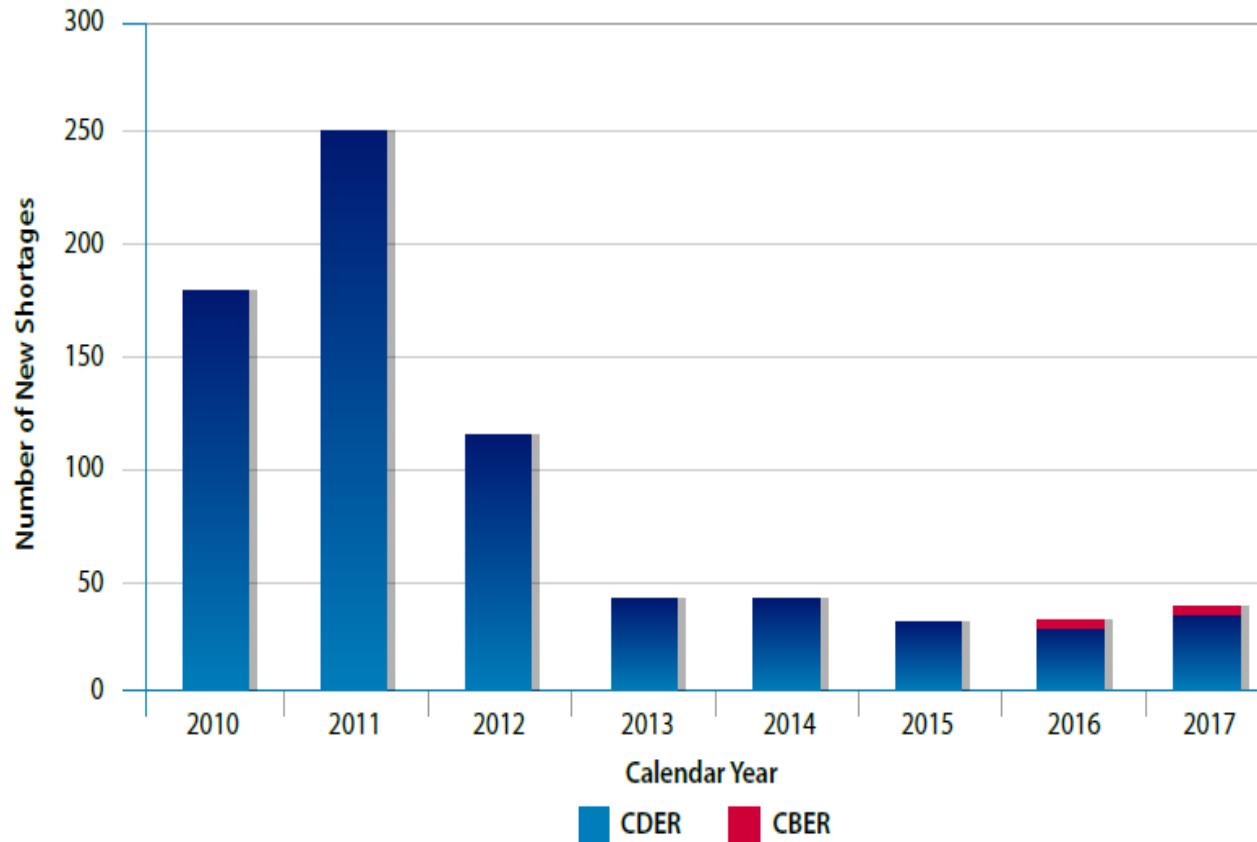
FDA working with manufacturers to bring additional products to market

- Expediting review of all related applications – new approvals from two other manufacturers for morphine and hydromorphone are now being launched
- Releasing Carpuject syringes with potential cracked needle hubs under regulatory discretion with instructions for healthcare professionals to inspect and withdraw contents with a filter needle before administering to patients
- Extending expiration dating for multiple opioid products listed on the FDA website based on data from the manufacturer
- Allowing temporary import of unapproved hydromorphone in coordination with DEA

# FDA Response to IV Opioids Shortage (cont)

- Coordinating with DEA on quota issues
  - FDA shares information with DEA through a Memorandum of Understanding
  - Providing a market assessment to DEA to assist them in their decision about whether to grant the quota

# Trends in New Drug Shortages 2010-2017



From FDA Drug Shortage Report to Congress, 2017  
<https://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM610662.pdf>

# What FDA Does to Address Drug Shortages



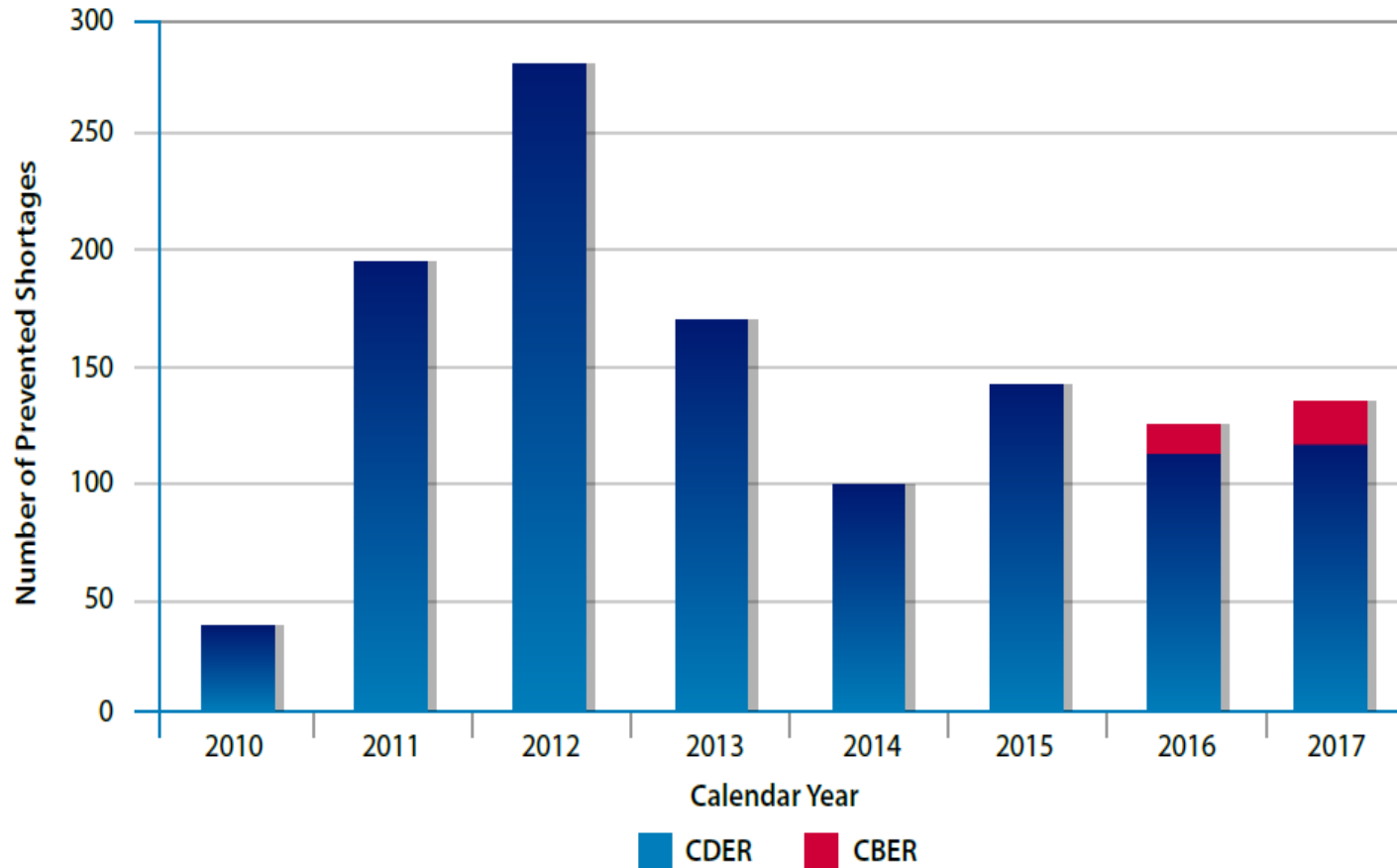
- Drug Shortage Staff focused on addressing drug shortages
- Facilitate temporary and long-term strategies to address shortages
- Coordinate timely and comprehensive risk/benefit decisions within FDA
  - Personnel across multiple FDA Offices involved in shortage response
- Distribute information (web posting, professional organizations):
  - <https://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm>
- **Goal: Maintain availability while minimizing risk to patients**

# What FDA Cannot Do to Address Drug Shortages

- FDA cannot require:
  - A company to disclose details of why a shortage occurs
  - A company to make a drug
  - A company to make more of a drug
  - How much and to whom the drug is distributed



# Trends in Preventing Drug Shortages 2010-2017 (FDA)



From FDA Drug Shortage Report to Congress, 2017  
<https://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM610662.pdf>

# Lessons Learned

- Availability of drugs for patients is critical for healthcare
  - Interruptions of drug manufacturing due to any reason can lead to drug shortages with devastating impact on public health
- Sources of drug shortages include manufacturing challenges and natural disasters
  - FDA response tailored to address underlying cause(s)
  - Communications and information sharing are critical both to preventing and to mitigating shortages
- Recovery from shortages takes time. Prevention is critical to reducing the numbers of drug shortages

# Ongoing FDA Shortage Work



- FDA Drug Shortage Taskforce
  - Announced July 2018
  - Goal of improved understanding of the forces leading to drug shortages and identify potential solutions
- Stakeholder Listening Sessions
  - ✓ Pharmacies and Hospitals
  - ✓ Manufacturing Groups
  - ✓ Medical Groups
  - ✓ GPO's and Distributors
- Public meeting November 2018
- Taskforce Members
  - Food and Drug Administration (CDER, CBER, CDRH, ORA)
  - Center for Medicare and Medicaid Services
  - The Office of the Assistant Secretary of Preparedness and Response
  - The Department of Veterans Affairs
  - The Department of Defense
  - The Federal Trade Commission

# Conclusions

- FDA's response to issues raised by opioids reflect unique challenges of how they are used, misused and abused
  - Addressing opioid abuse crisis a top priority for FDA
    - Multiple ongoing activities coordinated within a policy framework focused on public health impacts
  - Separately, injectable opioid shortages reflect the larger challenge of drug shortages today
    - FDA response is aimed at understanding and preventing shortages where possible, and at mitigating those that cannot be avoided

# Thank You

