FDA MedWatch and Patient Safety

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U S Food and Drug Administration

Food and Drug Administration
MEDWATCH

FDA MedWatch and Patient Safety

Some Context for this Presentation

- Patient Safety is on the agenda of many in recent years
  - Congress
  - Professional organizations
  - Academia [NEJM, JAMA]
- FDA is ‘in the news’ daily over its performance in post-marketing safety surveillance for drugs/devices
  - Vioxx [myocardial infarction]
  - Drug-eluting stents; ICD’s [defibrillators]

FDA MedWatch and Patient Safety

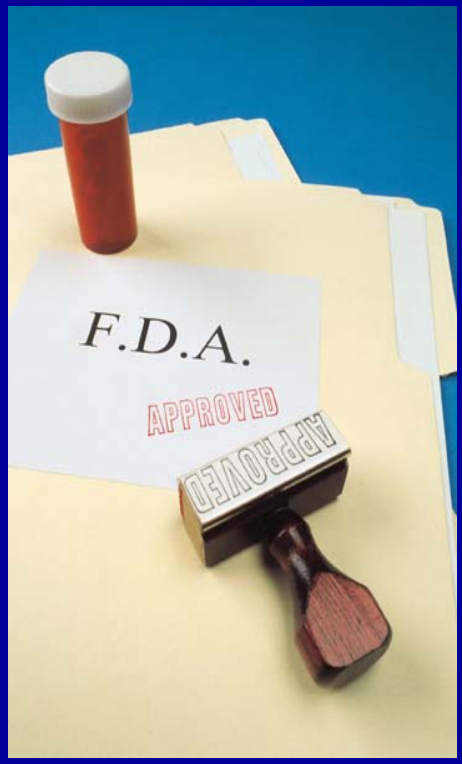
Some Context for this Presentation

- Patient safety is important to all healthcare providers
  - …..even while keeping current on the safety of the drugs, devices and diagnostics is getting more difficult
- FDA often is the first to learn about new safety issues critical to patient safety and wants to share this safety information with clinicians and their patients at the point of care
- These unexpected safety issues are identified and evaluated by FDA only with help from point of care providers and patients
- Postmarket events of interest to FDA:
  - ❖ Adverse Events for drugs and devices
  - ❖ Product Quality Problems
  - ❖ Medication and device use errors
  - ❖ Therapeutic failures/inequivalence

FDA MedWatch and Patient Safety

How FDA Monitors the Safety of Drugs and Devices

- Pre-Market Review and Approval
  - FDA does not develop or routinely test products itself
  - FDA reviews the results of laboratory, animal, and human clinical testing done by companies
- Post-Market Monitoring for Safety
  - Careful review of adverse experiences with products once they are marketed is essential



Why Postmarketing Adverse Event Surveillance is Necessary?

- Despite extensive evaluation of safety during drug development…

  there are significant limitations of phase 3 trials to identify safety signals before marketing

Limitations of phase 3 trials

The Five Too's

- **Too few - seldom more than 3000 pts**
- **Too simple –patients with complicated medical conditions excluded**
- **Too narrow – patients receiving concurrent meds are excluded**
- **Too median-aged –pediatric and elderly populations excluded**
- **Too brief – trials often no longer weeks to months; precluding identification of reactions due to long term use or latent effects**

Reporting In to MedWatch

What, when, how and why to report

- **What**
  - All clinical medical products
- **When**
  - If serious
- **How**
  - Online, or mail/fax/phone
- **Why**
  - Every report can make a difference

Reporting In to MedWatch

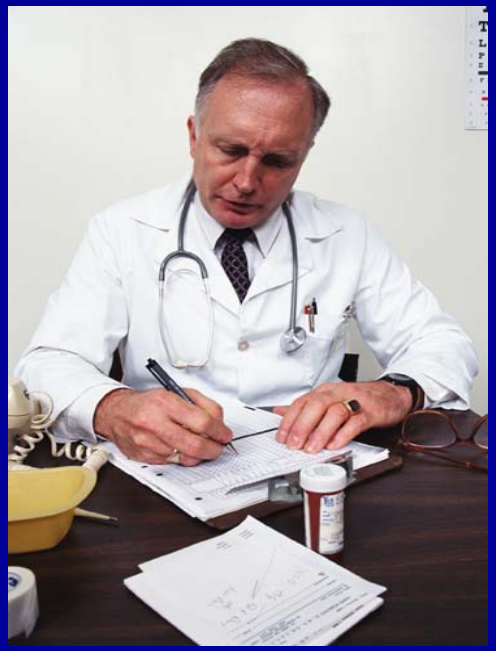
What products to report on

- **Drugs**
  - Prescription
  - Over the Counter
- **Medical Devices**
- **Biologics, except vaccines**
- **Special Nutritional Products**
  - Dietary supplements
  - Infant formulas
  - Medical foods
- **Cosmetics**

Reporting In to MedWatch

What To Report

- **Serious Adverse Events**
  - Drugs, biologics, devices, cosmetics and special nutritional products
- **Product Quality Problems**
  - Suspect counterfeit
  - Contamination, instability
  - Poor packaging, labeling
  - Defective components
  - Therapeutic failures
- **Medication and Device Use Errors**
- **Therapeutic Failures**



Reporting In to MedWatch

What is a serious adverse event

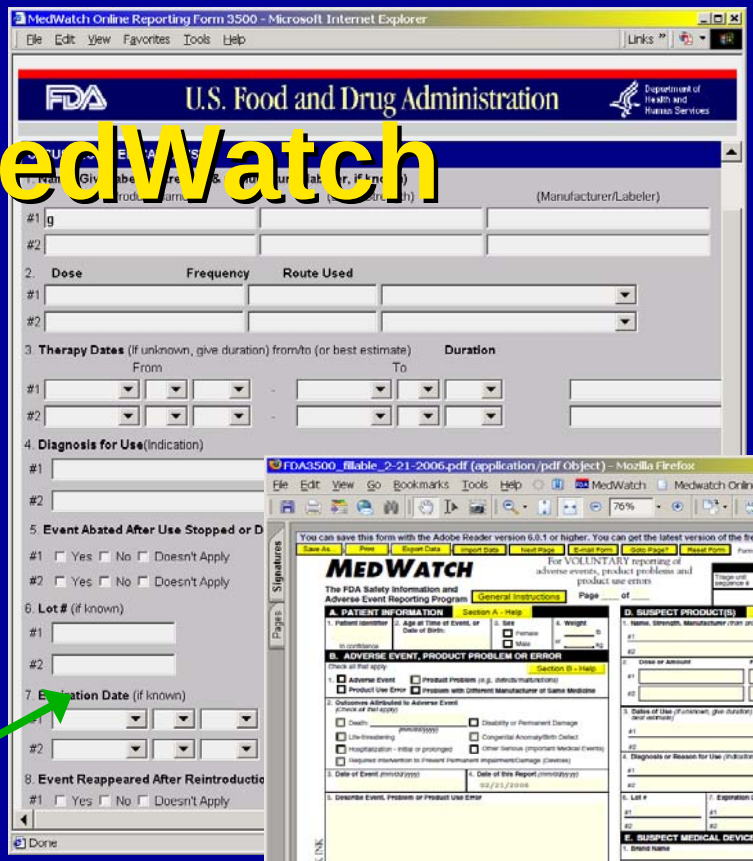
Any event that …

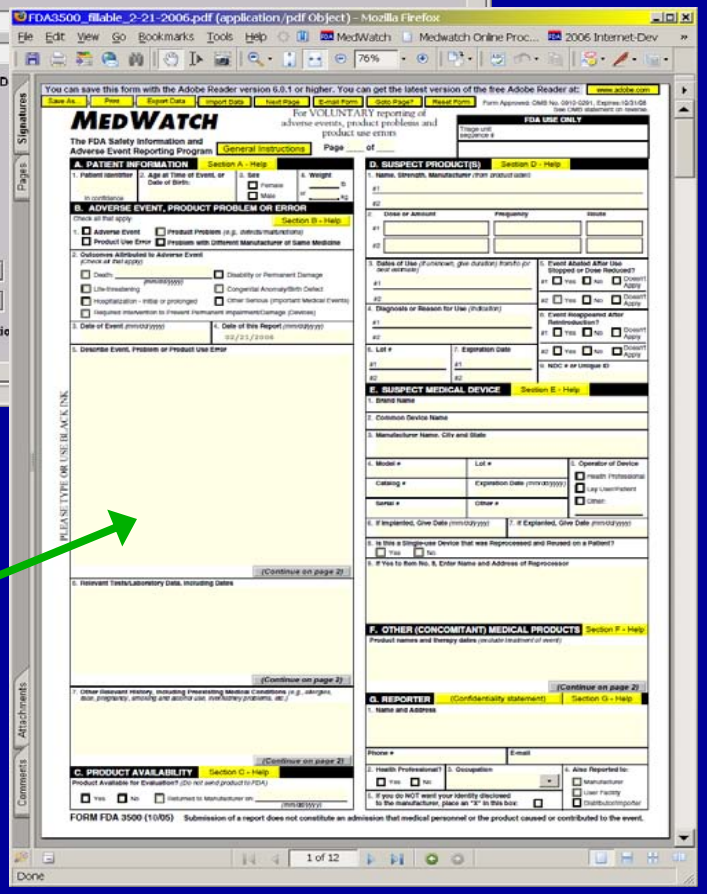
- Is fatal
- Is life-threatening
- Is permanently/significantly disabling
- Requires or prolongs hospitalization
- Causes a congenital anomaly
- Requires intervention to prevent permanent impairment or damage

Reporting to MedWatch

How to Report?

Phone (800-332-1088)
Fax
Mail





Online application for direct submission

www.fda.gov/medwatch/report.htm

Fillable pdf versions of voluntary form

offered for desktop use and submission by mail/fax

www.fda.gov/medwatch/getforms.htm

Reporting In to MedWatch

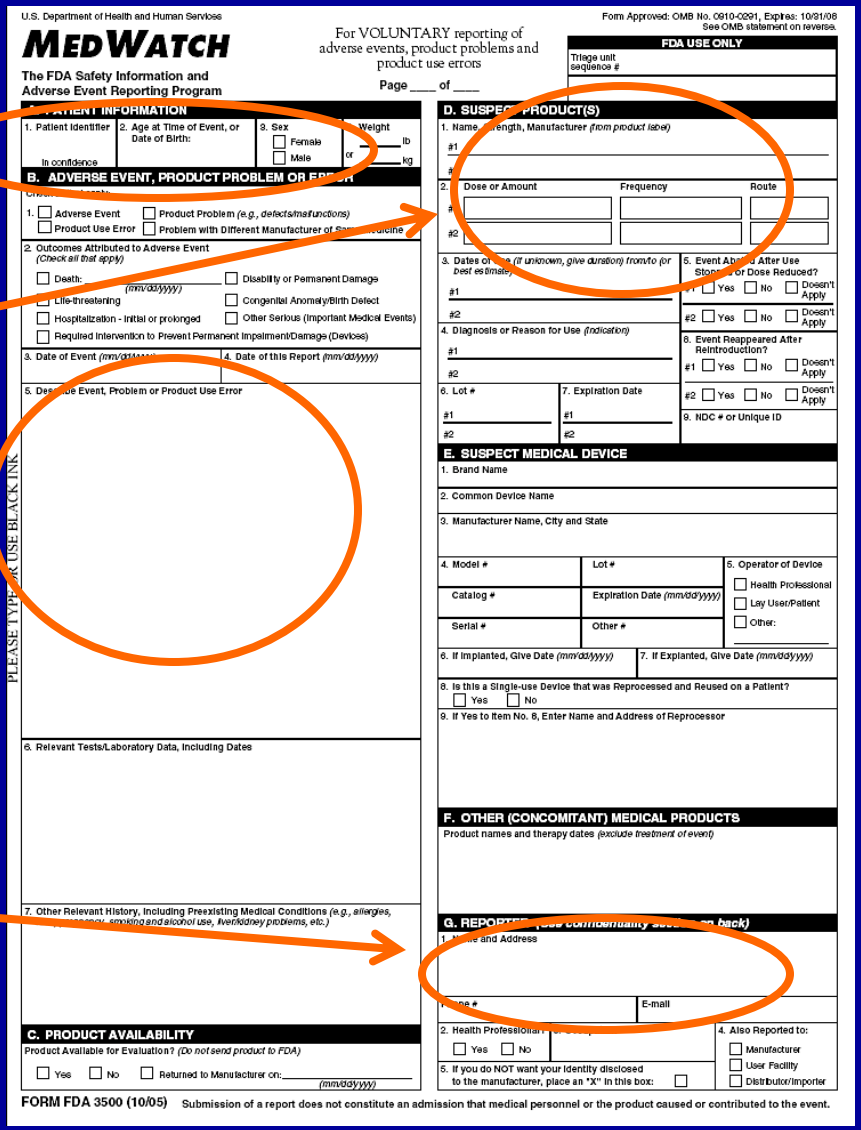
How to report

Patient

Product

Description of Event or Problem

Reporter



U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTARY reporting of adverse events, product problems and product use errors

Form Approved: OMB No. 0910-0291, Expires: 10/31/08
See OMB statement on reverse.

Page ___ of ___

FDA USE ONLY
Triage unit
sequence #

A. PATIENT INFORMATION
1. Patient Identifier
In confidence
2. Age at Time of Event, or Date of Birth:
3. Sex
Female
Male
Weight
lb
or
kg

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR
1. Adverse Event
Product Use Error
Product Problem (e.g., defects/malfunctions)
Problem with Different Manufacturer of Same Medicine
2. Outcomes Attributed to Adverse Event (Check all that apply)
Death: (mm/dd/yyyy)
Life-threatening
Hospitalization - Initial or prolonged
Required Intervention to Prevent Permanent Impairment/Damage (Devices)
Disability or Permanent Damage
Congenital Anomaly/Birth Defect
Other Serious (Important Medical Events)
3. Date of Event (mm/dd/yyyy)
4. Date of this Report (mm/dd/yyyy)
5. Describe Event, Problem or Product Use Error
6. Relevant Tests/Laboratory Data, Including Dates
7. Other Relevant History, Including Preexisting Medical Conditions (e.g., allergies, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)

C. PRODUCT AVAILABILITY
Product Available for Evaluation? (Do not send product to FDA)
Yes
No
Returned to Manufacturer on: (mm/dd/yyyy)

D. SUSPECT PRODUCT(S)
1. Name, Strength, Manufacturer (from product label)
#1
#2
2. Dose or Amount
Frequency
Route
3. Dates of Use (if unknown, give duration) from/to (or best estimate)
5. Event Abated After Use Stopped or Dose Reduced?
Yes
No
Doesn't Apply
4. Diagnosis or Reason for Use (Indication)
6. Event Reappeared After Reintroduction?
7. Lot #
8. Expiration Date
9. NDC # or Unique ID

E. SUSPECT MEDICAL DEVICE
1. Brand Name
2. Common Device Name
3. Manufacturer Name, City and State
4. Model #
Lot #
Catalog #
Expiration Date (mm/dd/yyyy)
Serial #
Other #
5. Operator of Device
Health Professional
Lay User/Patient
Other:
6. If Implanted, Give Date (mm/dd/yyyy)
7. If Explanted, Give Date (mm/dd/yyyy)
8. Is this a Single-use Device that was Reprocessed and Reused on a Patient?
Yes
No
9. If Yes to Item No. 8, Enter Name and Address of Reprocessor

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS
Product names and therapy dates (exclude treatment of event)

G. REPORTER (see confidentiality section on back)
1. Name and Address
Phone #
E-mail
2. Health Professional?
Yes
No
4. Also Reported to:
Manufacturer
User Facility
Distributor/Importer
5. If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box:

PLEASE TYPE OR USE BLACK INK

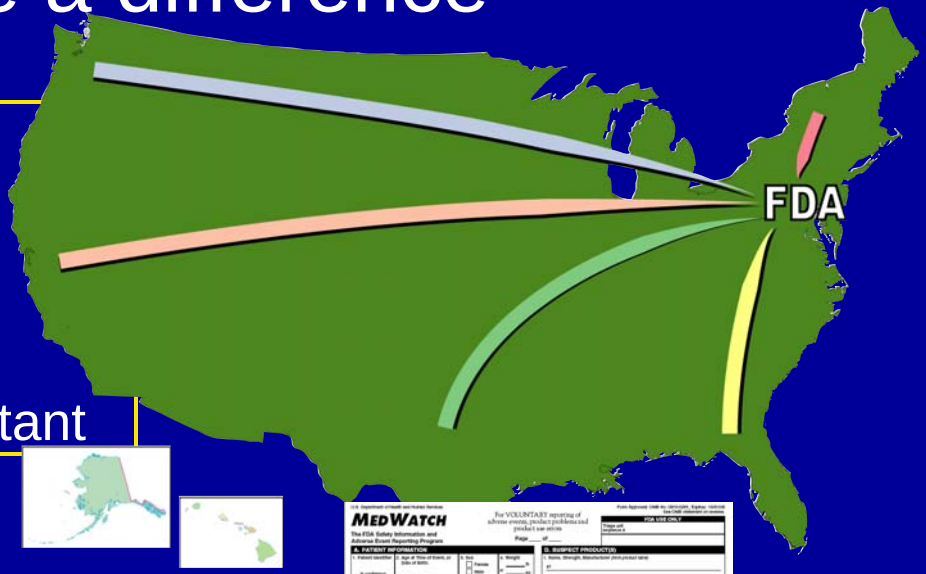
FORM FDA 3500 (10/05) Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Reporting In to MedWatch

Why Report?

Every report can make a difference

Walla Walla, WA – Oncologist
Sacramento, CA – Nurse
Houston, TX - Dentist
Tallahassee, FL – Pharmacist
Portland, ME – Physician Assistant



Even a few voluntary reports from individual reporters can become a ‘signal’ and lead to a label change or other FDA action.

What Happens to Your Report

- When you report an ADE for a drug or biologic
- When you report a product quality problem for a drug or device
- When you report a medication or device use error

What Happens to Your Report

When you report a serious adverse event

- Report captured in a database
- Database monitored by an FDA professional
- Review of a case series
- Consultation with medical review division and manufacturer
- Further epidemiological studies as needed

What Happens to Your Report

When you provide information on a serious ADE

Labeling or Educational Options

- Boxed Warning
  - Drug-drug, drug-food interaction warnings
  - Monitoring recommendations
  - Dosage adjustments for sub-populations
- Contraindications, Warnings, Precautions or Adverse Reactions
- Medication Guide

What Happens to Your Report

When you report a serious ADE

- **Special programs - REMS**
  - Prescribing or dispensing limitations
  - Laboratory testing documentation
  - Registries
- **Product withdrawal**

What Happens to Your Report

When you report a product quality problem

- **For problems due to:**
  - Product design
  - Manufacturing quality or distribution/storage
  - Counterfeit product
- **FDA can:**
  - Work with manufacturer to issue a recall of product
  - Request a modification in product design
  - Request a modification in manufacturing process
  - Improve instructions or warnings for use

What Happens to Your Report

When you report a medication or device use error

- **Errors and 'near misses'**
  - All reports are monitored and evaluated
- **For errors due to:**
  - Name confusion of drugs
  - Packaging or labeling of drugs
  - Device use
- **FDA can:**
  - Request name change or modification
  - Request packaging/labeling changes
  - Modify instructions for device use

Each Report Can Make a Difference

Every Report Can Make a Difference
Novantrone - mitoxantrone

- Single voluntary MedWatch report received by FDA
- Safety Evaluator review of AERS database
- Further evaluation of ongoing data in phase 4 study
- Revision of boxed warning to include new monitoring recommendations
- DHCP letter and MedWatch alert issued

Single voluntary MedWatch report received by FDA

- Direct Report made 9/18/2004
- A 34 year-old woman with multiple sclerosis developed cardiogenic shock with an ejection fraction of 5% after being treated with mitoxantrone for 2 and ½ years. The patient needed a heart transplant.

Safety Evaluator review of AERS database

- There appear to be cases of mitoxantrone-induced cardiac toxicity at cumulative doses less than the current monitoring threshold of 100 mg/m^2

Further evaluation of ongoing data in phase 4 study

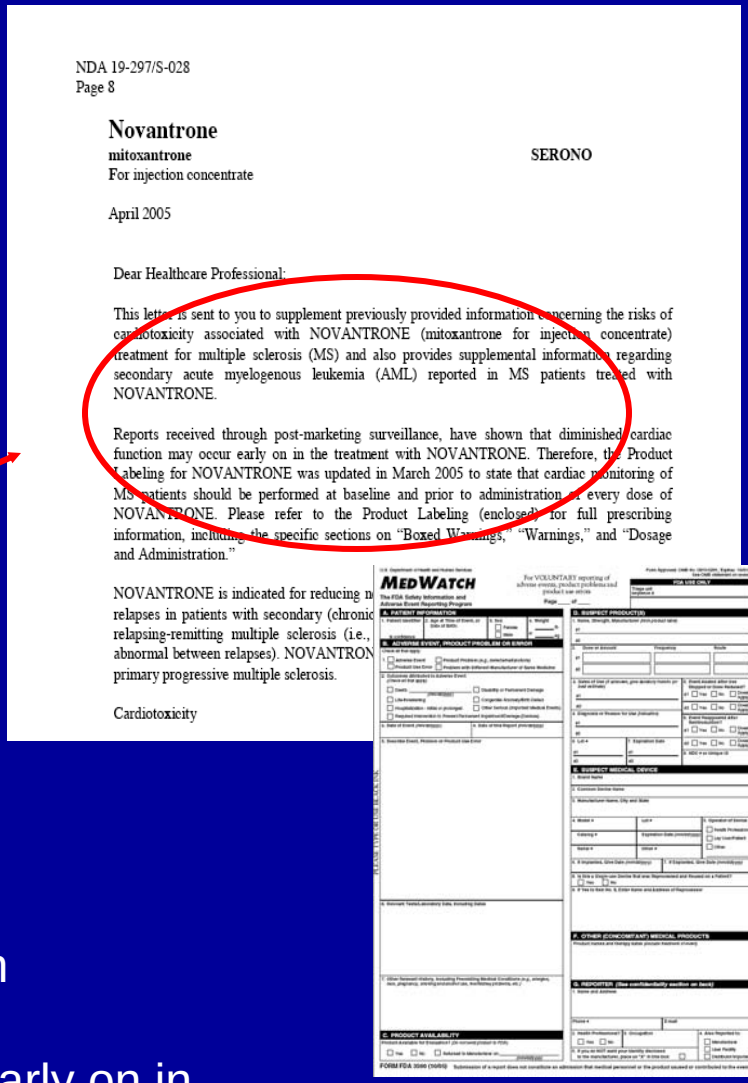
RENEW Interim Analysis

- 15 patients had a decline in LVEF to < 50%
  - Cumulative doses 47.6 – 126 mg/m^2
- 9 patients had LVEF measurements that decreased at least 10% but remained above 50% and mitoxantrone was discontinued
  - Cumulative doses 55.3 – 105.3 mg/m^2
- These LVEF screenings were done at the discretion of the investigator

Revision of boxed warning to include new monitoring recommendations

- LVEF should be reevaluated by echocardiogram or MUGA prior to each dose administered to patients with MS.
- Baseline evaluation of LVEF by echocardiogram or MUGA should be performed.
- MS patients with a baseline LVEF < 50% should not be treated with Novantrone.
- Additional doses should not be administered to MS patients with a drop in LVEF to below 50% or a clinically significant reduction in LVEF.

Novantrone
mitoxantrone
For injection concentrate



NDA 19-297/S-028
Page 8

Novantrone
mitoxantrone **SERONO**
For injection concentrate

April 2005

Dear Healthcare Professional:

This letter is sent to you to supplement previously provided information concerning the risks of cardiotoxicity associated with NOVANTRONE (mitoxantrone for injection concentrate) treatment for multiple sclerosis (MS) and also provides supplemental information regarding secondary acute myelogenous leukemia (AML) reported in MS patients treated with NOVANTRONE.

Reports received through post-marketing surveillance, have shown that diminished cardiac function may occur early on in the treatment with NOVANTRONE. Therefore, the Product Labeling for NOVANTRONE was updated in March 2005 to state that cardiac monitoring of MS patients should be performed at baseline and prior to administration of every dose of NOVANTRONE. Please refer to the Product Labeling (enclosed) for full prescribing information, including the specific sections on "Boxed Warnings," "Warnings," and "Dosage and Administration."

NOVANTRONE is indicated for reducing n
relapses in patients with secondary (chronic
relapsing-remitting multiple sclerosis (i.e.,
abnormal between relapses). NOVANTRON
primary progressive multiple sclerosis.

Cardiotoxicity

MedWatch
The FDA Safety Information and Adverse Event Reporting Program

April 2005

Dear Healthcare Professional:
This letter is sent to you to supplement previously provided information concerning **the risks of cardiotoxicity associated with NOVANTRONE** (mitoxantrone for injection concentrate) treatment for multiple sclerosis (MS) …… Reports received through postmarketing surveillance, have shown that diminished cardiac function may occur early on in the treatment with NOVANTRONE. ….. <u>cardiac monitoring of MS patients should be performed</u> at baseline and prior to administration of every dose of NOVANTRONE.

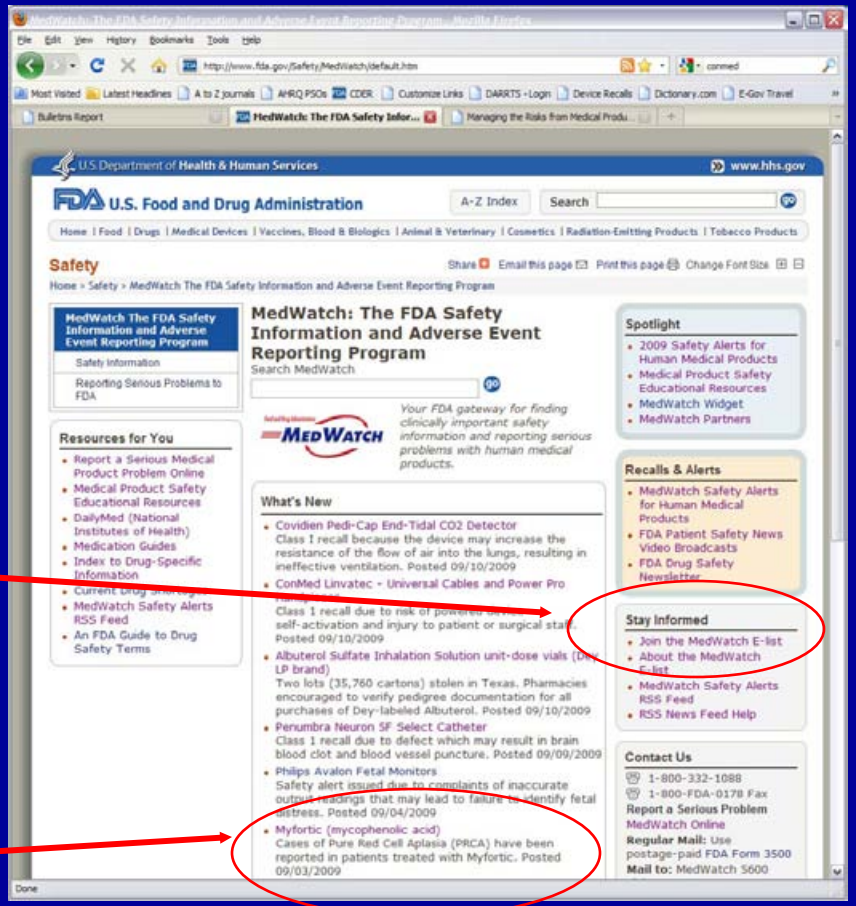
How MedWatch Sends Safety Information To You

MedWatch

E-list notification and RSS feeds

Listserve growth from 5K to 153,000 subscribers since 2002

RSS feed –over 1 million pageviews in December 2008

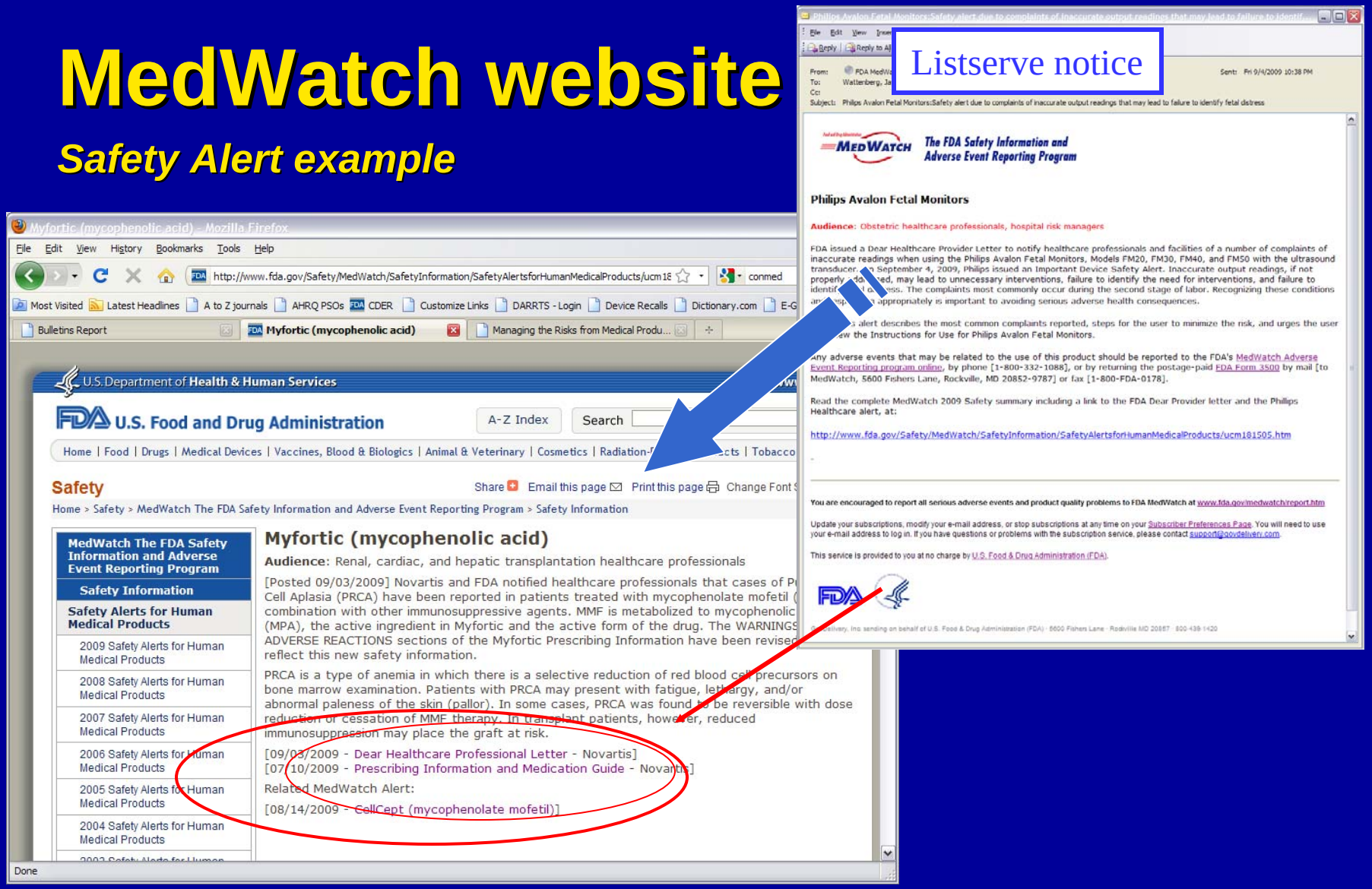


E-list notification example:

"Novartis and FDA notified healthcare professionals that cases of Pure Red Cell Aplasia (PRCA) have been reported in patients treated with mycophenolate mofetil (MMF) in combination with other immunosuppressive agents. MMF is metabolized to mycophenolic acid (MPA), the active ingredient in Myfortic and the active form of the drug. The WARNINGS and ADVERSE REACTIONS sections of the Myfortic Prescribing Information have been revised

MedWatch website

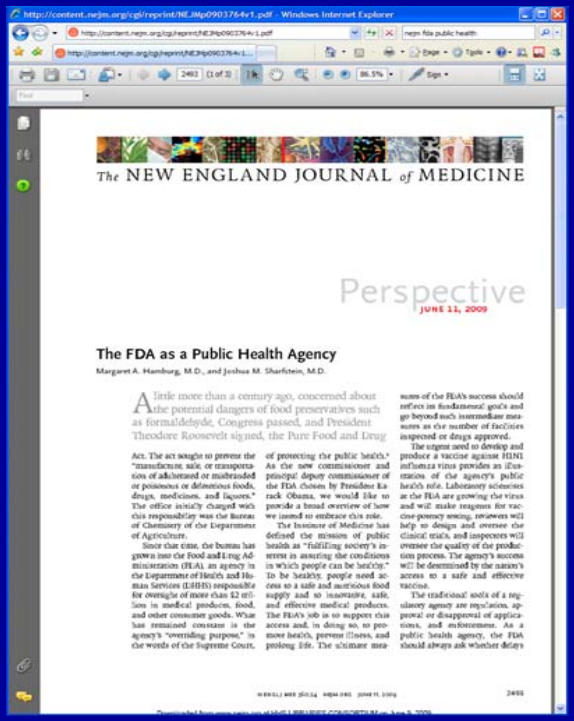
Safety Alert example



Drug Safety - FDA's Risk Management focus
Opportunities for improved risk communication

"Beyond the Label" strategies

- Request that sponsor send DHCP letter
- Announce the information to the press
- Post the information on the FDA website
- Notify targeted organizations and enlist their help in disseminating information to members
- Send a notification by email/text message to individual or RSS feed to work setting
- Incorporate notification into workflow at point at which provider is considering the product


The NEW ENGLAND JOURNAL of MEDICINE

Perspective

JUNE 11, 2009

The FDA as a Public Health Agency

Margaret A. Hamburg, M.D., and Joshua M. Sharfstein, M.D.

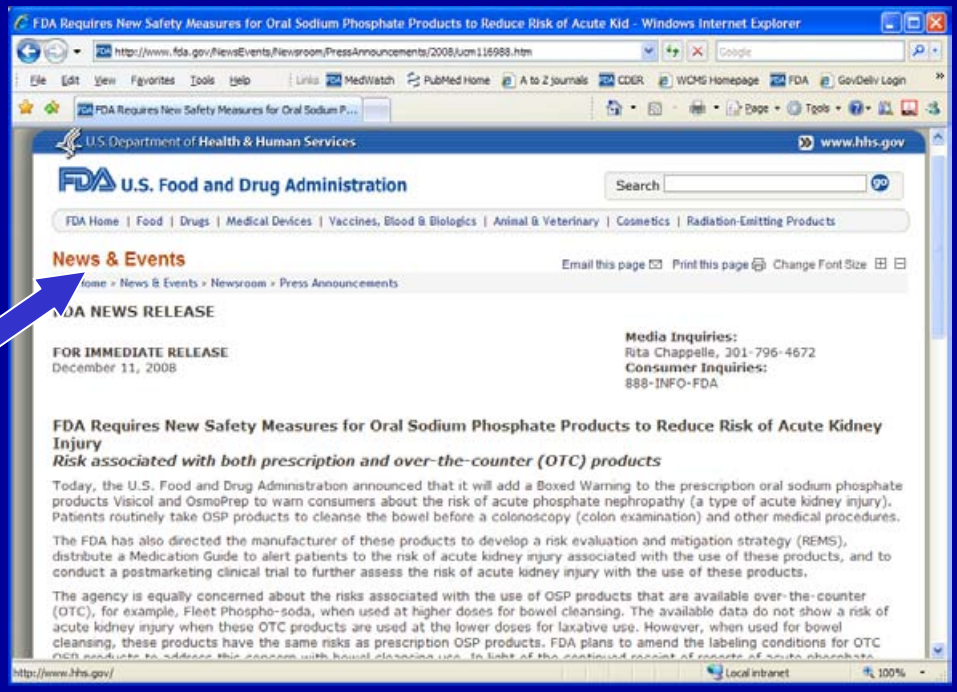
Transparency and public health role

Reaching Point-of-Care Providers With Timely and Actionable Safety Information

The Oral Sodium Phosphate example

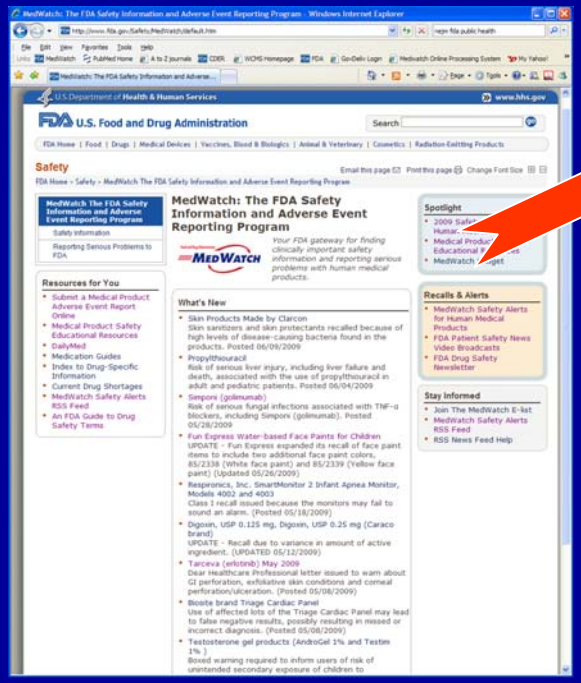
- ✓ Announce the information to the press

"As a result of new safety information received, FDA is requiring the manufacturer of Visicol and OsmoPrep, the two OSPs available by prescription only, to add a Boxed Warning to the labeling for these products. FDA is also requiring that the manufacturer develop and implement a risk evaluation……"

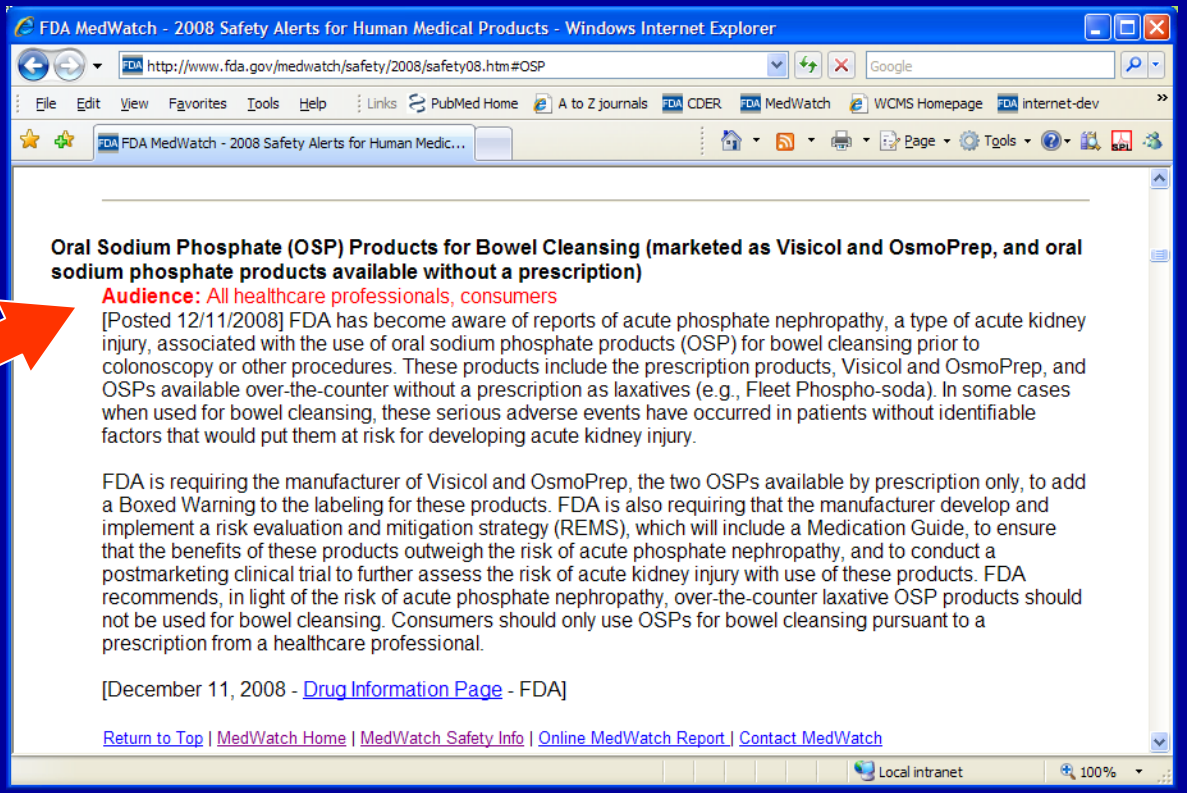


FDA MedWatch

Post the information on the FDA MedWatch website



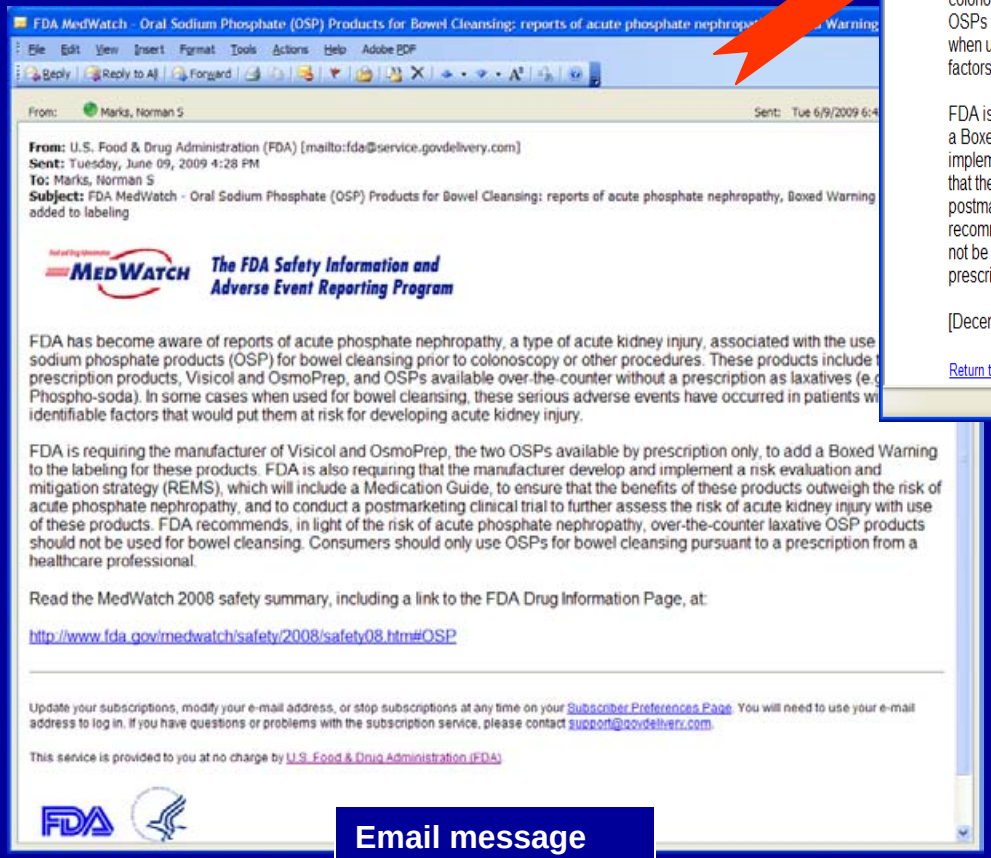
Homepage



Safety Alert item

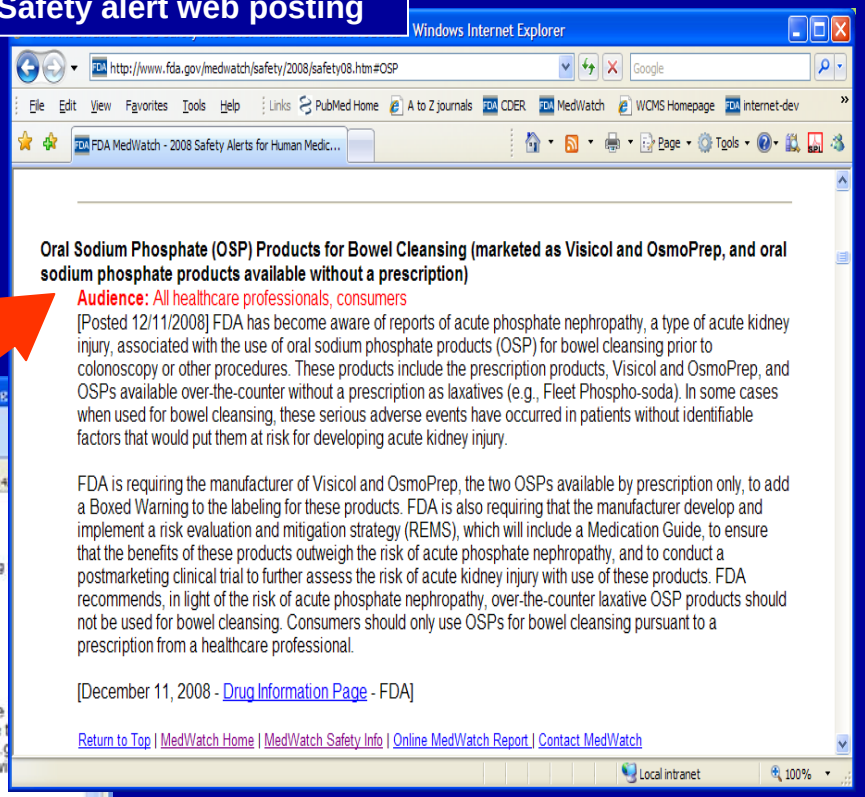
FDA MedWatch

Send notification by email/text message to individual or work setting



Email message

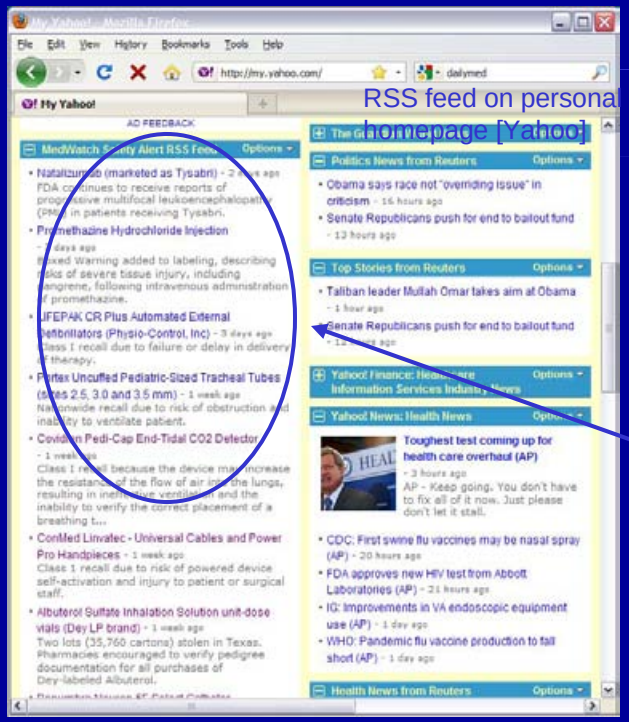
Safety alert web posting

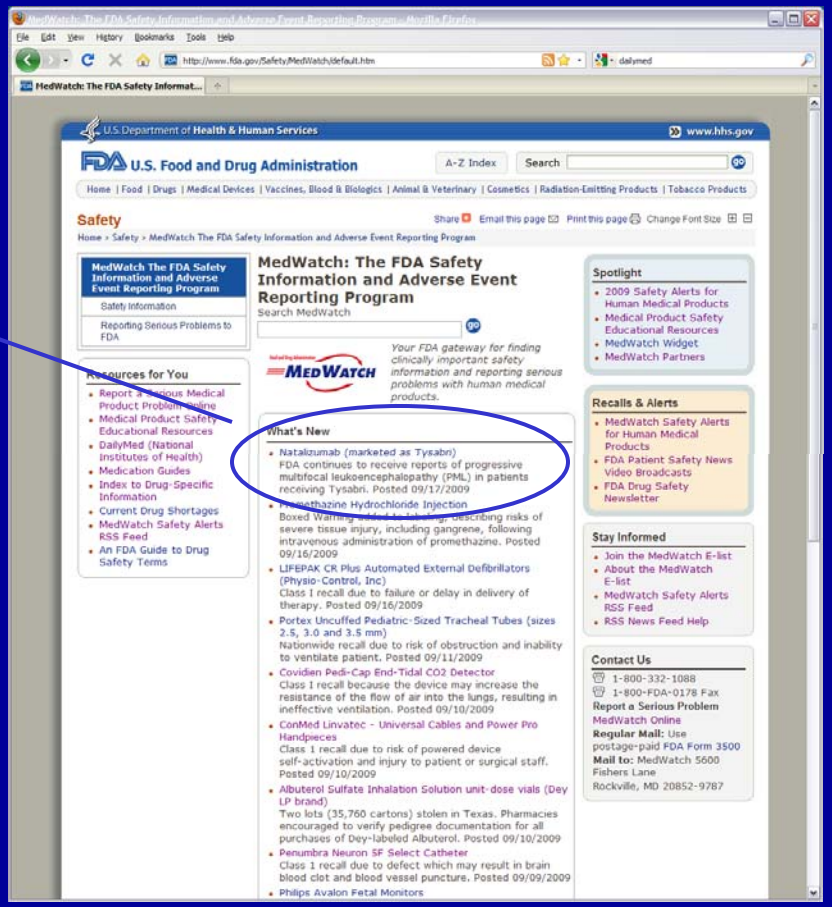


Listserve Notification GovDelivery distribution now reaches over 153,000 individuals

FDA MedWatch

Send notification by RSS feed to internet/intranet browsers

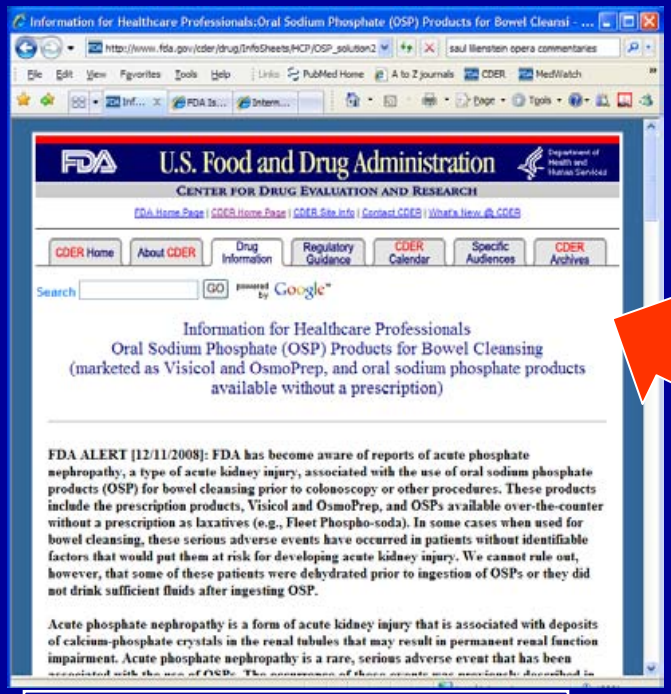




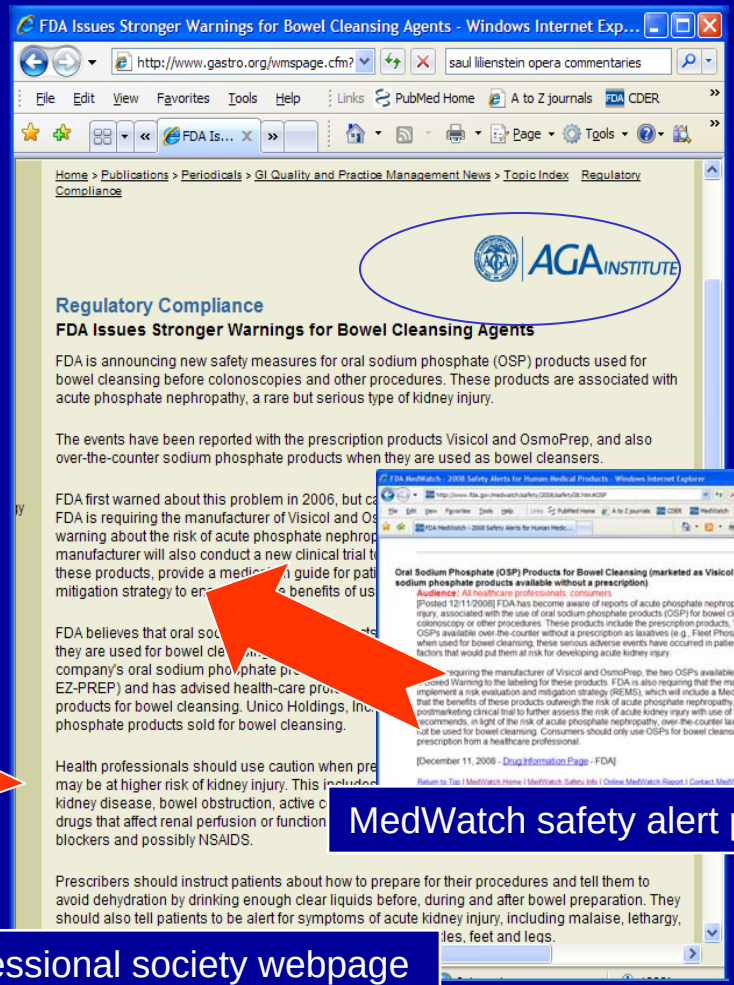
1. Alternative channel to individuals who want to avoid another email message
2. Automatic populating of intranet information for medical centers, hospital systems

FDA MedWatch

Notify targeted organizations and enlist their help in disseminating information to their members



Information for HCPs [FDA]



MedWatch safety alert posting

Professional society webpage

MedWatch Partners program

Am Gastroenterological Association

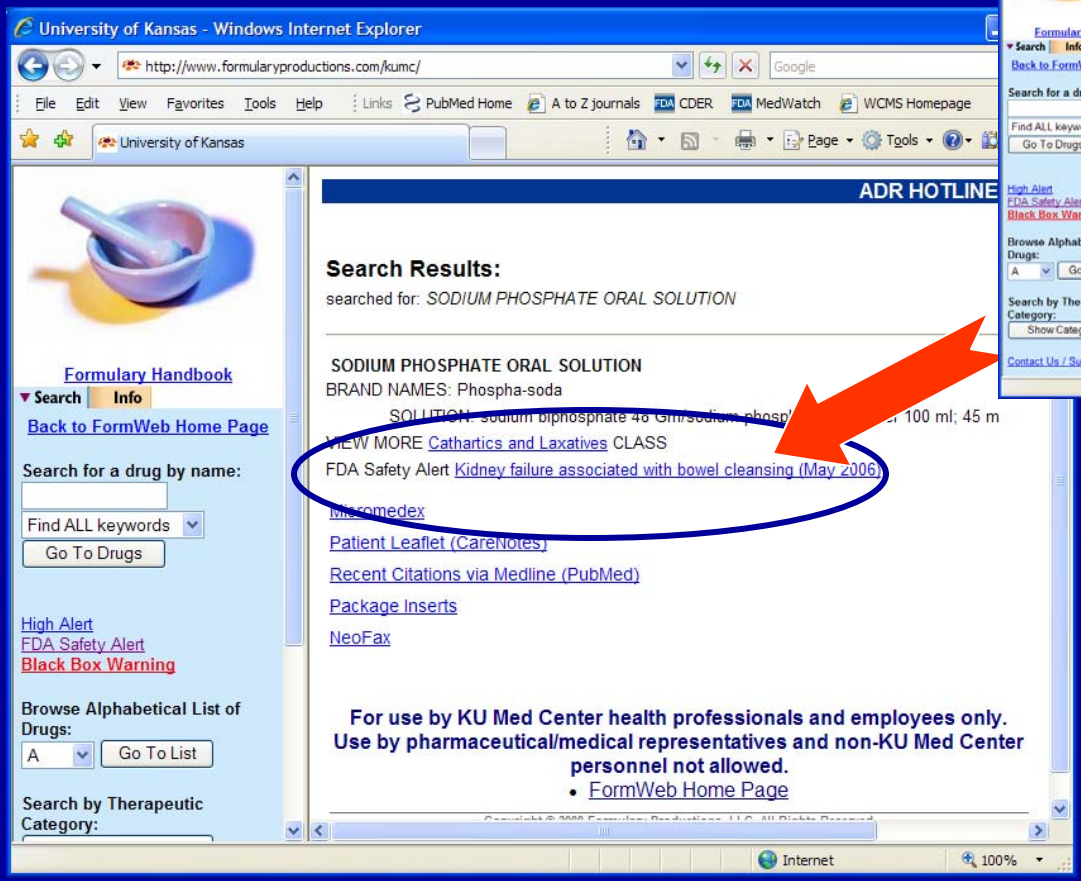
FDA MedWatch

Incorporate new safety information into workflow at point when provider is considering the product

- **Mobile drug references**
  - 650,000 registered users
  - 250,000 confirmed M.D.'s
  - 40,000 medical students
- **Regular updates of references weekly/monthly**
- ***DocAlerts*** notify physicians when updates are made, such as new drug approvals, additional indications,recalls
  - received by 5607 GI docs
  - received by over 131,000 primary care docs

FDA MedWatch

Incorporate new safety information into workflow at point when provider is considering the product



Kansas University Medical Center

FDA MedWatch and Patient Safety

Visit us online at

www.fda.gov/medwatch

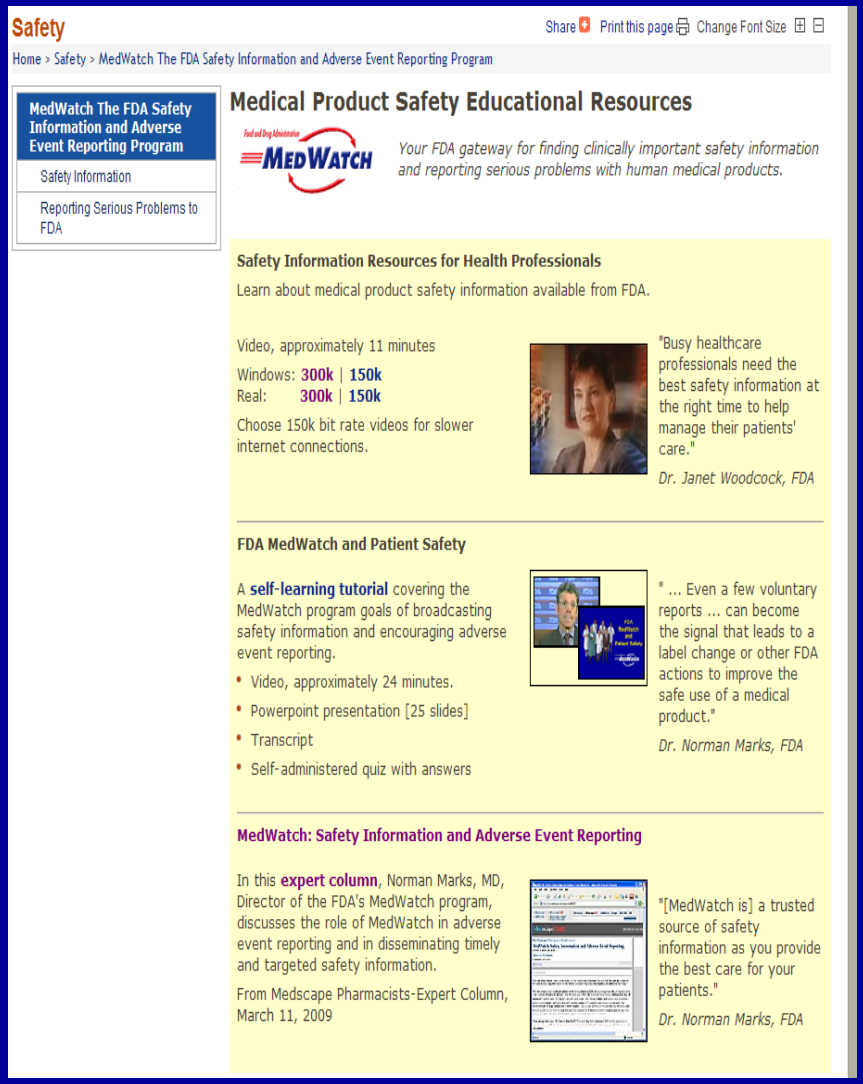
Food and Drug Administration

MEDWATCH

Safety Information Resources for HCPs

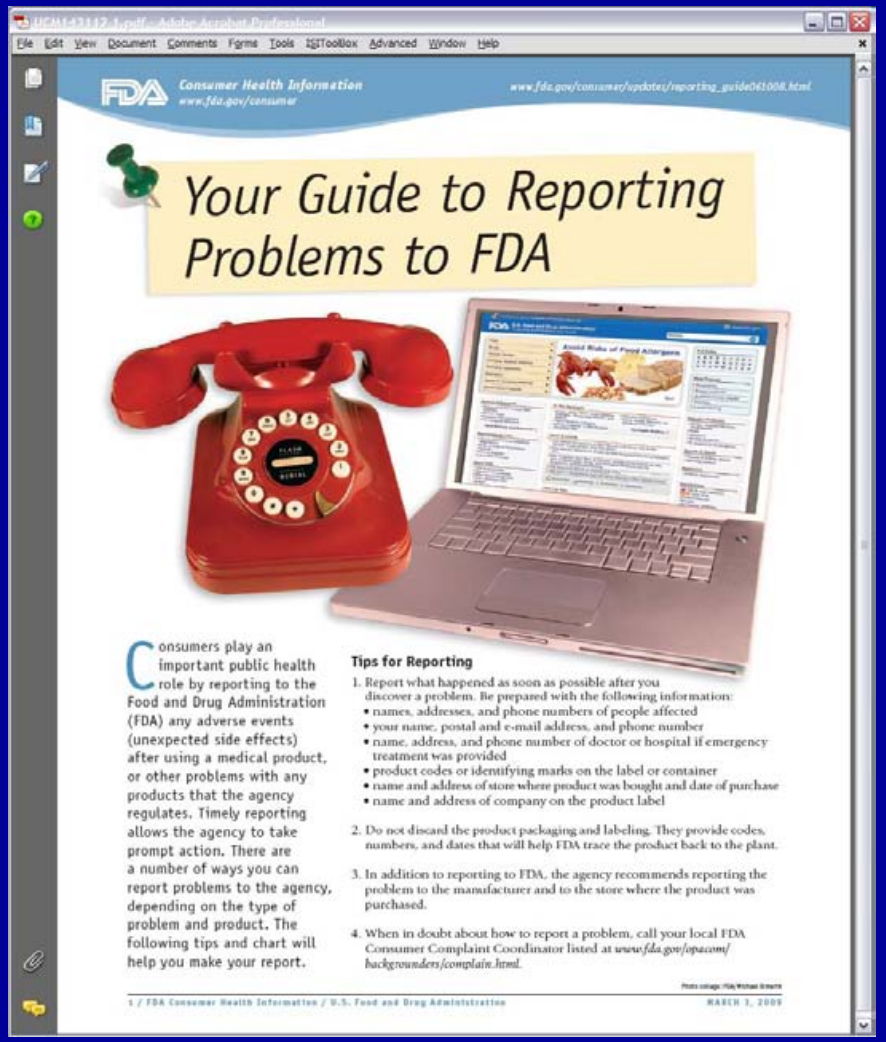
FDA MedWatch and Patient Safety

MedWatch: Safety Information and Adverse Event Reporting



http://www.fda.gov/Safety/MedWatch/ucm133050.htm

Your Guide to Reporting Problems to the FDA



Consumer Health Information
www.fda.gov/consumer

Your Guide to Reporting Problems to FDA

Consumers play an important public health role by reporting to the Food and Drug Administration (FDA) any adverse events (unexpected side effects) after using a medical product, or other problems with any products that the agency regulates. Timely reporting allows the agency to take prompt action. There are a number of ways you can report problems to the agency, depending on the type of problem and product. The following tips and chart will help you make your report.

Tips for Reporting

1. Report what happened as soon as possible after you discover a problem. Be prepared with the following information:
   - names, addresses, and phone numbers of people affected
   - your name, postal and e-mail address, and phone number
   - name, address, and phone number of doctor or hospital if emergency treatment was provided
   - product codes or identifying marks on the label or container
   - name and address of store where product was bought and date of purchase
   - name and address of company on the product label
2. Do not discard the product packaging and labeling. They provide codes, numbers, and dates that will help FDA trace the product back to the plant.
3. In addition to reporting to FDA, the agency recommends reporting the problem to the manufacturer and to the store where the product was purchased.
4. When in doubt about how to report a problem, call your local FDA Consumer Complaint Coordinator listed at *www.fda.gov/ora/com/backgrounders/complain.html*.

1 / FDA Consumer Health Information / U.S. Food and Drug Administration MARCH 3, 2009

http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM143112.pdf