U.S. Food and Drug Administration
Protecting and Promoting Public Health
www.fda.gov

FDA Update

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APhA Annual Meeting (New Orleans, LA)
March 11, 2012

Objectives

At the completion of this activity, participants will be able to:

- Describe FDA activities during the last year.
- State how changes in FDA regulations and actions will affect participant's practice.

Overview

- FDA mission
- Approval and actions
- Drug safety information
- Safe Use Initiative
- REMS/Medication Guides
- Patient Medication Information (PMI)
- Sentinel Initiative
- OTC News
- Recalls
- Drug shortages
- Supply chain integrity
- What's Next

FDA: What we do

Mission: Promote and protect the public health

- FDA's primary responsibility is to protect the American people from unsafe or mislabeled food, drugs, and other medical products and to make sure consumers have access to accurate, science - based information about the products they need and rely on every day.

- FDA/CDER (Center for Drug Evaluation and Research) ensures that safe and effective and high quality drugs are available for U.S. patients


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U.S. Food and Drug Administration
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Animal & Veterinary
Cosmetics
Radiation-Emitting Products
Tobacco Products
Statin safety labeling changes
FDA Approves Changes to Statin Labels
Some important changes are coming to the safety labels on cholesterol-lowering drugs known as statins.
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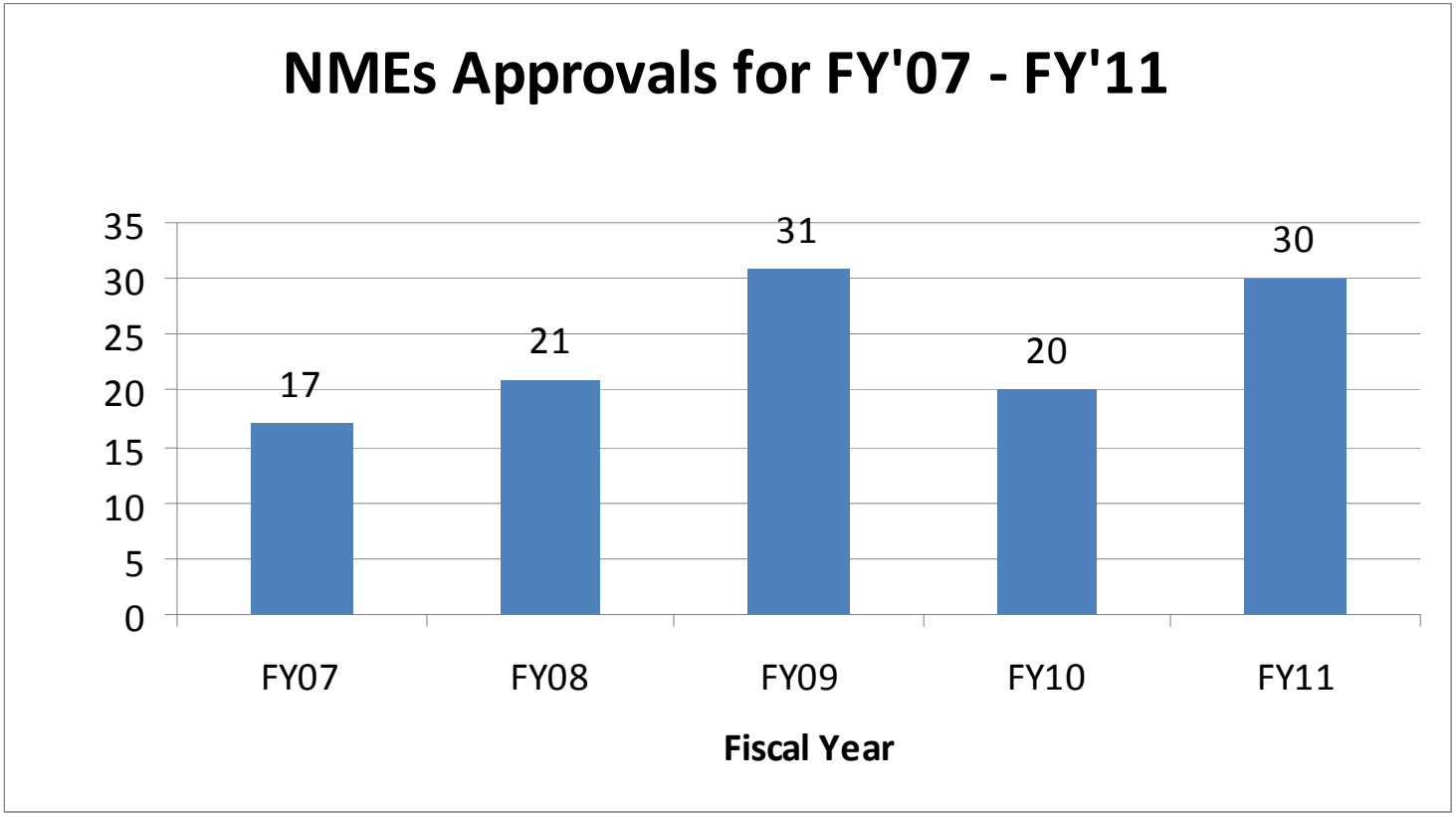
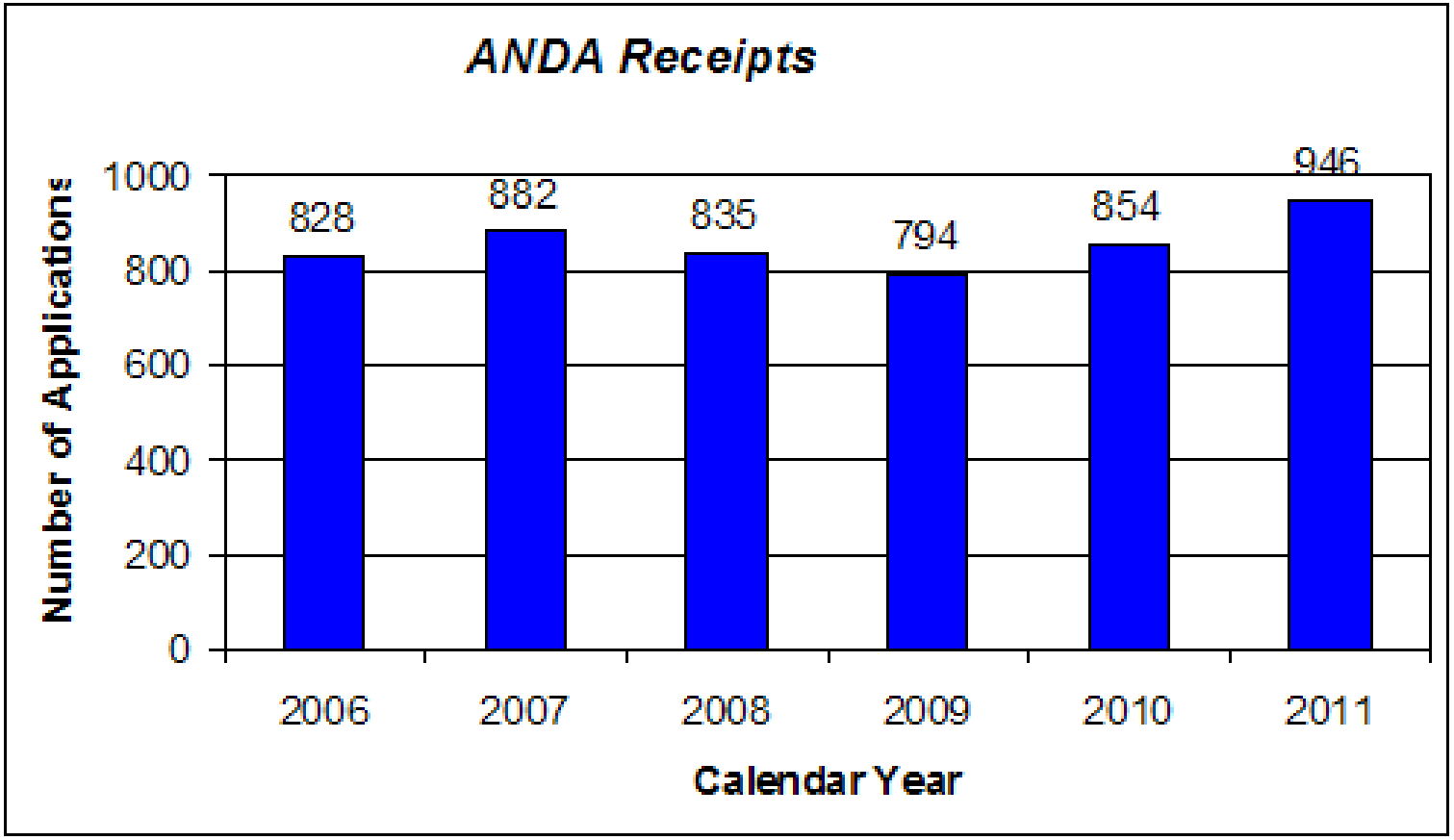
For Consumers & Patients
Updates and information for staying safe and healthy
For Health Professionals
Medical product safety information, adverse event/problem reporting and more
For Scientists & Researchers
NCTR, pediatrics, clinical trials, Critical Path Initiative and more
For Industry
Guidance, registration and listing, import programs and more
Recalls & Alerts
Approvals & Clearances
Report a Problem
Recalls & Safety Alerts
MedWatch: Safety Alerts
Enforcement Report
Industry Recall Guidance
Identifying Recalled Products
FDA Recall Email Alert
FDA Initiatives
Innovation
Globalization
Food Safety
Regulatory Science

New Molecular Entities (NMEs)* approved by CDER



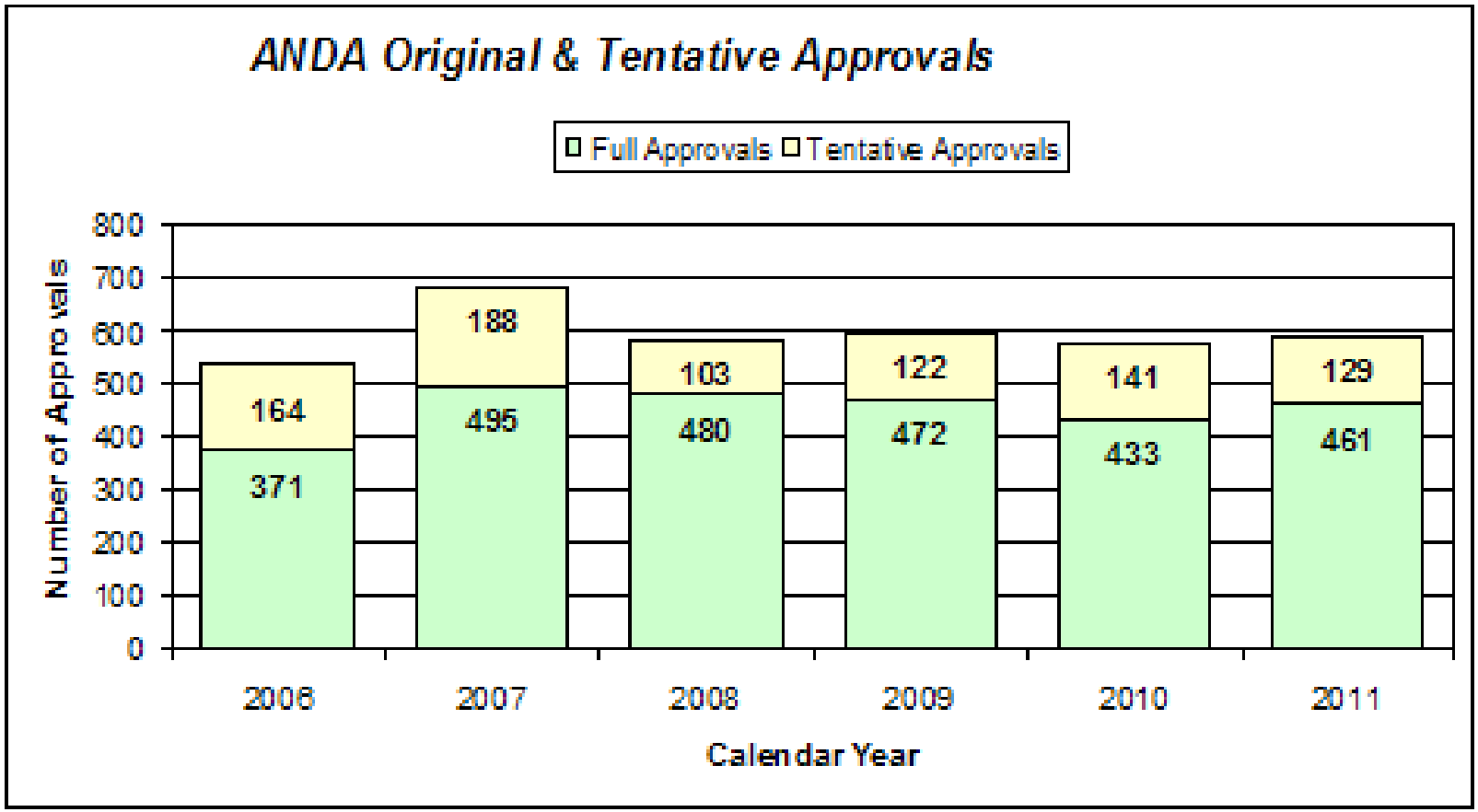
*Represents applications for New Molecular Entities (NMEs) filed under New Drug Applications (NDAs) and therapeutic biologics filed under Original Biologic License Applications (BLAs)

Generic Drug Applications



ANDA = Abbreviated New Drug Application

Generic Drug Applications



ANDA = Abbreviated New Drug Application

Look to FDA for Drug Safety Information

- for Healthcare Professionals
- for Consumers (Patients)
- for Industry

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FDA's Safety Information and Adverse Event Reporting System

HOW FDA FINDS OUT ABOUT POST MARKETING RISK AND SAFETY ISSUES

- **Reports of serious adverse events** (death, life-threatening, required hospitalization, disability or permanent damage, birth defect)
- **Reports of medication errors** (wrong dose, wrong medication…)
- **Reports of product quality issues** (contamination, counterfeit, poor packaging or labeling, product mix-ups, device malfunction…)

HOW YOU FIND OUT ABOUT POST MARKETING RISK AND SAFETY ISSUES

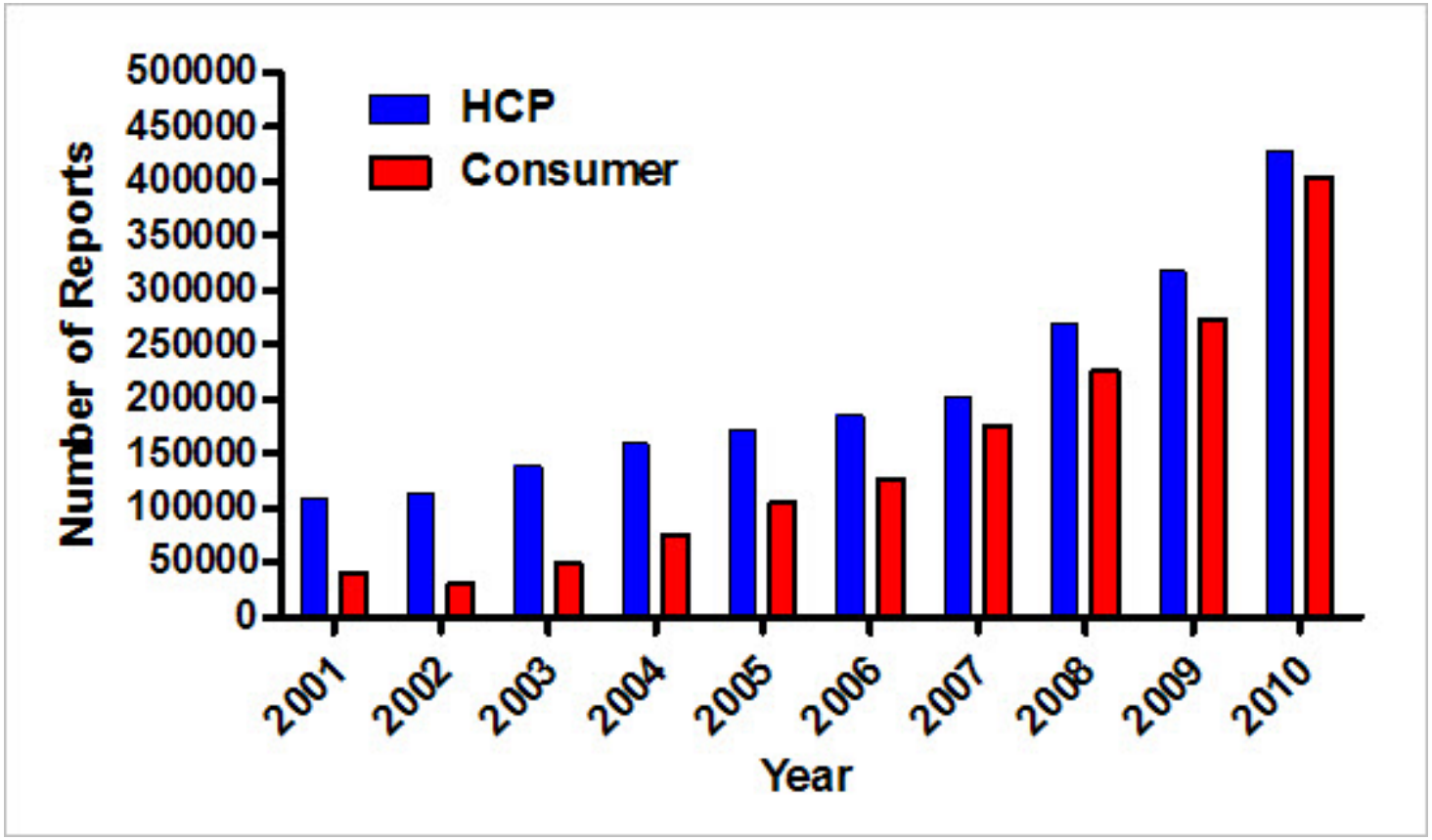
MedWatch Safety Alerts

- receive concise, timely clinically important medical product alerts by

  Email, text, Twitter, RSS Feed to your desktop, webpage

  http://www.fda.gov/Safety/MedWatch/default.htm

MedWatch Reporting

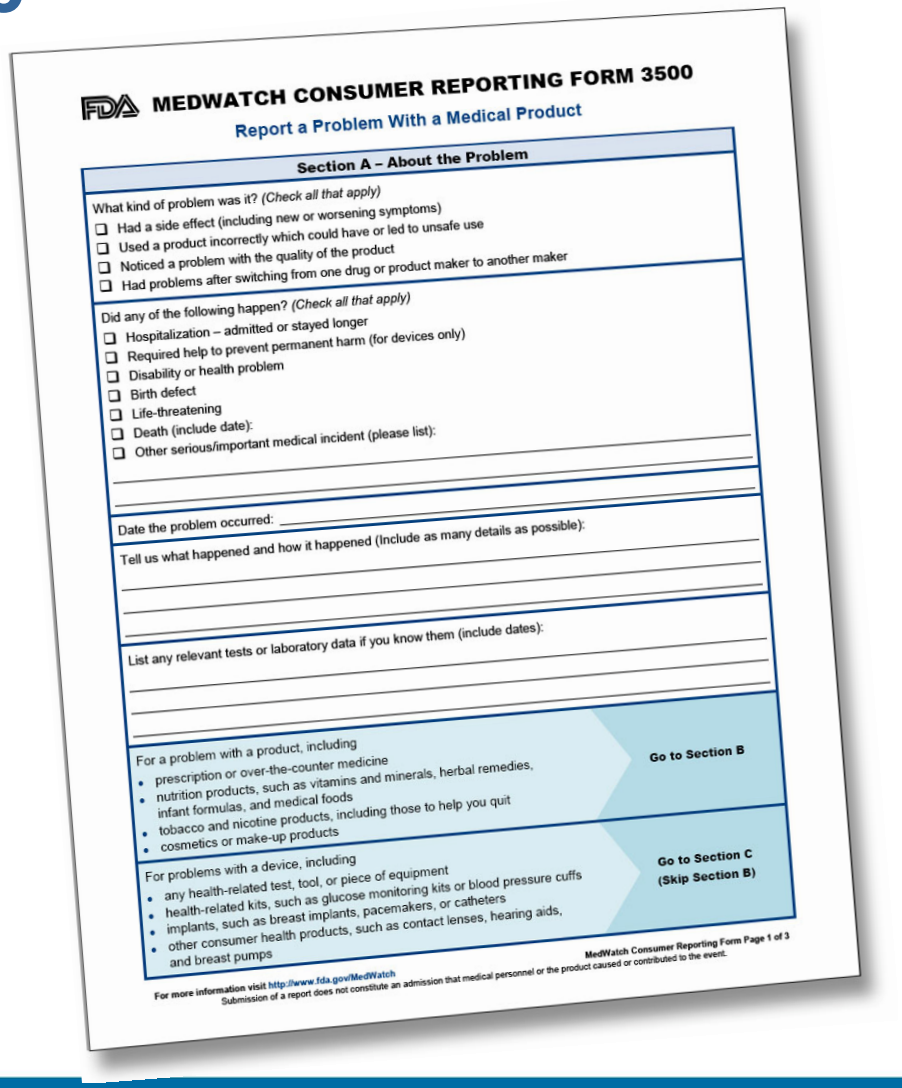


HCP = Health care providers

http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm070456.htm

Proposed New Consumer MedWatch Form 3500

- Developed because of current form was written and formatted at a literacy level that exceeding recommending level for general public
- Proposed in 2011 for public comment



FDA MEDWATCH CONSUMER REPORTING FORM 3500

Report a Problem With a Medical Product

Section A – About the Problem

What kind of problem was it? *(Check all that apply)*

- ❑ Had a side effect (including new or worsening symptoms)
- ❑ Used a product incorrectly which could have or led to unsafe use
- ❑ Noticed a problem with the quality of the product
- ❑ Had problems after switching from one drug or product maker to another maker

Did any of the following happen? *(Check all that apply)*

- ❑ Hospitalization – admitted or stayed longer
- ❑ Required help to prevent permanent harm (for devices only)
- ❑ Disability or health problem
- ❑ Birth defect
- ❑ Life-threatening
- ❑ Death (include date):
- ❑ Other serious/important medical incident (please list):

Date the problem occurred:

Tell us what happened and how it happened (Include as many details as possible):

List any relevant tests or laboratory data if you know them (include dates):

For a problem with a product, including
- prescription or over-the-counter medicine
- nutrition products, such as vitamins and minerals, herbal remedies, infant formulas, and medical foods
- tobacco and nicotine products, including those to help you quit
- cosmetics or make-up products

Go to Section B

For problems with a device, including
- any health-related test, tool, or piece of equipment
- health-related kits, such as glucose monitoring kits or blood pressure cuffs
- implants, such as breast implants, pacemakers, or catheters
- other consumer health products, such as contact lenses, hearing aids, and breast pumps

Go to Section C (Skip Section B)

For more information visit http://www.fda.gov/MedWatch
Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.
MedWatch Consumer Reporting Form Page 1 of 3

Safety Alerts

http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/default.htm

Drug Safety Communications

http://www.fda.gov/Drugs/DrugSafety/ucm199082.htm

- Labeling Change
  - Dosing changes
  - Risk information
- Product Quality Issues
  - Contamination
  - Mix-ups
  - Recalls

Safe Use Initiative

- **What?** FDA's non-regulatory activities to reduce risks (*preventable* harm) from prescription and over-the-counter medicine
- **Why?** FDA's regulatory authority alone is not sufficient to prevent harm
- **How?** Partnering with those involved in healthcare who can control, modify or influence behavior and practices

Goal: to reduce preventable harm by identifying specific, preventable medication risks and developing, implementing and evaluating cross-sector interventions with partners who are committed to safe medication use.

www.fda.gov/safeuseinitiative

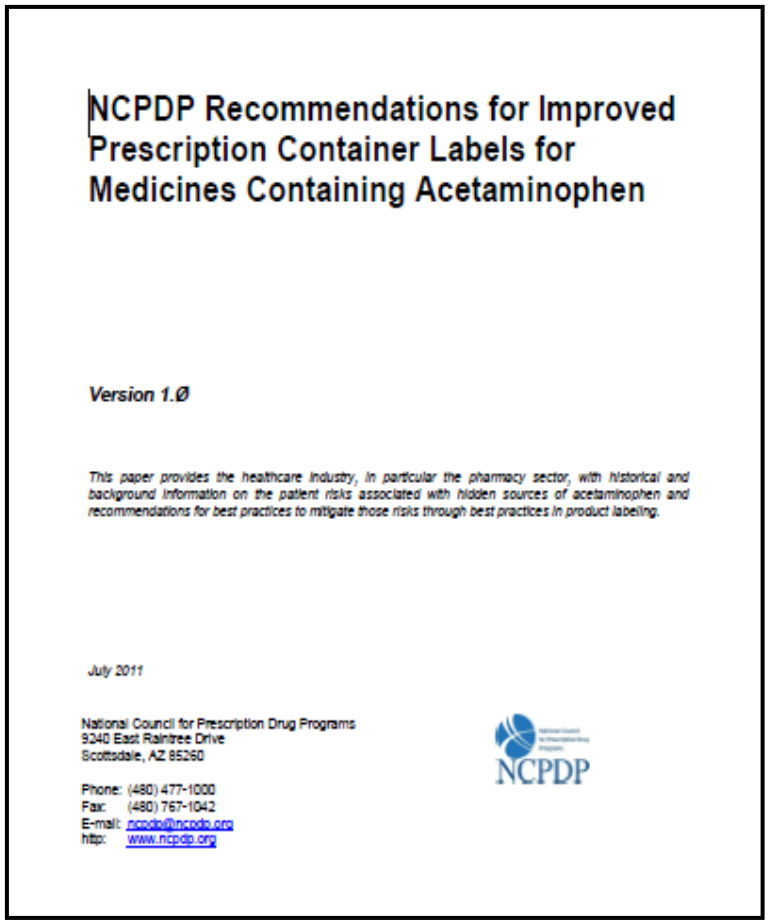
SAFE USE

SAFE USE Updates

Acetaminophen Toxicity

- Under the leadership of the National Council for Prescription Drug Programs (NCPDP), FDA's Safe Use Initiative and a broad group of stakeholders came together to form the Acetaminophen Best Practices Task Group to write the white paper.

- Since the publication of the white paper in August 2011, there has been continued efforts by pharmacy system stakeholders to respond to the call to action.



NCPDP Recommendations for Improved Prescription Container Labels for Medicines Containing Acetaminophen

Version 1.0

This paper provides the healthcare industry, in particular the pharmacy sector, with historical and background information on the patient risks associated with hidden sources of acetaminophen and recommendations for best practices to mitigate those risks through best practices in product labeling.

July 2011

National Council for Prescription Drug Programs
9240 East Raintree Drive
Scottsdale, AZ 85260

Phone: (480) 477-1000
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E-mail: ncpdp@ncpdp.org
http: www.ncpdp.org

NCPDP

www.fda.gov/downloads/Drugs/DrugSafety/UCM266631.pdf

SAFE USE

Collaborative Efforts

- Acetaminophen Toxicity
- Antipsychotic use in elderly with dementia-related psychosis
- Long-Acting Sustained Release Opioids
- NSAIDs for treatment of pain in elderly patients
- Prescription opioids
- Psychotropic medications in pediatric populations
- Safe disposal of needles and other sharps outside of healthcare facilities
- Safe Injection Practices
- Surgical Fires
- Unintentional medication overdoses in children
- Medication Adherence

Risk Evaluation and Mitigation Strategies (REMS)

- Required risk management plan - uses risk minimization strategies beyond professional labeling
- Can be required:
  - Before approval to ensure that benefits outweigh risks
  - Post-approval if **new safety information** makes REMS necessary to ensure that benefits outweigh risks
- A REMS can include:
  - Medication Guide or PPI
  - Communication Plan for HCPs
  - Elements to Assure Safe Use (Generally include some type of restricted distribution)
  - Implementation System
- Must include a timetable for assessment of the REMS

REMS Update

- Opioid REMS Meeting with Industry Working Group (IWG)

  discussed prescriber training, Medication Guides, REMS assessment plan, and administrative requirements (May 2011)

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

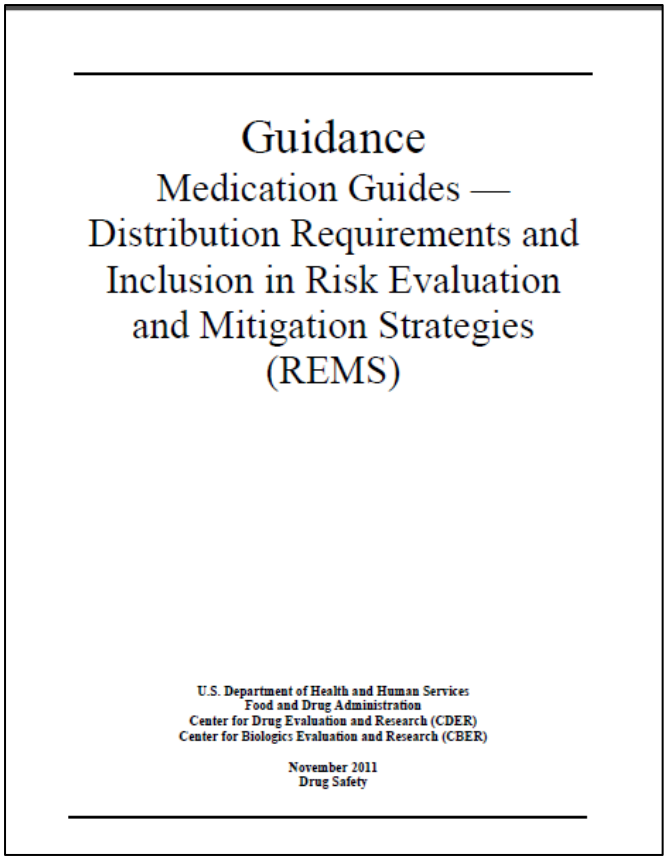
  contains core messages for use by continuing education (CE) providers to develop educational materials to train prescribers under the required risk evaluation and mitigation strategy (REMS) (November 2011)

- Final Medication Guide Guidance for Industry

  Medication Guides – Distribution Requirements and Inclusion in REMS (November 2011)

Medication Guides

http://www.fda.gov/Drugs/DrugSafety/UCM085729



Guidance

Medication Guides — Distribution Requirements and Inclusion in Risk Evaluation and Mitigation Strategies (REMS)

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

November 2011
Drug Safety

Medication Guides Guidance

- Finalized November 2011
- Clarifies when FDA intends to exercise enforcement discretion regarding when MG must be provided with drug/biological product that is dispensed to *HCP* for administration to patient
- Clarifies when a MG will be required as part of REMS

Patient Medication Information (PMI)

Goals and Objectives

- Patients need to receive clear, actionable medication information in order to use their prescription medications safely and effectively

- Under the current system, patients receive several types of information developed by different sources that may be duplicative, incomplete, or difficult to read and understand

- Considering a new regulation to require all prescription drugs to have a single PMI document standardized in content and format that will provide accurate and balanced prescription medication risk and benefit information in a consistent and easily understood format

PMI Updates

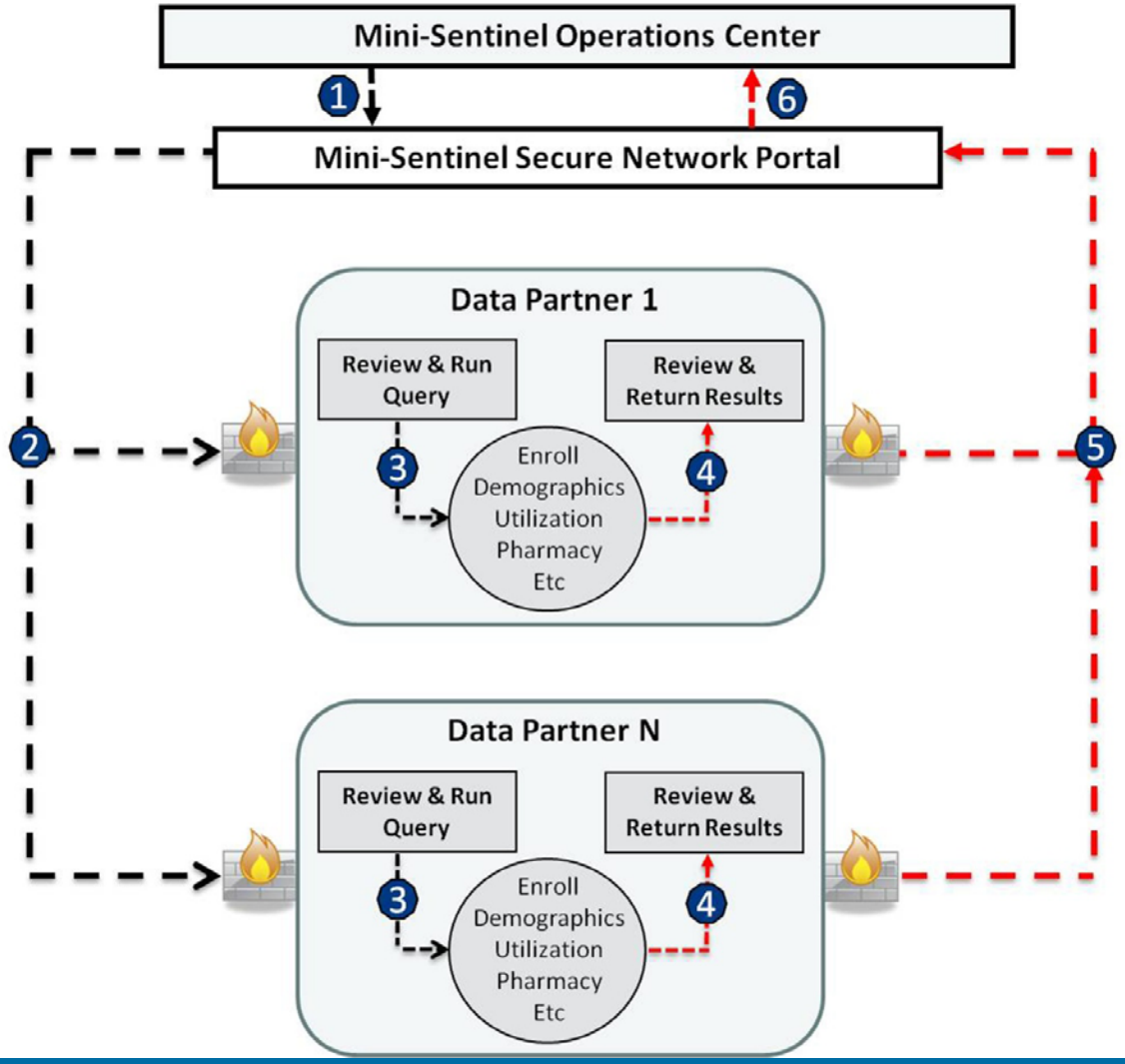
- Study to test single-document PMI prototypes initiated November 2011
- Collaborative effort with Engelberg Center for Health Care Reform at Brookings to develop distribution pilots
- Continue stakeholder outreach through public meetings
- Continue developing framework for PMI
  - Standardize content and format
  - Create Central Repository to store PMI (collaborative effort with National Library of Medicine)
  - Identify and assess mechanisms to ensure distribution
  - Regulation of compliance and quality

Sentinel Initiative

- A tool designed to enable safety scientists to have access to medical product *data* to help them assess complex safety issues
- Adds to FDA's existing tools for gathering and analyzing data

- Mini-Sentinel
  - Partner with academia, health systems, insurance, research, industry, etc
  - Creates coordinating center with continuous access to automated healthcare data systems to develop scientific methods for active medical product safety surveillance
  - Distributed Database includes
    - 126 million individuals (as of December 2011)
    - 345 million person-years of observation time (2000-2011)
    - 3 billion dispensings and accumulating 37 million dispensings per month
  - Data development in progress to expand base population, incorporate data from immunization registries and HER, outcome detection and validation for 18 systematic reviews on vaccine safety

Mini-Sentinel Distributed Analysis



1- User creates and submits query (a computer program)

2- Data partners retrieve query

3- Data partners review and run query against their local data

4- Data partners review results

5- Data partners return results via secure network

6 Results are aggregated

Mini-Sentinel Action Items

- Active Surveillance Activities
  - Characterize populations, treatments, and health events
  - For older products, assess concerns arising from any source
  - Assess impact of FDA actions
  - For new products, monitor accumulating experience for pre-specified potential adverse outcomes

- Challenges
  - Many different exposures, outcomes, patient types, and diverse data environments
  - Need for timeliness in both detection and follow-up
  - Need to avoid false alarms
  - Need for simultaneous activities and surge capacity

- FDA's Sentinel Web Page
  http://www.fda.gov/Safety/FDAsSentinelInitiative/default.htm
- Mini-Sentinel Web Page
  http://mini-sentinel.org

OTC News

Sunscreens

- Labeling changes (front and back)
- Only Broad Spectrum or SPF 15 or higher – reduce risk of skin cancer and early skin aging
- A product that is not Broad Spectrum, or that is Broad Spectrum with an SPF between 2 to 14 - required to have a warning stating that the product has not been shown to help prevent skin cancer or early skin aging
- All will have a Drug Facts label
- No more “sunblocks”

OTC News

Sunscreens – Drug Facts Label

For Broad Spectrum SPF 15 or higher:

Use(s)
- helps prevent sunburn
- if used as directed with other sun protection measures (see ***Directions***), decreases the risk of skin cancer and early skin aging caused by the sun

Directions
Sun Protection Measures. Spending time in the sun increases your risk of skin cancer and early skin aging. To decrease this risk, regularly use a sunscreen with a Broad Spectrum SPF value of 15 or higher and other sun protection measures including:
- limit time in the sun, especially from 10 a.m. - 2 p.m.
- wear long-sleeved shirts, pants, hats, and sunglasses

For non-Broad Spectrum or SPF<15:

Use(s)
- helps prevent sunburn

Warnings
Skin Cancer/Skin Aging Alert: Spending time in the sun increases your risk of skin cancer and early skin aging. This product has been shown only to help prevent sunburn, **not** skin cancer or early skin aging

Expanding Access to Nonprescription Drugs - Overview

Utilizing Innovative Technologies and Other Conditions of Safe Use To Expand Access to Nonprescription Drugs – Public Hearing
March 22-23, 2012

- What is the purpose of this public hearing?

  FDA is seeking input on a new paradigm being considered that would allow certain drugs that would otherwise require a prescription to be approved for nonprescription use under conditions of safe use

- What are examples of conditions of safe use?
  - Pharmacist intervention to ensure appropriate selection of drug or to provide follow-up monitoring during continued use
  - Innovative technologies such as kiosks or computer algorithms that would allow consumers to self-diagnose
  - Diagnostic tests that would be approved for use in the pharmacy or other setting
- Each drug approved under the paradigm would be approved with individualized conditions of safe use

Why are we considering a new paradigm?

- Undertreatment of many common diseases or conditions is a well recognized public health problem (e.g., high cholesterol, hypertension)

- Requirements to visit a practitioner one or more times to obtain a prescription for medication and, in some cases, for routine monitoring may contribute to undertreatment of certain conditions

- Conditions of safe use could eliminate or reduce the number of routine visits to healthcare practitioners and could
  - Improve health outcomes for consumers getting and/or staying on necessary medication
  - Reduce burdens on overburdened health care system
  - Allow more time to be spent on more seriously ill patients
  - Reduce health care costs

Input requested

- FDA is requesting input from consumers, pharmacists, physicians and other members of the medical community, regulated industry, insurers, managed care organizations and other interested members of the public

- Broad areas of input requested are:
  - Types of technology and conditions of safe use
  - Pharmacy, consumer, and health care provider issues
  - Other related issues

Questions on which FDA is seeking input

- Are there specific medical conditions or diseases for which it would be beneficial to make medication available under this paradigm?
- What type of technologies are in development (e.g., algorithms, diagnostics) and what other conditions of safe use could ensure safe and effective use of nonprescription drugs?
- Is there existing information on:
  - the use of conditions of safe use and the impact on health care, access to medication, or increased disease and treatment education?
  - how expanded access or education could affect consumer behavior or health outcomes generally?
- What types of studies could be conducted to evaluate:
  - the effects of conditions of safe use on the safety and efficacy of particular drugs and on behavior and health outcomes?
  - the safety and efficacy of any technologies that could be relied upon as conditions of safe use?

Questions for pharmacy, consumer, and health care providers (1)

- Would this new paradigm increase access to necessary medial care?
- Would increasing access reduce the burden on emergency rooms and individual health care providers, or otherwise reduce the burden on the health care system?
- Are data available about how many consumers requiring drug therapy do not take it due to burdens associated with obtaining a prescription?
- How might concerns regarding lack of oversight by a physician be addressed?
- How might this paradigm affect consumers financially or otherwise affect access to and delivery of health care?

Questions for pharmacy, consumer, and health care providers (2)

- How might pharmacy operations be affected?
- Would additional specialized training for pharmacists be needed?
- Would this new paradigm create any confusion or difficulties for consumers?
- What experiences have you had with state-authorized arrangements that expanded access to prescription drugs?
- What are the public health and regulatory implications of using in vitro diagnostics to be used in a pharmacy as conditions of safe use?

Other questions

- How would insurance coverage and out-of-pocket costs be affected?
- Will this new paradigm increase liability concerns for pharmacists or increase the cost of services?
- What barriers (e.g., proprietary, technological, economic) might impede implementation of this paradigm and how could any barriers be avoided?
- Would overall health care costs decrease if this paradigm were instituted?

Public hearing and comment details

- Date and Location of Public Hearing
  - March 22-23, 2012 at FDA's White Oak Campus, Silver Spring, MD
- Attendance/participation
  - Free
  - Seating will be on a first-come, first-served basis.
  - Registration required only if you want to speak (Deadline was March 9)
  - Written comments welcome; comment period ends May 7, 2012
- For more info on the meeting or how to submit comments, see:

  http://www.fda.gov/Drugs/NewsEvents/ucm289290.htm

  or

  Federal Register meeting notice - 39 FR 12059 (February 28, 2012)

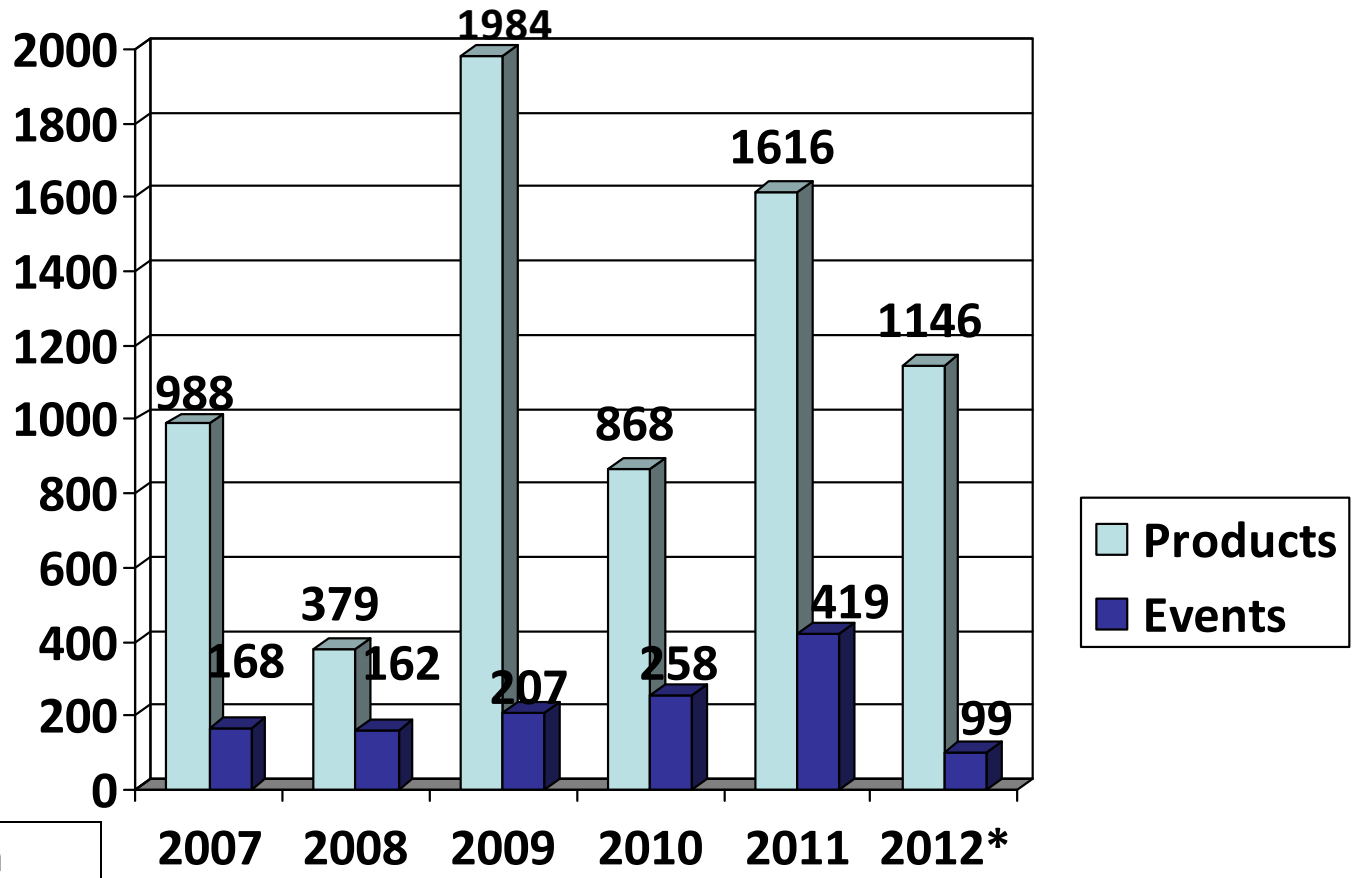
Recall definitions

- **Class I recall:** a situation in which there is a reasonable probability that the use of or exposure to a violative product will cause serious adverse health consequences or death.

- **Class II recall:** a situation in which use of or exposure to a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

- **Class III recall:** a situation in which use of or exposure to a violative product is not likely to cause adverse health consequences

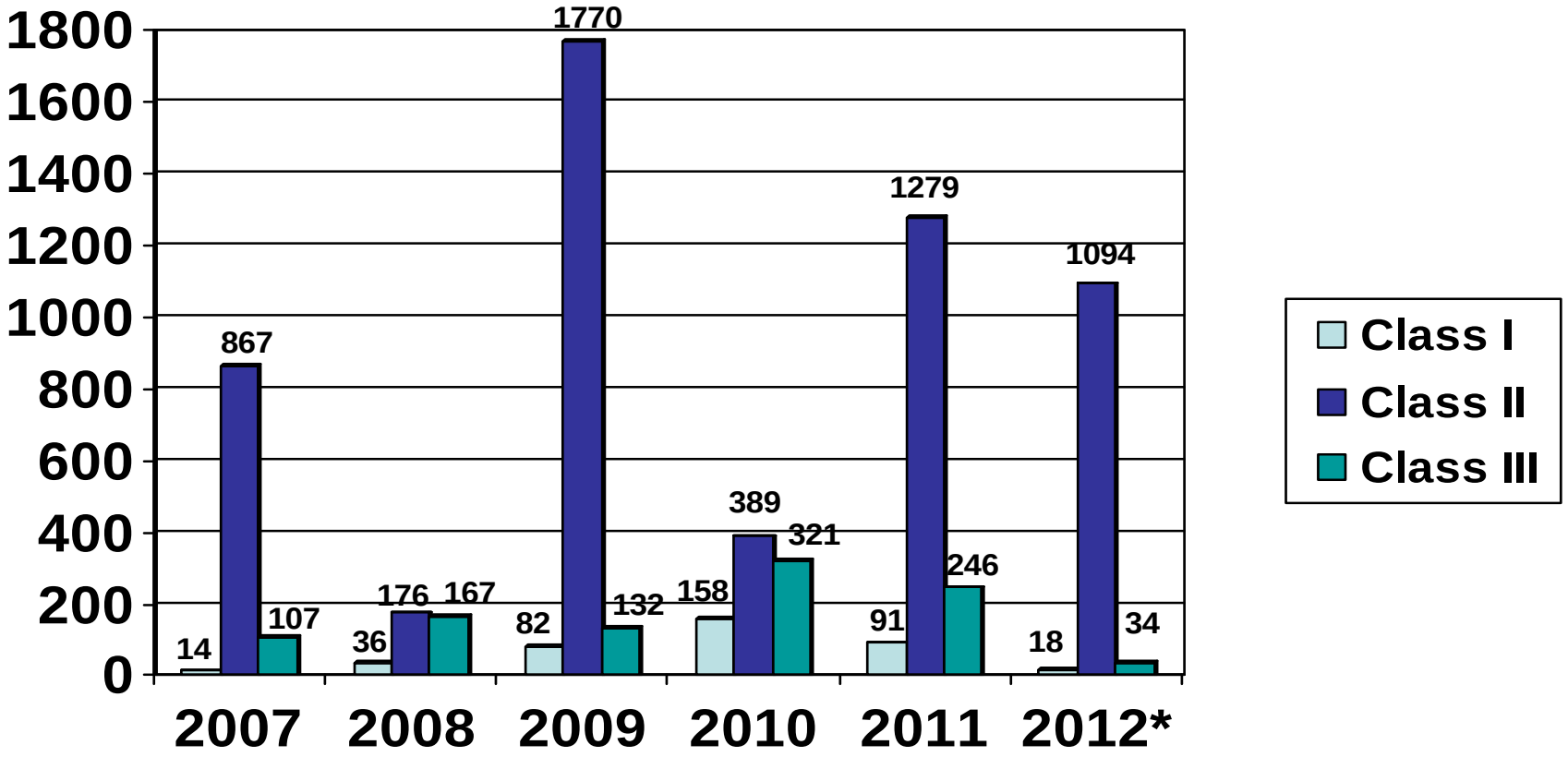
Total number of recall events and product recalls - FY 2007 to 2012*



Data extracted from Recall Enterprise System Jan. 5th, 2012

2012* - first quarter

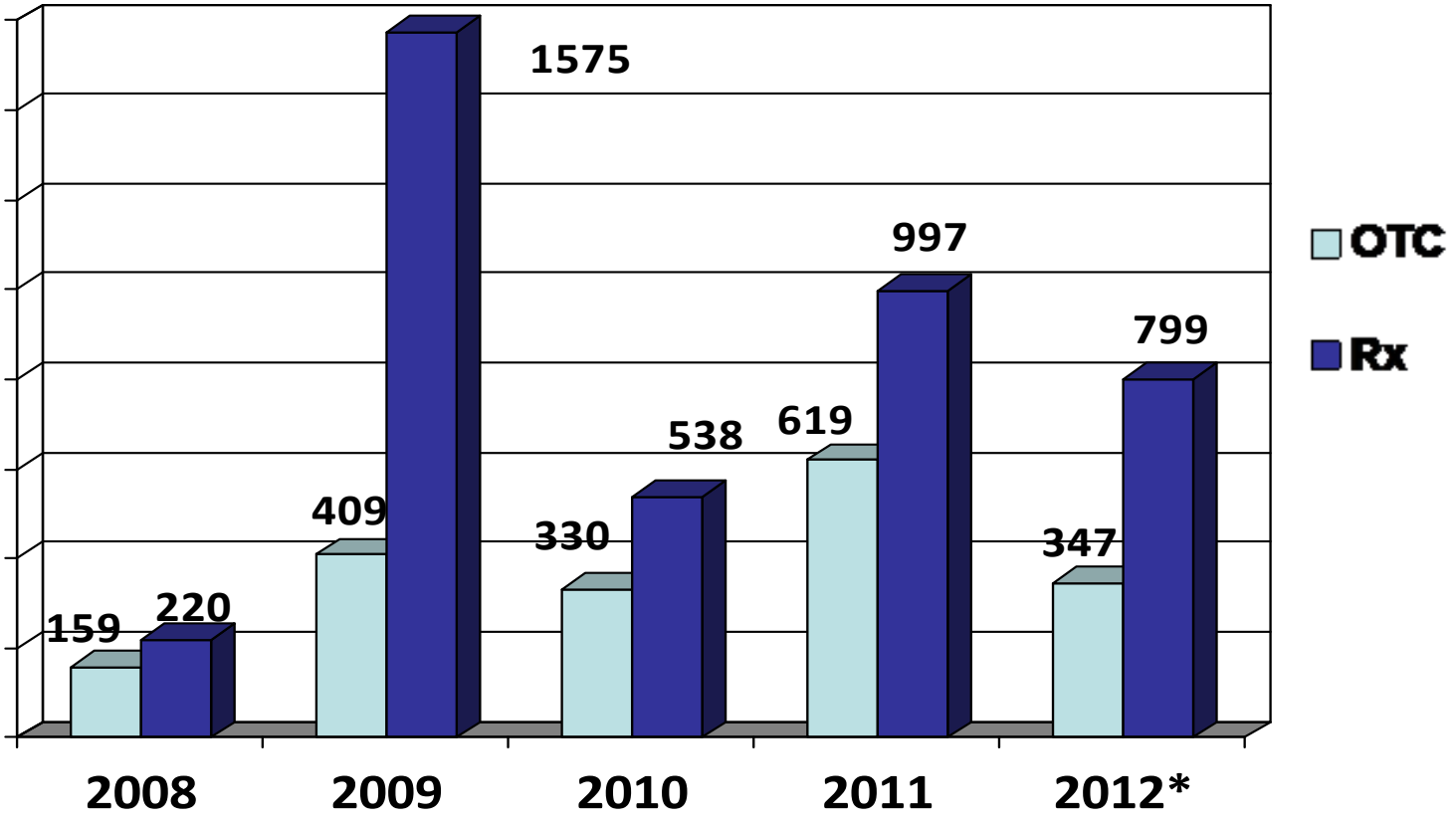
Total number of product recalls by classification - FY 2007 to 2012*



Data extracted from Recall Enterprise System Jan. 5th, 2012

2012* - first quarter

Total number of product recalls by product type - FY 2008 to 2012*



Data extracted from Recall Enterprise System Jan 5th 2012

Dietary Supplements Embedded in Rx/OTC Totals

2012* - first quarter

Major reasons for recalls (OTC and Rx) - FY 2010 – 2012*

Year	Top Reasons
2010	GMP Deviations
	Temperature Abuse
	Marketed without an Approved NDA/ANDA
2011	Penicillin Cross Contamination
	GMP Deviations
	Marketed without an Approved NDA/ANDA
2012*	Penicillin Cross Contamination
	Microbial Contamination of Non-Sterile Products
	GMP Deviations

2012* - as of 3/7/2012

U.S Department of **Health & Human Services** a A A

U.S. Food and Drug Administration

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Drugs

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Drug Safety and Availability

- Drug Shortages
- Current Drug Shortages
- How to Report a Shortage or Supply Issue
- Resolved Drug Shortages
- Drugs to be Discontinued
- Frequently Asked Questions About Drug Shortages

Resources for You

- Drug Shortage Manual of Policies and Procedures

Drug Shortages

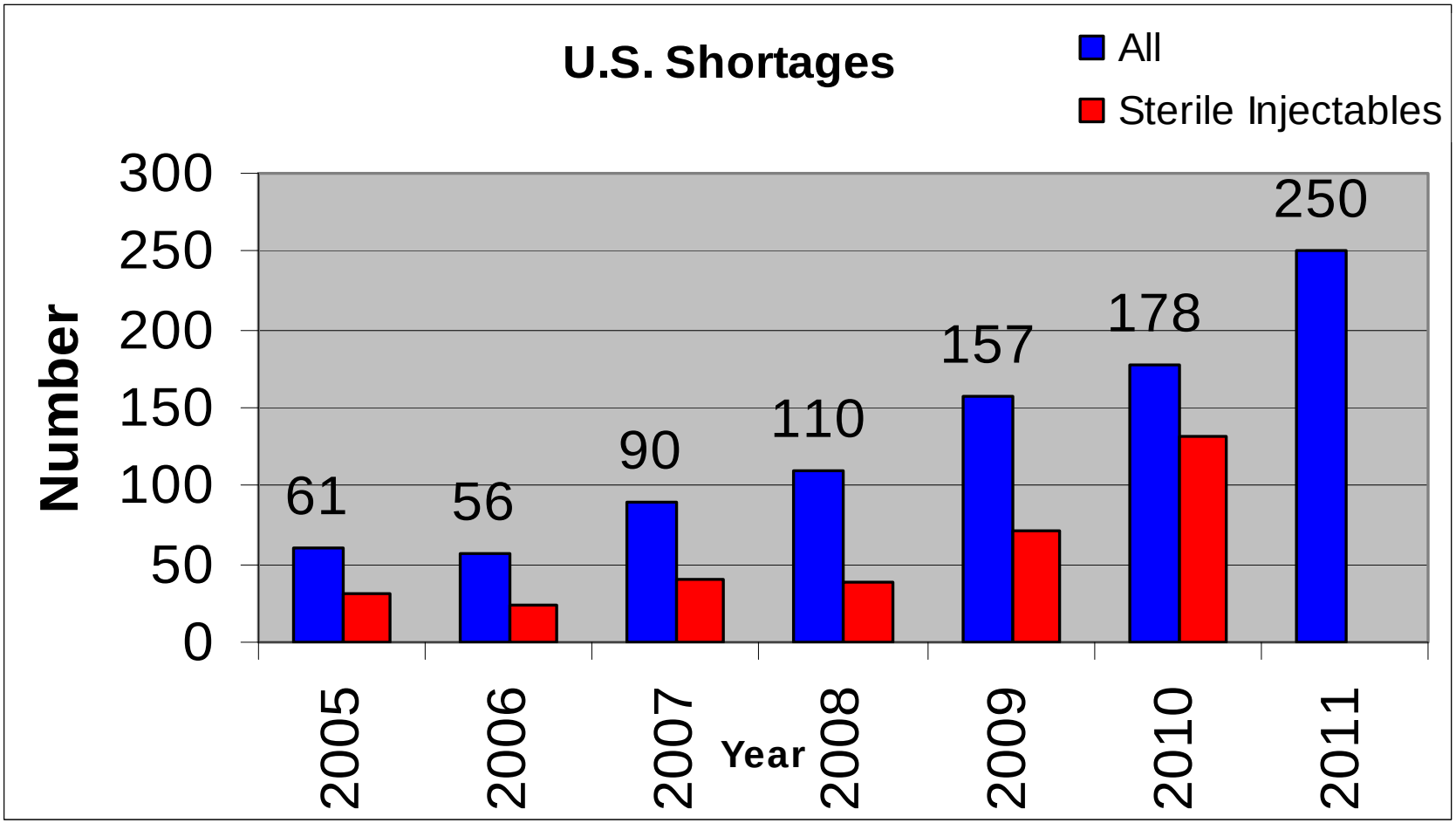
FDA takes great efforts, within its legal authority, to address and prevent drug shortages, which can occur for many reasons, including manufacturing and quality problems, delays, and discontinuations. The agency works closely with manufacturers of drugs in short supply to communicate the issue and to help restore availability. FDA also works with other firms who manufacturer the same drug, asking them to increase production, if possible, in order to prevent or reduce the impact of a shortage.

Manufacturers are not required to report information, such as reasons for shortages or the expected duration of shortages. However, many companies voluntarily provide shortage information that FDA posts on its website. FDA encourages and appreciates all reporting of shortages by manufacturers. Shortage notifications and updates may be reported to FDA at drugshortages@fda.hhs.gov.

Spotlight

- FDA acts to bolster supply of critically needed cancer drugs
- Notification to FDA of Issues that May Result in a Prescription Drug or Biological Product Shortage (PDF - 225KB)
- Bedford Product Availability
- FDA Report: A Review of FDA's Approach to Medical Product Shortages
- Statement from FDA and HHS on Drug Shortages

http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm



Most shortages do get resolved.

Reasons for shortages: Sterile injectables

- State of the industry
  - Seven (7) manufacturers make up most of market
  - Contract manufacturers – firms contract out manufacturing as well as acting as contract manufacturers
- Lack of redundancy
  - Multiple products made on existing manufacturing lines
  - 24/7 production with no “cushion”
- Complex manufacturing process
  - No simple fixes
  - Problems typically affect multiple products
- Investment economics question
  - e.g., propofol 20ml sells for $0.48/vial

FDA authorities are very limited

What we can require

- Notification by sole source manufacturers*
  - Discontinuance of certain products
  - 6 months in advance or immediately if not foreseen
  - No penalty for not reporting
- Notification of manufacturing changes

What we can't require

- A company to make a drug or make more
- Notification of all production delays for all products
- How much and to whom drug is sold or distributed

FDA drug shortages program largely depends on voluntary notification by manufacturers and the public.

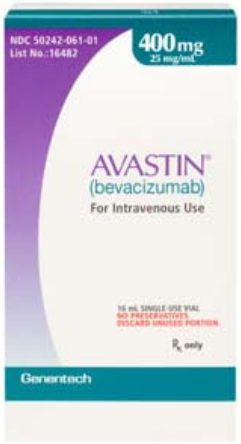
FDA's approach to prevention/mitigation

- Prioritize products that are medically necessary
- Risk/Benefit of the drug always considered
- Do everything possible to continue availability while minimizing risk to patients.
- Work with firm to address
  - We can advise, assist and expedite, but only the manufacturer can fix the problem
  - Why we encourage early notification so we are aware of problems quickly
- Be flexible and creative – and fast

FDA tool box

- Regulatory discretion: allow manufacture of medically necessary product(s) to continue
  - Minor, low risk issues usually best suited for this tool
  - In some cases require additional safety controls
    - Filters packaged with product; extra testing at plant; 3rd party oversight of production; special instructions for safe use
- Request other firms to ramp up manufacturing.
- Expedite any review of company proposals
  - New manufacture site, increased expiry, new raw material source, changes in specifications, etc.
- In rare cases, temporary importation from unapproved sources
  - 2010 propofol
  - 2011 foscarnet, ethiodol, thiotepa, norepinephrine, Xeloda, levoleucovorin, leucovorin
  - 2012 liposomal doxirubicin

Authentic Avastin



Counterfeit Avastin

Images from Genentech, Inc.

Counterfeit/falsified, diverted or stolen or unapproved drugs may be dangerous

- May contain harmful ingredients
- May be ineffective (contain no or little drug)
- May cause adverse events (due to ingredients or wrong strength)
- May have lost potency (due to improper storage)
- May be expired
- May be produced under filthy conditions…etc.

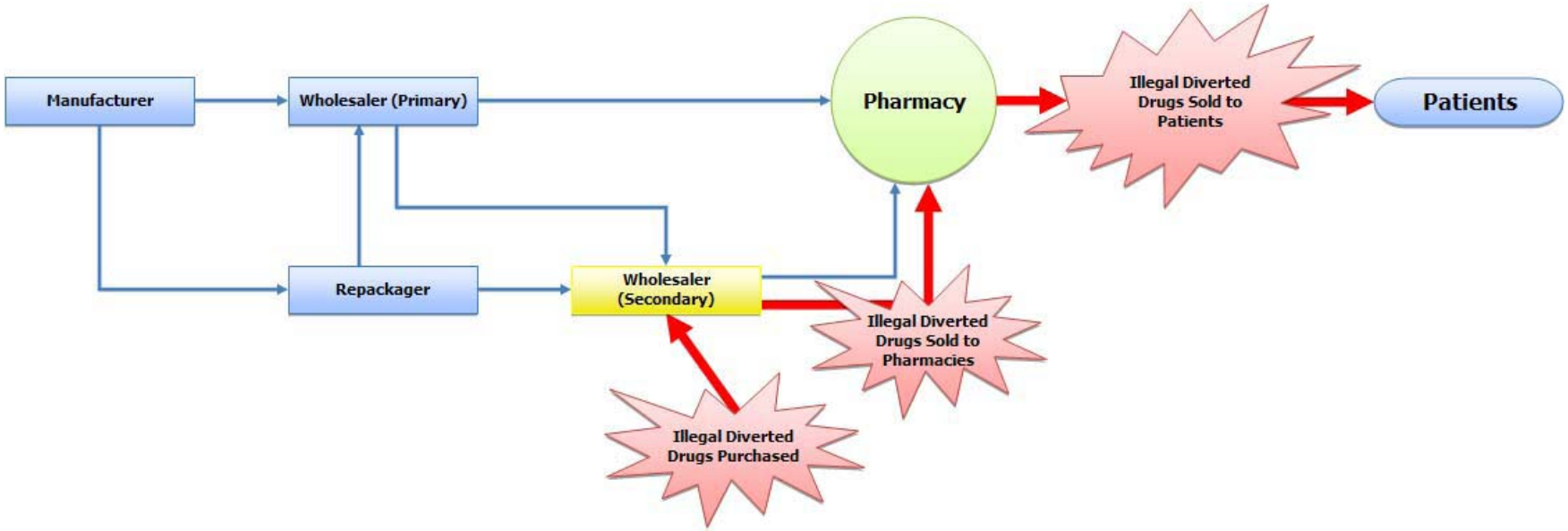
= Harm to public health

What's FDA doing to protect public health?

Preliminary review of OCI cases

Report highlights

- Examples of diversion and counterfeit schemes



- Drug products involved (solid oral dosage forms)
- Type of entities involved (wholesalers, pharmacist, doctor etc.)

Overview of a track and trace system

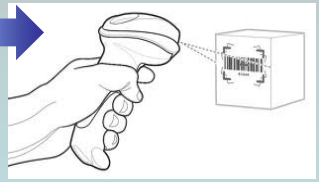
or

Manufacturer/ packaging line

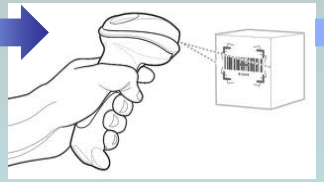
Distributor

Distributor

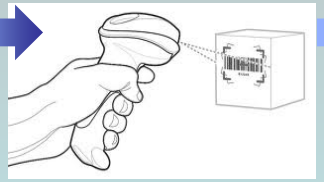
Pharmacy



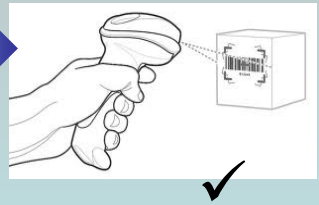
- Serialize
- Record SNI and product info



- **Track** product
- **Authenticate**



- **Track** product
- **Authenticate**



- **Track** product
- **Authenticate**

Track and trace database
centralized or decentralized (distributed)

What's next?

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