



FDA and Opioids: What's a Regulator to Do?

Pain Care Forum

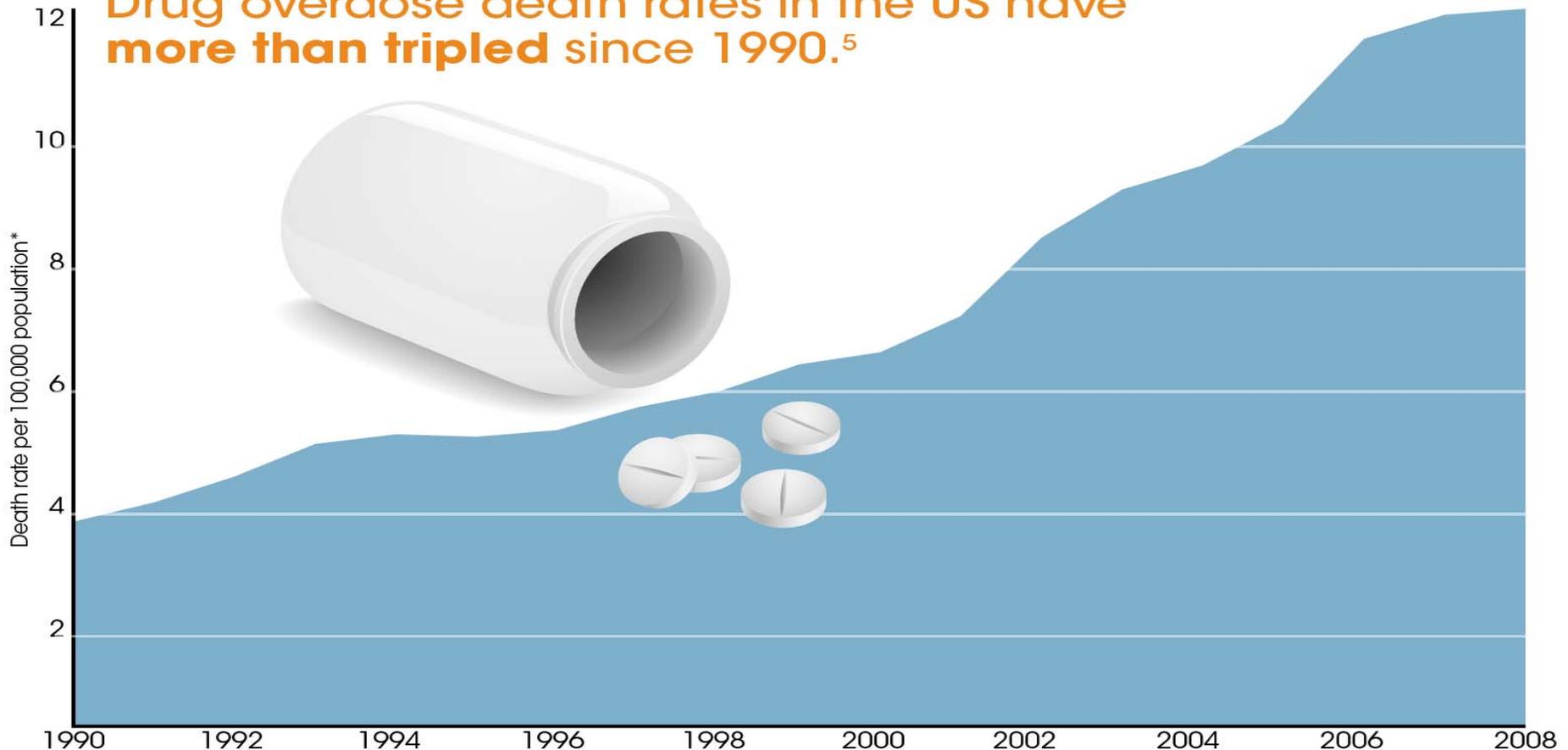
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Deputy Director, CDER, FDA**

June 14, 2012



A Major Public Health Problem

Drug overdose death rates in the US have **more than tripled** since 1990.⁵



*Deaths are those for which poisoning by drugs (illicit, prescription, and over-the-counter) was the underlying cause.

Opioid Deaths Are the “Tip of the Iceberg”

In 2008, there were **14,800** prescription painkiller deaths.⁴

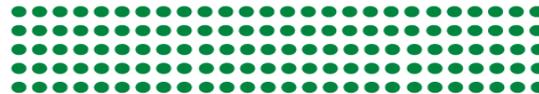
For every **1** death there are...



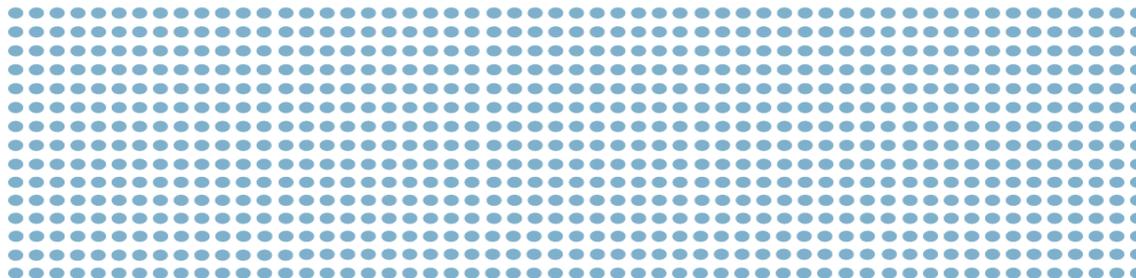
10 treatment admissions for abuse⁹



32 emergency dept visits for misuse or abuse⁶

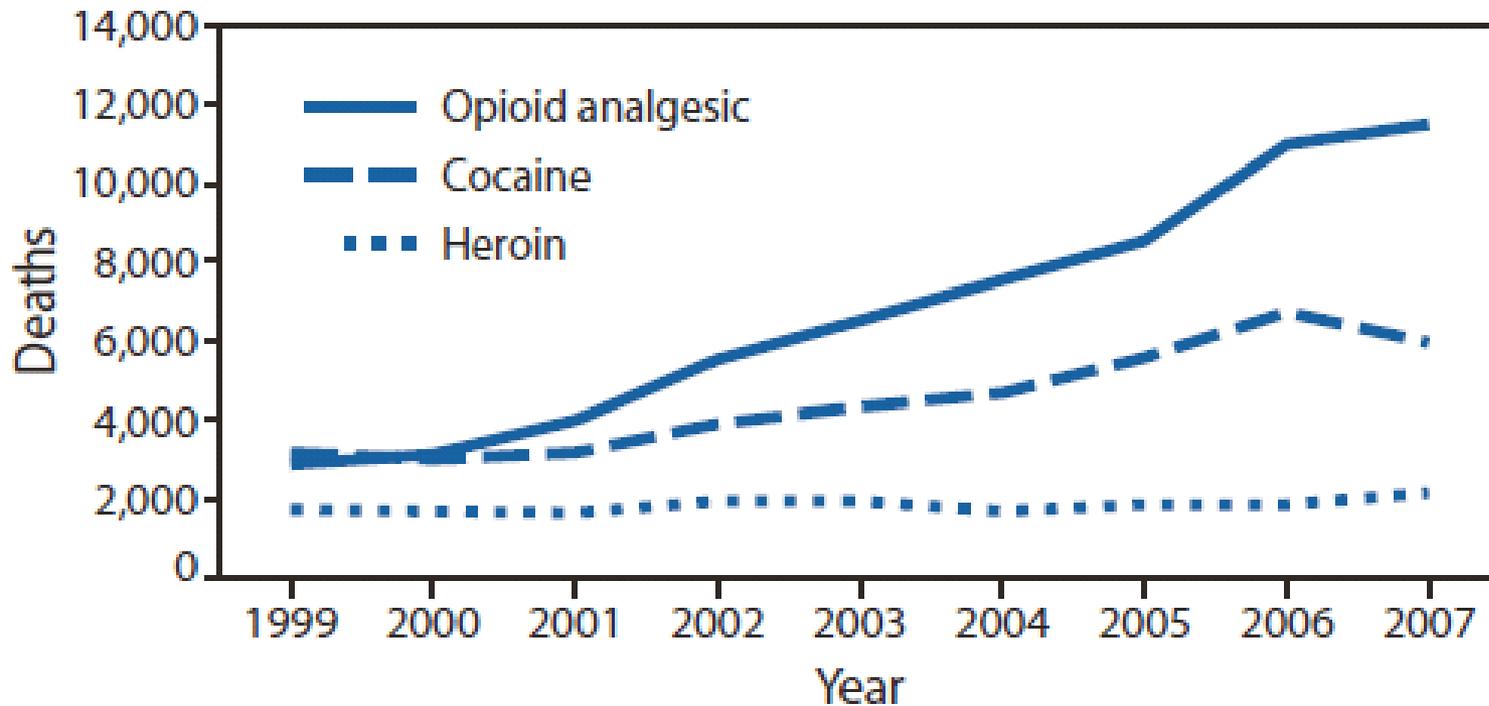


130 people who abuse or are dependent⁷



825
nonmedical users⁷

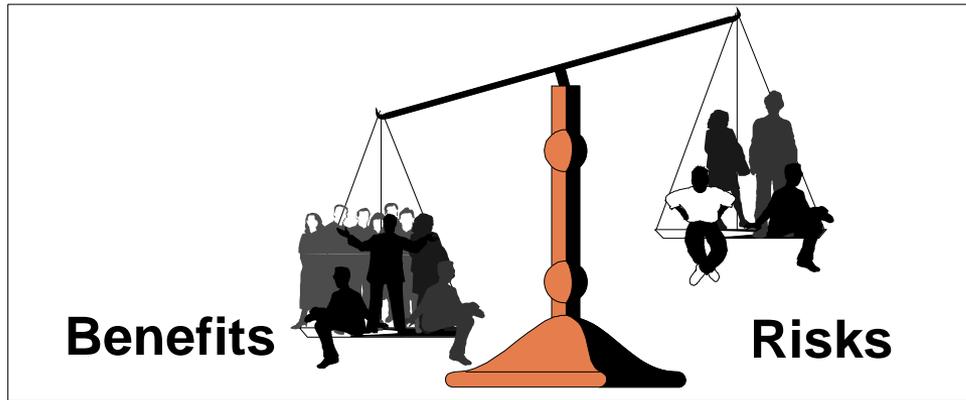
Causes of Unintentional Drug Overdose Deaths — United States, 1999–2007



Opioids: FDA One of Many Stakeholders

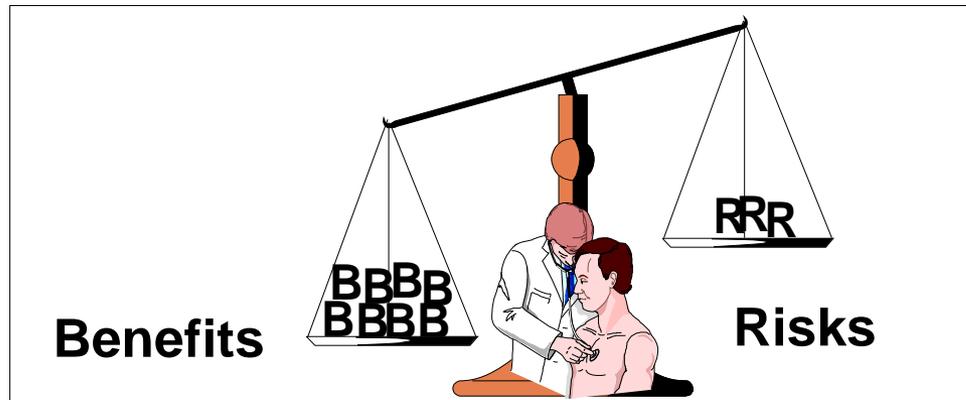
FDA

evaluates
benefits/risks
for the population



Provider

evaluates
benefits/risks
for a patient



Patient/Advocates

evaluates
benefits/risks
in terms of
personal values

Benefits Risks

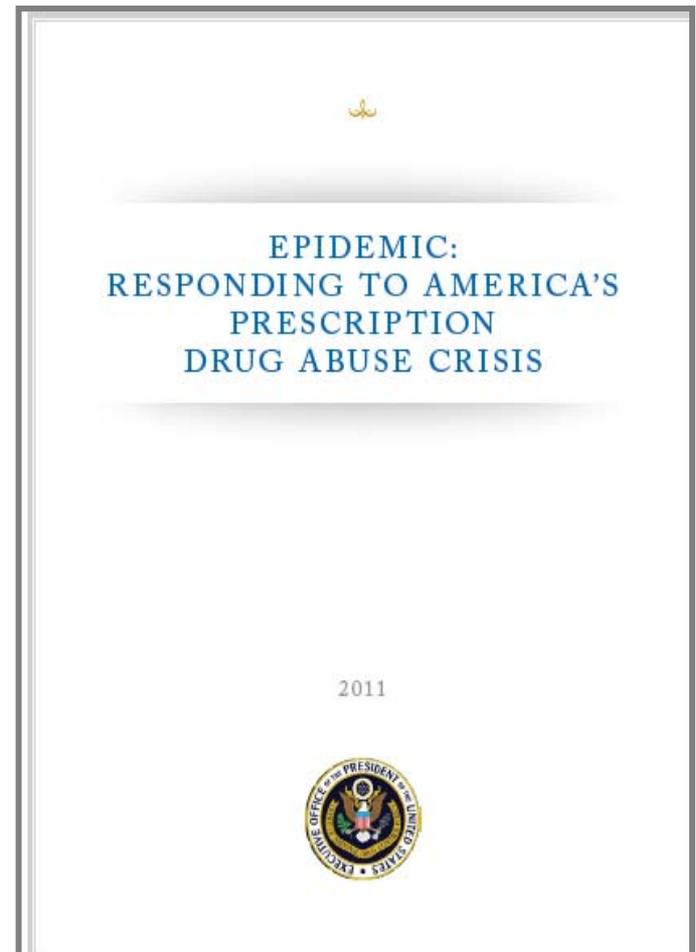


What's A Regulator to Do?

- We have an important role among the many groups with important roles to play
 - FDA role extends beyond strictly regulatory activities—broad range of activities
 - Unintended consequences are important to try to avoid
 - Need to avoid inefficient, burdensome systems
 - Focus on highly-impacted groups to hear concerns and anticipate issues
 - Unintended consequences may happen
 - Willingness to listen and change essential

FDA Within Larger Governmental Response

- April 2011 - Obama Administration National Drug Abuse Prevention Plan
- Four major areas of focus to reduce prescription drug abuse and other harm from drugs
 - Education
 - Monitoring
 - Proper medication disposal
 - Enforcement



FDA Commitments in ONDCP Plan

- Improved prescriber education through Opioid REMS
- Guidance on development of abuse-resistant formulations of opioids
- Public meeting to discuss best uses of naloxone in the treatment of opioid overdose

FDA's Regulatory Response

U.S. Department of Health & Human Services | www.hhs.gov

FDA U.S. Food and Drug Administration | A-Z Index | Search [] go

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Home > Drugs > Drug Safety and Availability > Information by Drug Class

Drug Safety and Availability
Information by Drug Class

Resources for You

- Office of National Drug Control Policy (ONDCP)
- Responding to America's Prescription Drug Abuse Crisis (ONDCP)
- Background on Opioid REMS
- Current State of Opioid Drug

Opioid Drugs and Risk Evaluation and Mitigation Strategies (REMS)

Opioids are at the center of a major public health crisis of addiction, misuse, abuse, overdose and death. FDA is taking action to protect patients from serious harm due to these drugs. **This action represents a careful balance between continued access to these necessary medications and stronger measures to reduce their risks.**

Update on Implementation of Opioids REMS

After notifying the sponsors of long-acting and extended-release (LA/ER) opioid drugs that they were required to submit a risk evaluation and mitigation strategy (REMS), FDA has been working with the sponsors that market these products on the required REMS. The central component of the Opioid REMS is an education program for prescribers (e.g., physicians, nurse practitioners, physician assistants) so that LA/ER opioid drugs can be prescribed and used safely. FDA expects the prescriber training to be conducted by accredited, independent continuing education (CE) providers, without cost to the healthcare professionals, under unrestricted grants to accredited CE providers funded by the sponsors.

On November 4, 2011, FDA announced the availability for public comment of a draft "Blueprint." The Blueprint, developed by FDA with advice from other Federal agencies, is a basic outline and the core messages that FDA believes should be conveyed to prescribers in a basic two to three hour educational module. After it is completed and approved as part of the REMS, the Blueprint will be posted on the FDA Web site for use by CE providers in developing CE courses.

For further information, please contact: OpioidREMS@fda.hhs.gov.

FDA Action on Opioid Drugs

- Draft Blueprint for Prescriber Education for the Long-Acting/Extended-Release Opioid Class-wide

Go to [FDA.GOV](http://www.fda.gov) and type opioid REMS in search box

or

<http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm163647.htm>

Opioids: FDA Risk Evaluation and Mitigation Strategy (REMS)

- Focus is long-acting and extended-release opioids (ER/LA opioids)
 - Disproportionate share of misuse and abuse
- February 2009 to present: Listening, Analysis, Proposals, Implementation

Goals of ER/LA Opioids REMS

- Help address the significant increase in inappropriate prescribing, misuse and abuse of these products over the past decade
- Minimize the burden on the healthcare system of having all these products with a different REMS

Opioids: REMS and Education

- Potential approaches chosen on evidence of what will make a difference within FDA regulatory authority
- Education about ER/LA Opioids
 - Improved labeling including Medication Guides
 - Outline of content that is important to be included in educational activities ('blueprint')*
 - Educational materials available for patients to help improve use and disposal

*<http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM277916.pdf>¹²

ER and LA Opioid REMS Prescriber Education*

- General information about the use of the class of LA/ER opioids to aid in patient selection and counseling
- Specific information about the individual drugs in this class.
- Information about how to recognize the potential for and evidence of addiction, dependence, and tolerance.
- Information on proper storage and disposal

* From draft FDA 'Blueprint'₁₃

Opioids REMS In Context

- Opioid REMS: proposed education for prescribers is not mandatory
- Paired with a separate Administration goal in ONDCP plan to link mandatory effective prescriber training to DEA registration to prescribe controlled substances
 - Legislation required

Other Regulatory Activities

- Guidance on development of abuse-resistant formulations of opioids
 - Provide regulatory guidance on development of abuse-deterrent formulations and on post-marketing assessment of their performance
 - Many challenging scientific issues!
 - **Incentivize product development**
 - **Avoid negative impact on Generics development**
- Labeling revision to reflect new data
- Priority reviews for promising products

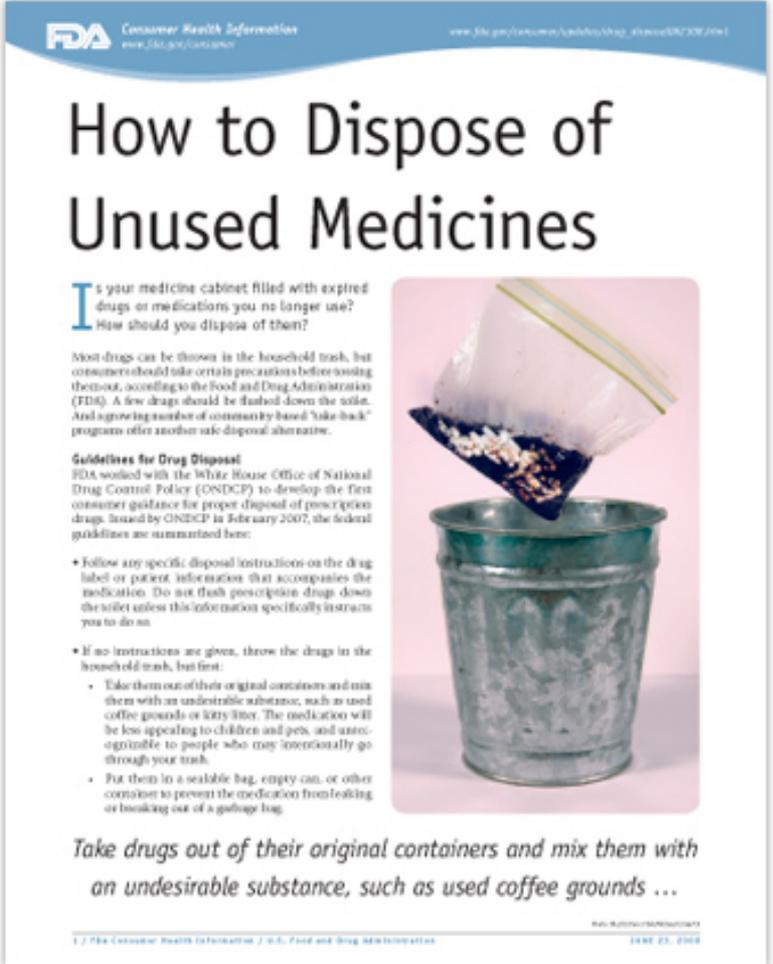
Other Regulatory Activities

- PDUFA Reauthorization
 - Variety of proposals related to controlled substances under discussion
- Advisory Committee to discuss hydrocodone combination product upscheduling October 29-30, 2012
 - <http://www.gpo.gov/fdsys/pkg/FR-2012-06-08/pdf/2012-13868.pdf>

Other Regulatory Activities: Disposal

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

FDA focus on flushing of selected high-potency drugs that can kill with a single dose to improve human safety
Example: recent fentanyl patch communication



The poster features the FDA logo and the text 'Consumer Health Information' at the top. The main title is 'How to Dispose of Unused Medicines'. Below the title, there is a paragraph starting with 'Is your medicine cabinet filled with expired drugs or medications you no longer use?' followed by a question 'How should you dispose of them?'. A second paragraph explains that most drugs can be thrown in the household trash, but certain precautions should be taken, and some drugs should be flushed down the toilet. It also mentions 'take-back' programs. A section titled 'Guidelines for Drug Disposal' states that 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 guidelines are summarized in a list of bullet points. To the right of the text is a photograph of a clear plastic bag being poured into a green glass jar. Below the photograph, there is a quote: 'Take drugs out of their original containers and mix them with an undesirable substance, such as used coffee grounds ...'. At the bottom, there is a small footer with the text 'U.S. Food and Drug Administration' and 'JUNE 23, 2008'.

FDA Consumer Health Information
www.fda.gov/consumers
www.fda.gov/consumers/updates/ucm101653.html

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 containers 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 ...

U.S. Food and Drug Administration
JUNE 23, 2008

What's A Regulator To Do (Cont): Non-Regulatory Activities

- Patterns of drug use and information flow are more complex than ever
 - Influencing behavior requires multiple inputs
- FDA need to work in partnership with other parts of the healthcare system to promote the best uses of drugs
 - FDA Safe Use Initiative—Focus on Collaboration

Improving Analgesics Use Requires Collaboration/ Safe Use



- Medicines are essential for the treatment of an important human condition (pain)
- Pain has both medical and social aspects to its treatment
 - No single entity or institution ‘owns’ the problem
- Multiple tx modalities exist, including several classes of drugs (Rx and OTC): opiates, NSAIDs, APAP.....
 - The available drugs all have ‘challenges’
- Complex social, regulatory and legal issues

Safe Use Activities on Opioids

- Physician Patient Agreement (PPA) development
 - Partnership with multiple groups to craft and test a model PPA to be used when valuable
 - FDA convened pain management specialists, GPs, pharmacists, dentists and nurse practitioners to work on templates
- PDMPs and Data-sharing
 - Collaborating with Brandeis University to pilot and test a surveillance tool using integrated PDMP data from 5 states

What's A Regulator To Do (Continued): Additional Scientific Work

- Pharmacology of methadone cardiac toxicity
 - FDA scientists created an exposure-response model for methadone effects on QT interval
 - Links dose of methadone to CV risk to inform risk mitigation strategies
- Naloxone use in preventing overdose deaths
 - FDA/CDC/NIDA public meeting April 2012
- Efficacy of opioids in treating chronic non-cancer pain
 - FDA/NIH public meeting May 2012

Priority Needs

- Improved data collection
 - DAWN transition
 - Definitional standards
- Measurement tool to assess access to pain medicines
- Diagnostic and therapeutic biomarkers for pain
- Improved data on efficacy of chronic opioids—
who benefits, who doesn't?
 - ACTION Network

Summary

- FDA is taking the issues around appropriate use of all medicines, including opioids, seriously. Opioids and other complex medical issues have shifted the paradigm
 - Broadened the scope of our involvement after drug approval for complex drugs issues
 - Reinforced need to be prepared to change course where necessary
 - Regulatory and Non-Regulatory Roles for FDA
 - Collaborative model absolutely essential

Conclusion: Role of the FDA?

- Fulfill our role: one among many
- Assure all voices are heard
- Remember that the status quo is not acceptable: we must stem this tide of misuse, abuse and death before it imperils future access to essential therapies for pain