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

Pain Care Forum

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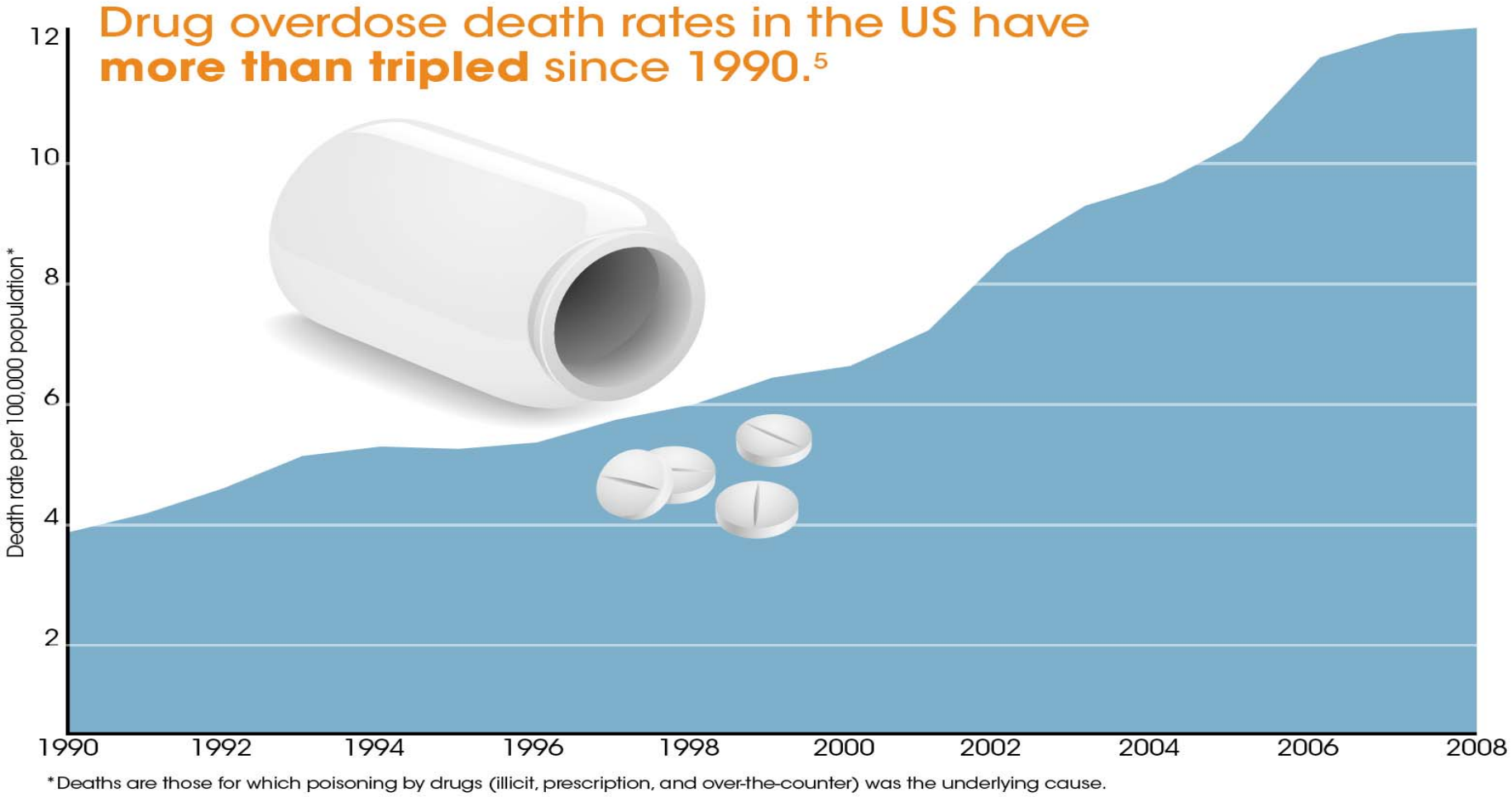
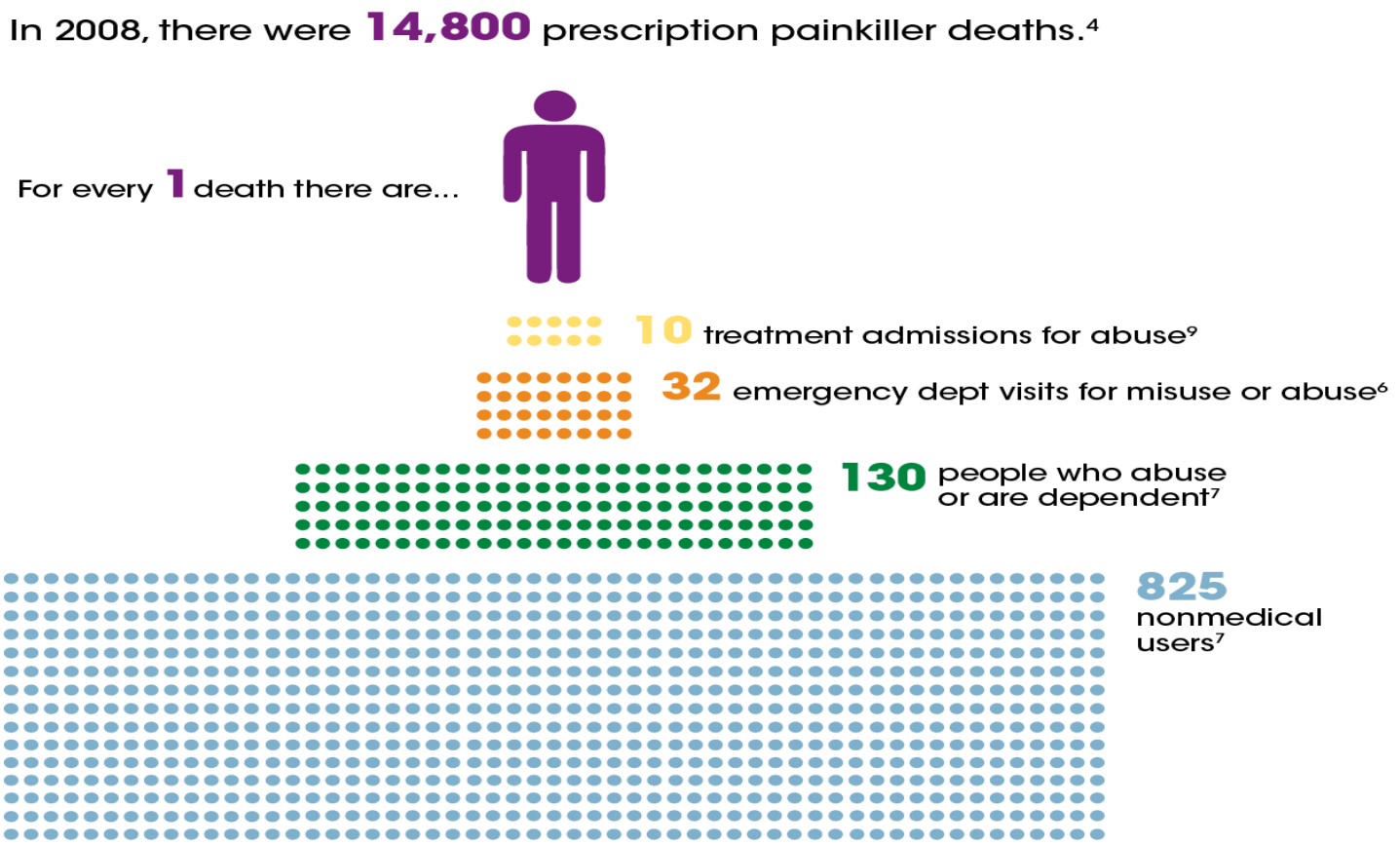
A Major Public Health Problem



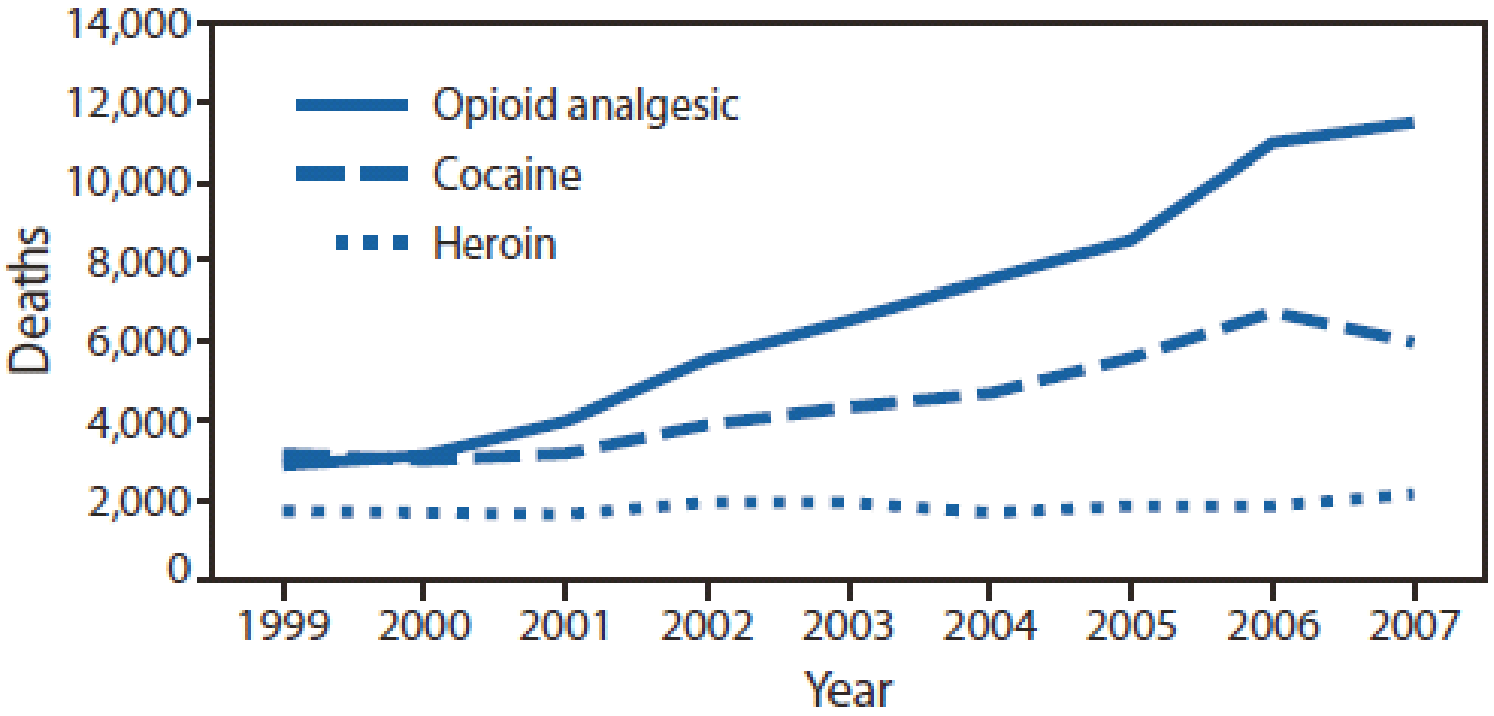
Source: CDC NCIPC November 2011

Opioid Deaths Are the "Tip of the Iceberg"



Source: CDC NCIPC November 2011

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

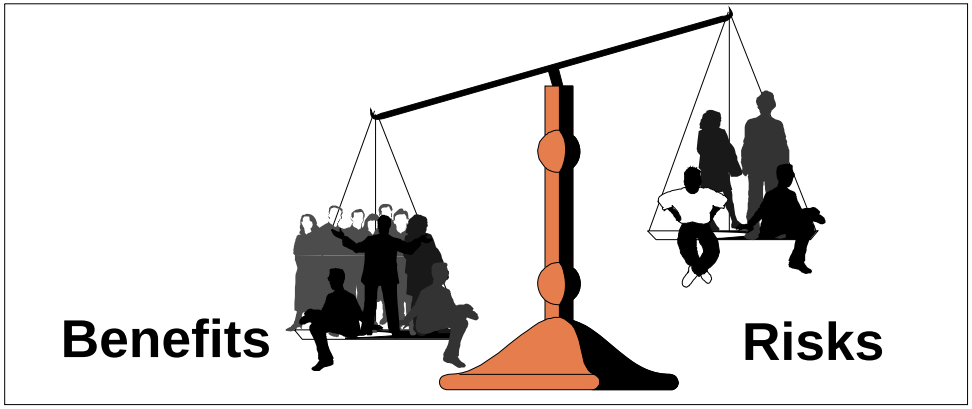


Source: National Vital Statistics System

Opioids: FDA One of Many Stakeholders

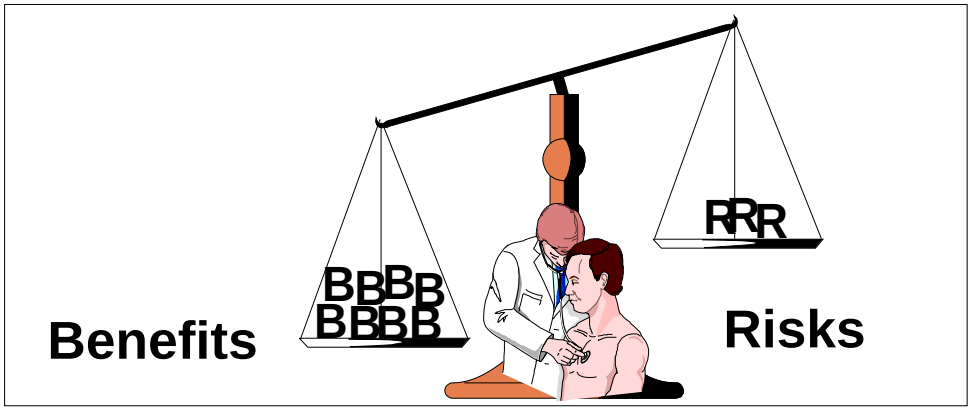
FDA

evaluates
benefits/risks
for the population



Provider

evaluates
benefits/risks
for a patient



Patient/Advocates

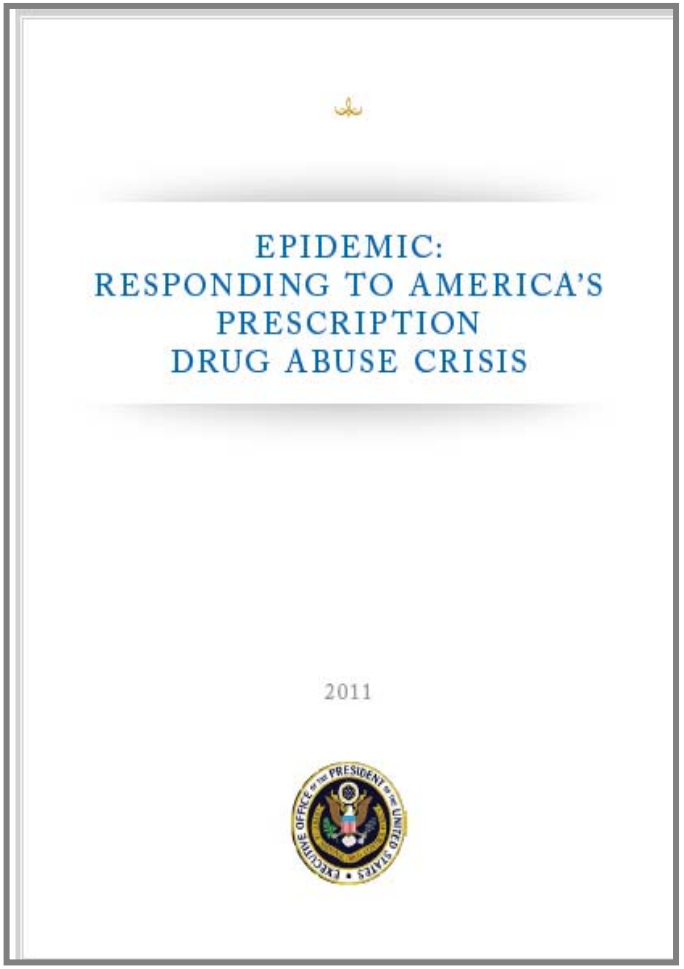
evaluates
benefits/risks
in terms of
personal values

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

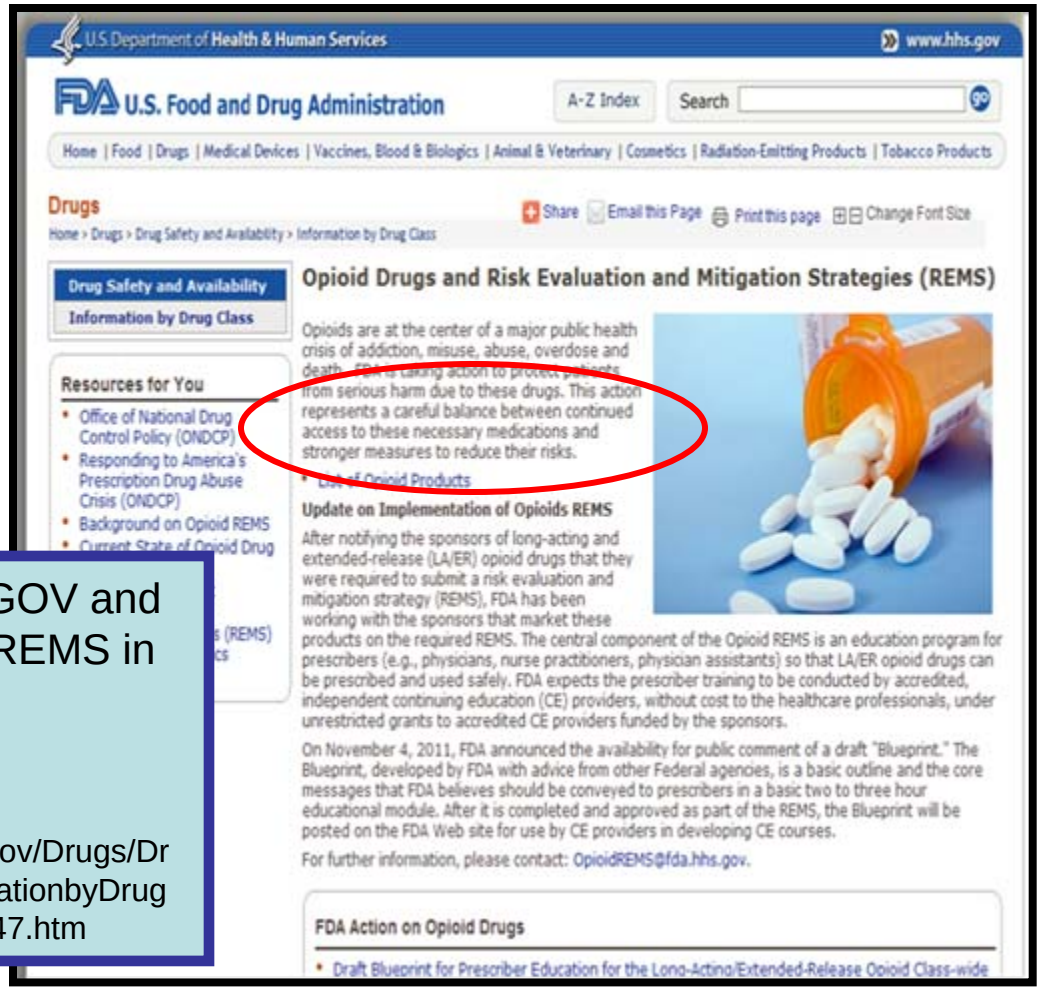
- April 2011 - Obama Administration National Drug Abuse Prevention Plan
- Four major areas of focus to reduce prescription drug abuse and other harm from drugs
  - Education
  - Monitoring
  - Proper medication disposal
  - Enforcement



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



Go to 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

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'

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

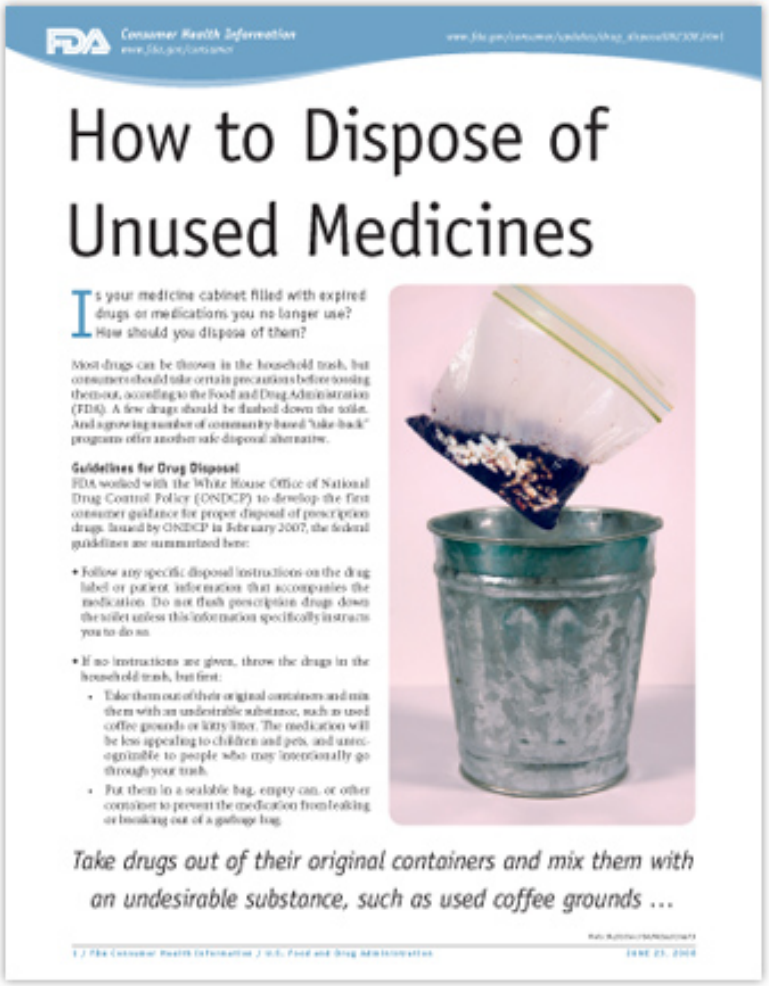
- PDUFA Reauthorization
  - Variety of proposals related to controlled substances under discussion
- Advisory Committee to discuss hydrocodone combination product upscheduling October 29-30, 2012
  - http://www.gpo.gov/fdsys/pkg/FR-2012-06-08/pdf/2012-13868.pdf

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



FDA Consumer Health Information

www.fda.gov/consumer

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.

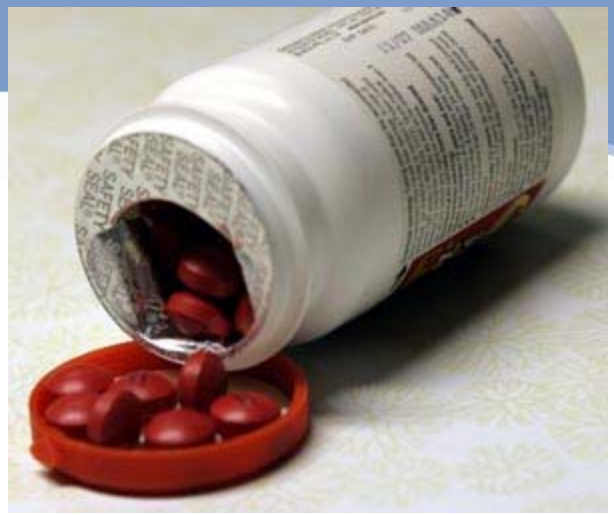
Take drugs out of their original containers and mix them with an undesirable substance, such as used coffee grounds …

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

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?
  - ACTTION 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