FDA's MedWatch Adverse Event Reporting Program - Opportunities to Collaborate -

Steve L. Morin R.N., B.S.N.
CDR United States Public Health Service
Office of Health and Constituent Affairs
Office of External Affairs

March 2018

Today's Presentation

- About FDA Public Health Mission
- About the MedWatch Program
- Ways to Engage with FDA
- Challenges to Meaningful Engagement

FDA's Public Health Mission

- Ensure the safety, effectiveness, and security of human and animal drugs, biological products and medical devices
- Ensure the safety of foods, cosmetics, and radiation-emitting products
- Regulate tobacco products

FDA Regulates $2.4 Trillion Worth of Products a Year

Every morning when you wake up and

brush your teeth
put in your contact lenses
microwave your breakfast
take your medicine
feed your pet
select a sunscreen
go grocery shopping
get a flu shot or a mammogram….

You have been touched by the
U. S. Food and Drug Administration.

Approximately 20 cents on every dollar spent in the U.S.

FDA's Oversight Responsibilities

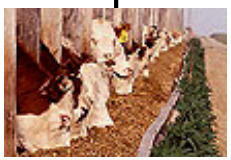
- 75 % of U.S. food supply
- 300,000 registered facilities, more than 80% of them abroad
- Over 17,000 prescription drug products
- Over 6,000 categories of medical devices

- Over 320 FDA-licensed biologic products
- Over 4,500 currently regulated tobacco products

Office of the Commissioner

Office of Foods

Center for Food Safety & Applied Nutrition



Center for Veterinary Medicine

Office of Medical Products & Tobacco

Center for Devices & Radiological Health

Center for Biologics Evaluation & Research

Center for Drug Evaluation & Research

Center for Tobacco Products

Office of Global Regulatory Operations & Policy

Office of Regulatory Affairs

What is MedWatch?

1. A way to send information you observe or experience from regulated medical products to FDA
2. A way to stay up-to-date on recently reported safety information from FDA

www.fda.gov/medwatch

Who Can Report to MedWatch?

Healthcare Professionals

Consumers and Patients

https://www.fda.gov/Safety/MedWatch/default.htm or https://go.usa.gov/xnuQy

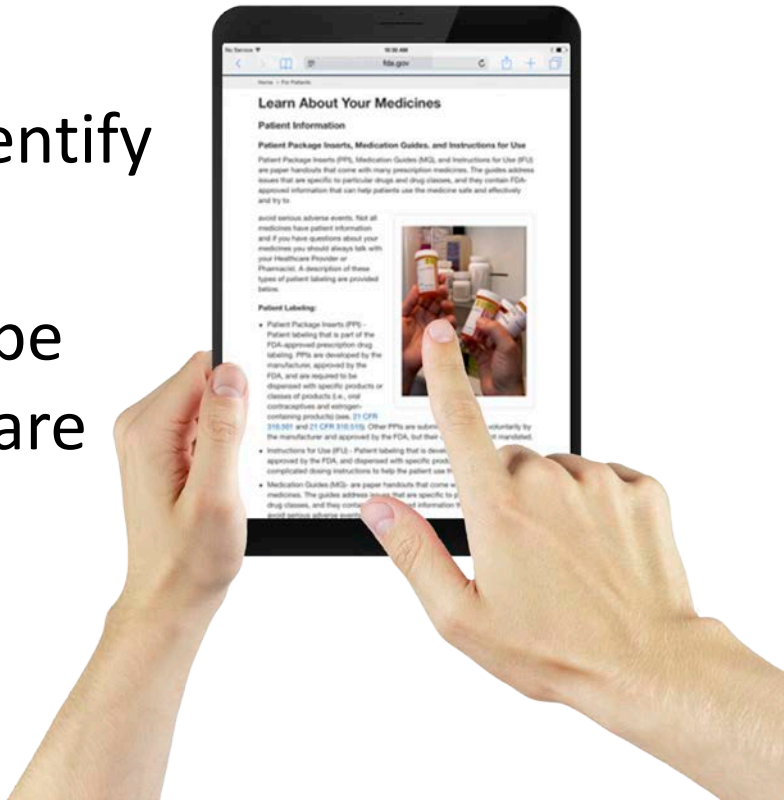
Why Report to MedWatch?

“Every product that FDA approves carries some risk…Sometimes there are risks that only come to light after a medical product gets on the market and is used in a larger number of patients, for a longer period of time, and in patients whose health characteristics are different from those of the patients studied before approval."

- Norman Marks, M.D., retired MedWatch Medical Officer

Why Report to MedWatch?

- Not all products have clinical data/trials before clearance to market
- Limitations of clinical trials to identify safety signals before marketing
- Number of patients tested may be too small to detect serious but rare problems
- Trials are brief



MedWatch: Safety Information *IN*

One person can make a difference

MedWatch *Safety Alerts*

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Total	128	139	169	138	140	203	181	149	164	159

Safety Alerts will update you on new information about:

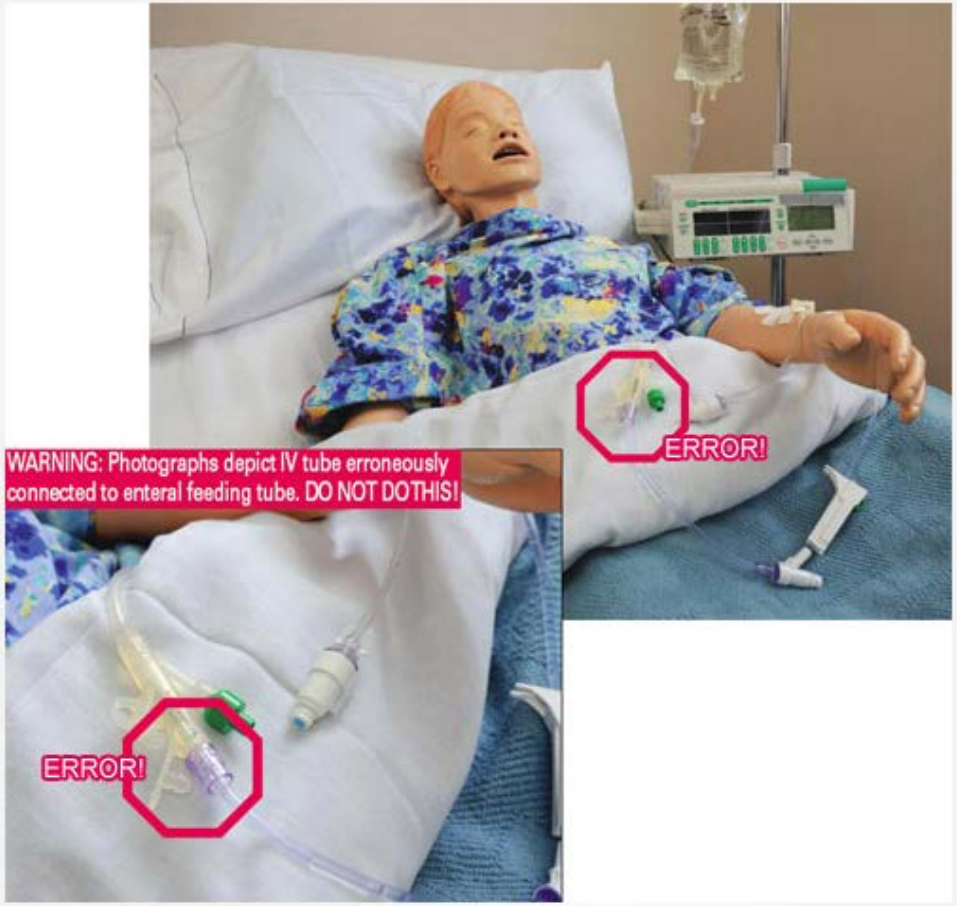
- *Drugs and Therapeutic Biologics*
- *Medical devices*
- *Nutritional products*
- *Cosmetics*
- *Products with undeclared drugs*
- *Tobacco*

MedWatch - What to Report

- Serious events such as:
  - death
  - life-threatening
  - permanently disabling
  - prolongs hospitalization
  - birth defect
  - Requires intervention to prevent permanent impairment or damage
- Medication errors
- Product quality problems
- Potential for error
- Non-serious events

Potential Harm

IV tubing erroneously connected to enteral feeding tube

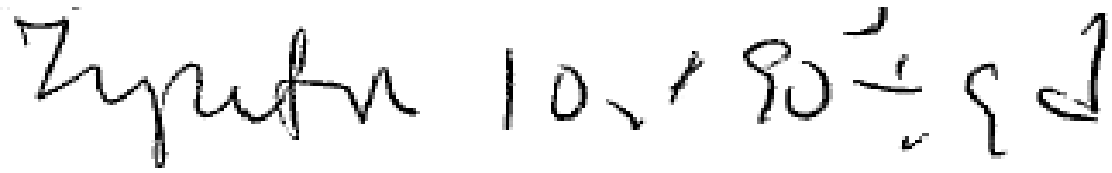


CASE STUDY

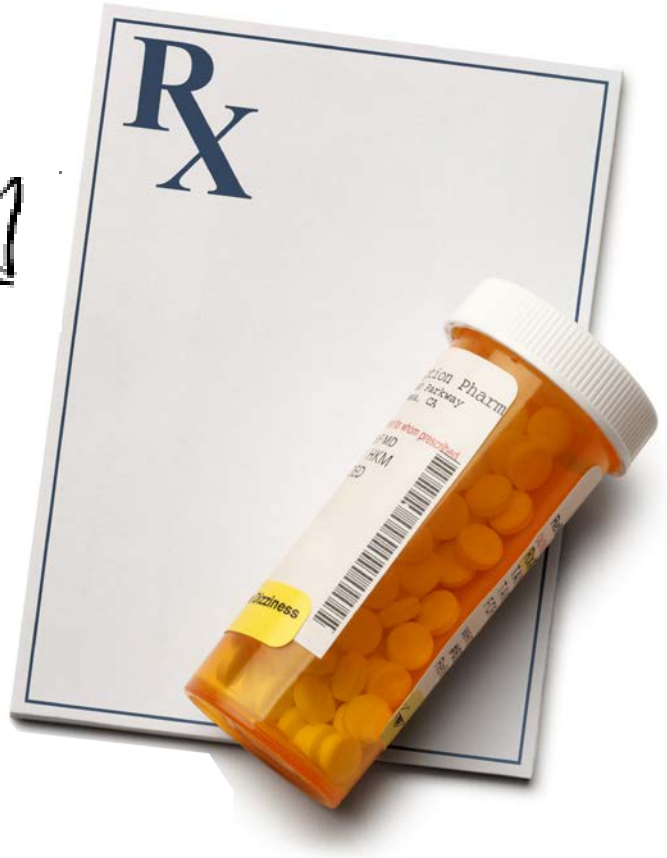
- A child had both a gastric feeding tube for nutrition and an IV for medicine and hydration
- When the child's gown was changed, a family member inadvertently attached the IV tubing to the gastric feeding tube

Potential Errors

- Prescribing
  - handwriting, abbreviations

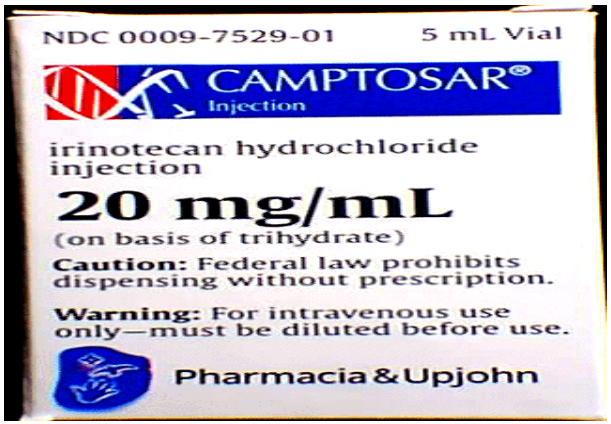


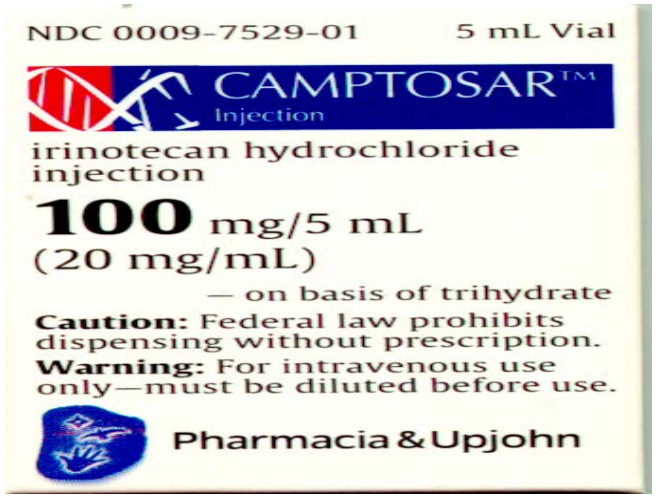
- Miscommunication of Orders/ Nomenclature
  - sound alike, look alike



Potential Errors

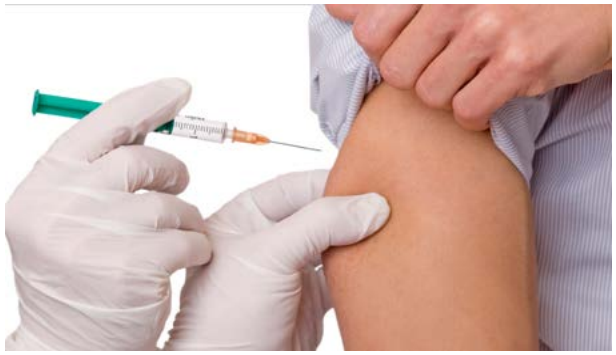
- Label/Packaging
  - placement of information
  - expression of strength/ dose
  - readability of label
  - inappropriate labeling during repackaging





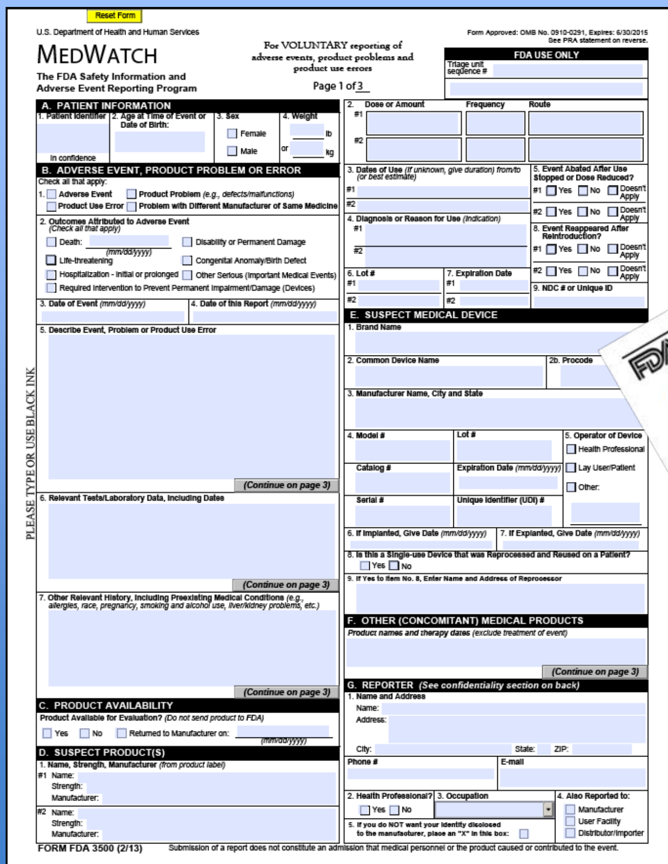
MedWatch - What *Not* to Report

- Tobacco Products
- Vaccines
- Investigational Drugs
- Dietary Supplements
- Veterinary Medicine

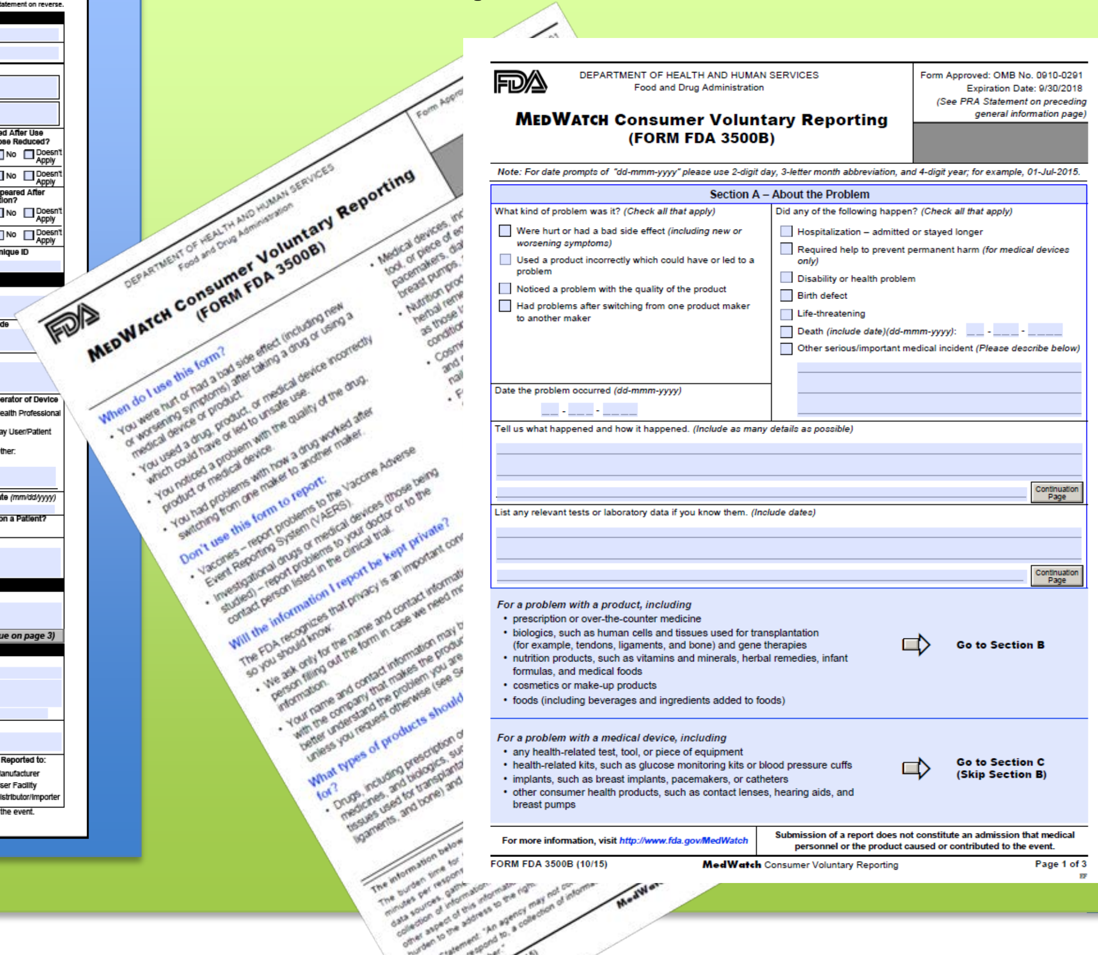


How to Report to MedWatch?

Clinician Form 3500

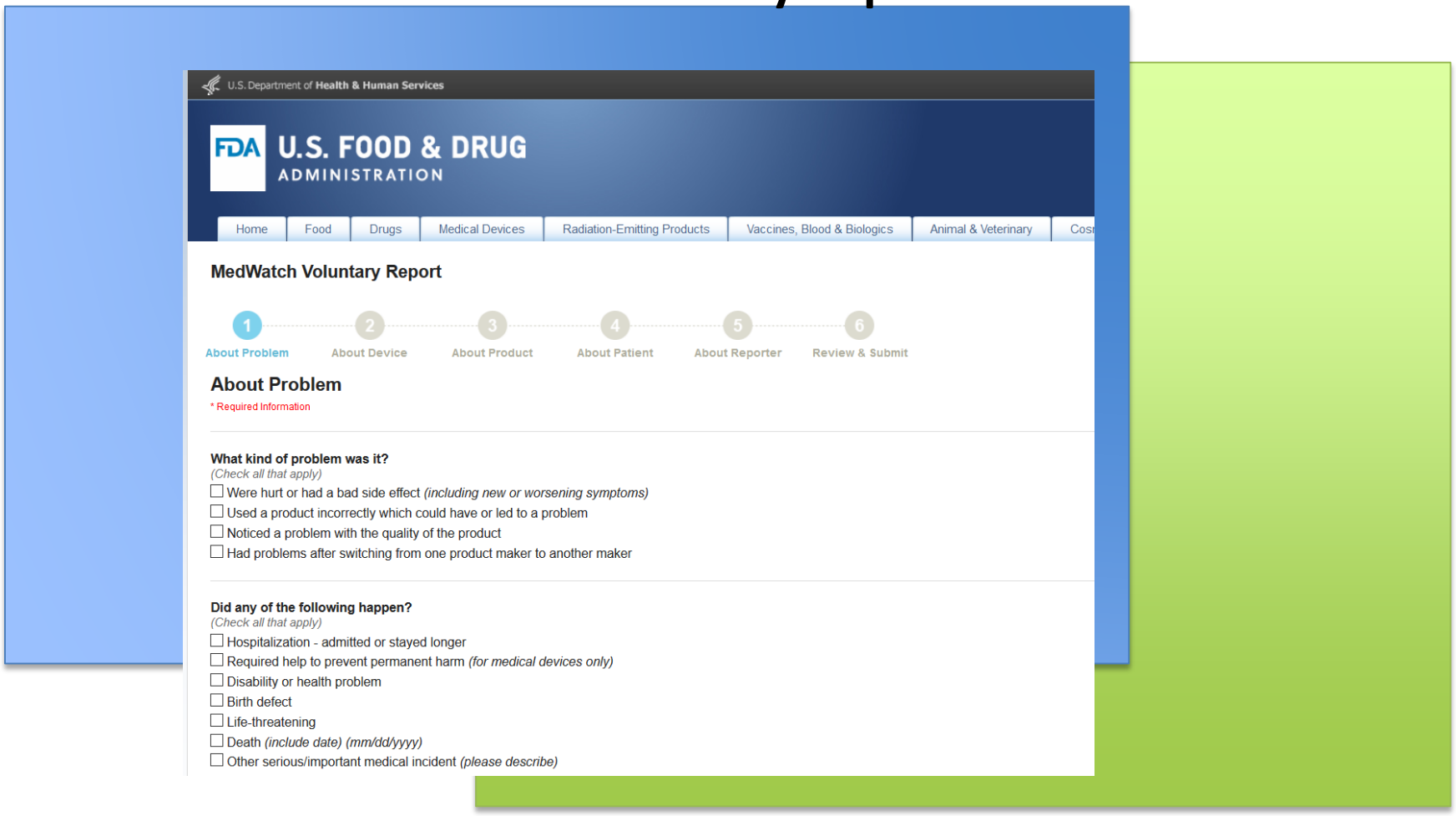


Consumer/Patient Form 3500B

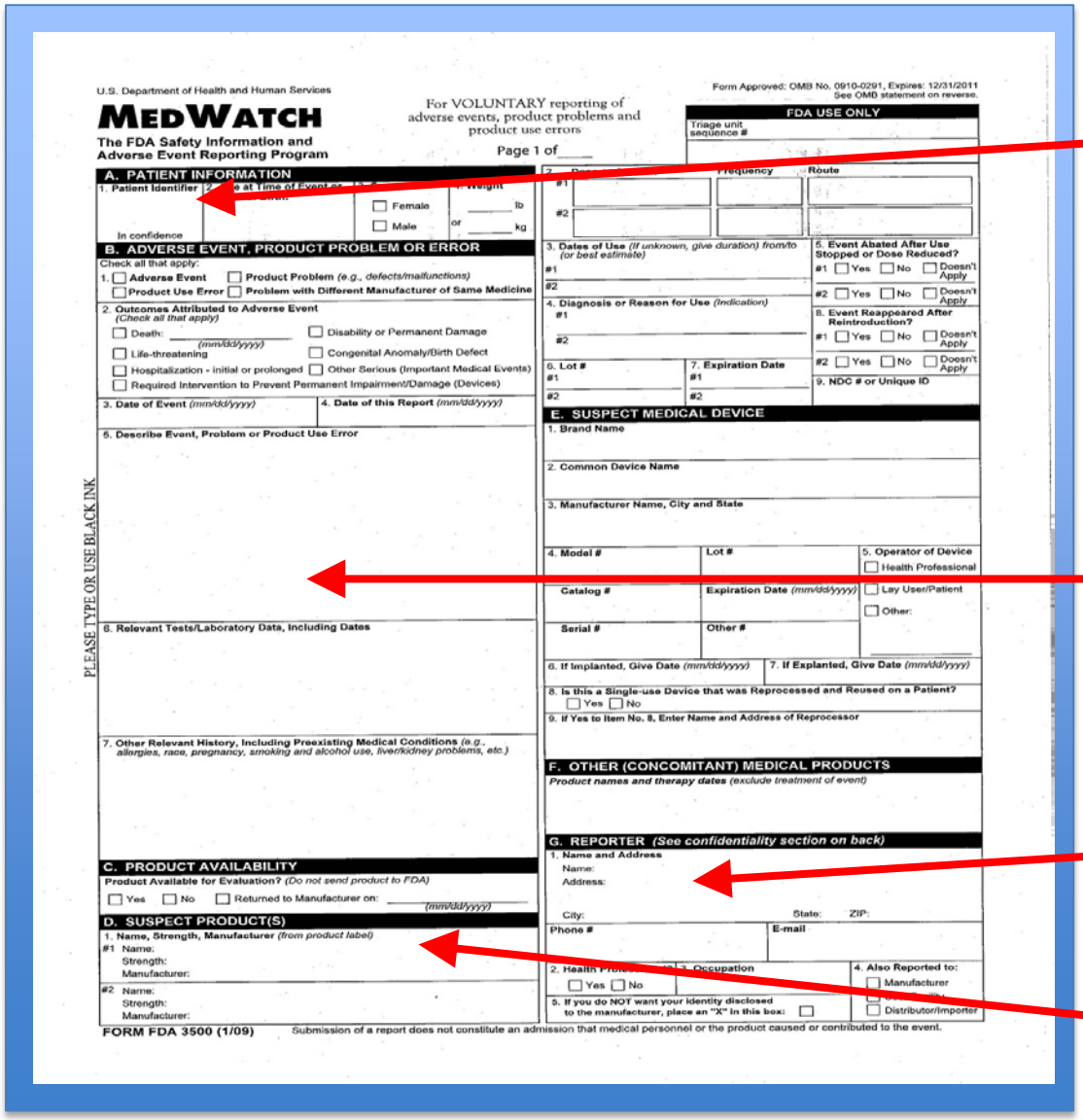


How to Report to MedWatch?

Online Voluntary Report



MedWatch Form



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

Page 1 of ___

Form Approved: OMB No. 0910-0291, Expires: 12/31/2011
See OMB statement on reverse.

FDA USE ONLY

Triage unit
seqüence #

A. PATIENT INFORMATION

1. Patient Identifier | 2. Age at Time of Event or Date of Birth | 3. Weight

In confidence

☐ Female ☐ Male

or _____ lb _____ kg

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR

Check all that apply:

1. ☐ Adverse Event ☐ Product Problem (e.g., defects/malfunctions)
☐ Product Use Error ☐ Problem with Different Manufacturer of Same Medicine

2. Outcomes Attributed to Adverse Event (Check all that apply)
☐ Death: _____ (mm/dd/yyyy)
☐ Disability or Permanent Damage
☐ Life-threatening
☐ Congenital Anomaly/Birth Defect
☐ Hospitalization - initial or prolonged
☐ Other Serious (Important Medical Events)
☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)

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, race, 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 Name:
Strength:
Manufacturer:

#2 Name:
Strength:
Manufacturer:

	Dose	Frequency	Route
#1			
#2			

3. Dates of Use (If unknown, give duration) from/to (or best estimate)
#1
#2

4. Diagnosis or Reason for Use (Indication)
#1
#2

5. Event Abated After Use Stopped or Dose Reduced?
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

8. Event Reappeared After Reintroduction?
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

6. Lot #	7. Expiration Date
#1	#1
#2	#2

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 #	5. Operator of Device
Catalog #	Expiration Date (mm/dd/yyyy)	☐ Health Professional ☐ Lay User/Patient ☐ Other:
Serial #	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
Name:
Address:
City: State: ZIP:
Phone # | E-mail

2. Health Profession ☐ Yes ☐ No | 3. Occupation | 4. Also Reported to: ☐ Manufacturer ☐ 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 (1/09)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Patient Identifier

Event or Problem

Reporter

Product

Quality is Key: Case #1

- Health care worker ST reported male patient ABC123 started Drug X at 5 mg daily for type 2 diabetes on February 11, 2015.
- The patient developed liver failure.

Question: Does Case #1 contain the four elements?

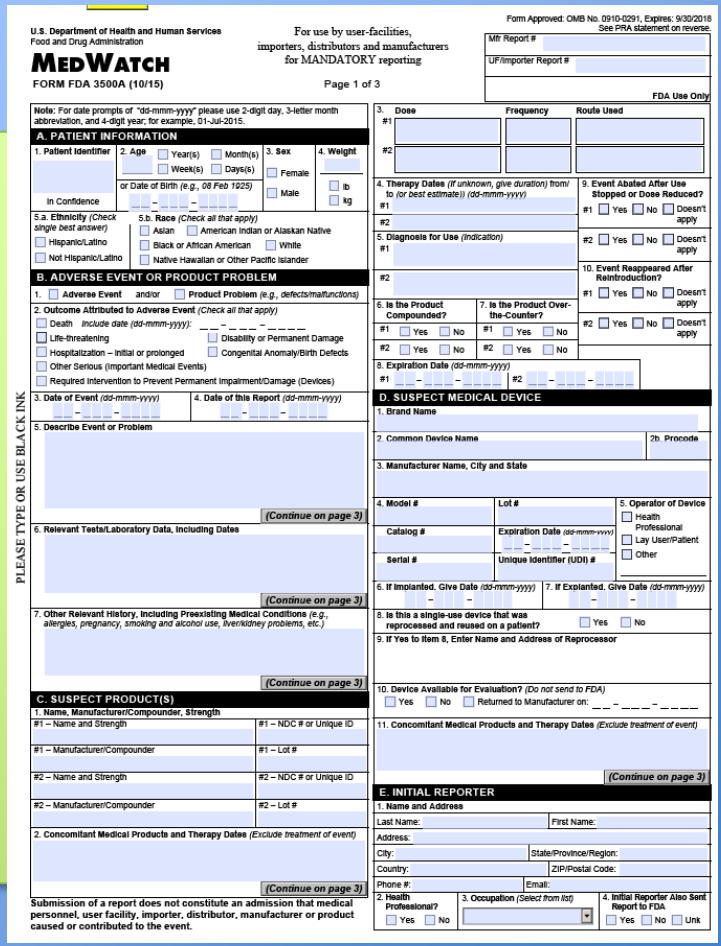
Quality is Key: Case #1

- Health care worker ST reported male patient ABC123 started Drug X at 5 mg daily for type 2 diabetes on February 11, 2015.
- The patient developed liver failure.

MedWatch Reporting- *MANDATORY*

MANDATORY Form 3500A

- User Facilities (medical devices)
- Manufacturers
  - Drugs
  - Biologics
  - Human Cell and Tissue Products
  - OTC Products
  - Medical Devices



U.S. Department of Health and Human Services
Food and Drug Administration

MEDWATCH

FORM FDA 3500A (10/15)

For use by user-facilities, importers, distributors and manufacturers for MANDATORY reporting

Page 1 of 3

Form Approved: OMB No. 0910-0291, Expires: 9/30/2018
See PRA statement on reverse.

Mfr Report #

UF/Importer Report #

FDA Use Only

Note: For date prompts of "dd-mmm-yyyy" please use 2-digit day, 3-letter month abbreviation, and 4-digit year; for example, 01-Jul-2015.

A. PATIENT INFORMATION

1. Patient Identifier / In Confidence
2. Age / or Date of Birth (e.g., 08 Feb 1925)
3. Sex: Female, Male
4. Weight: lb, kg
5.a. Ethnicity (Check single best answer): Hispanic/Latino, Not Hispanic/Latino
5.b. Race (Check all that apply): Asian, American Indian or Alaskan Native, Black or African American, White, Native Hawaiian or Other Pacific Islander

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. Adverse Event and/or Product Problem (e.g., defects/malfunctions)
2. Outcome Attributed to Adverse Event (Check all that apply): Death (include date (dd-mmm-yyyy)), Life-threatening, Hospitalization – initial or prolonged, Other Serious (Important Medical Events), Required Intervention to Prevent Permanent Impairment/Damage (Devices), Disability or Permanent Damage, Congenital Anomaly/Birth Defects
3. Date of Event (dd-mmm-yyyy)
4. Date of this Report (dd-mmm-yyyy)
5. Describe Event or Problem (Continue on page 3)
6. Relevant Tests/Laboratory Data, Including Dates (Continue on page 3)
7. Other Relevant History, Including Preexisting Medical Conditions (e.g., allergies, pregnancy, smoking and alcohol use, liver/kidney problems, etc.) (Continue on page 3)

C. SUSPECT PRODUCT(S)

1. Name, Manufacturer/Compounder, Strength
#1 – Name and Strength / #1 – NDC # or Unique ID
#1 – Manufacturer/Compounder / #1 – Lot #
#2 – Name and Strength / #2 – NDC # or Unique ID
#2 – Manufacturer/Compounder / #2 – Lot #
2. Concomitant Medical Products and Therapy Dates (Exclude treatment of event) (Continue on page 3)

Submission of a report does not constitute an admission that medical personnel, user facility, importer, distributor, manufacturer or product caused or contributed to the event.

3. Dose / Frequency / Route Used
4. Therapy Dates (If unknown, give duration) from/to (or best estimate)) (dd-mmm-yyyy)
5. Diagnosis for Use (Indication)
6. Is the Product Compounded?
7. Is the Product Over-the-Counter?
8. Expiration Date (dd-mmm-yyyy)
9. Event Abated After Use Stopped or Dose Reduced?
10. Event Reappeared After Reintroduction?

D. SUSPECT MEDICAL DEVICE

1. Brand Name
2. Common Device Name / 2b. Procode
3. Manufacturer Name, City and State
4. Model # / Lot # / Catalog # / Expiration Date (dd-mmm-yyyy) / Serial # / Unique Identifier (UDI) #
5. Operator of Device: Health Professional, Lay User/Patient, Other
6. If Implanted, Give Date (dd-mmm-yyyy)
7. If Explanted, Give Date (dd-mmm-yyyy)
8. Is this a single-use device that was reprocessed and reused on a patient?
9. If Yes to Item 8, Enter Name and Address of Reprocessor
10. Device Available for Evaluation? (Do not send to FDA) / Returned to Manufacturer on:
11. Concomitant Medical Products and Therapy Dates (Exclude treatment of event) (Continue on page 3)

E. INITIAL REPORTER

1. Name and Address
Last Name: / First Name:
Address:
City: / State/Province/Region:
Country: / ZIP/Postal Code:
Phone #: / Email:
2. Health Professional?
3. Occupation (Select from list)
4. Initial Reporter Also Sent Report to FDA

PLEASE TYPE OR USE BLACK INK

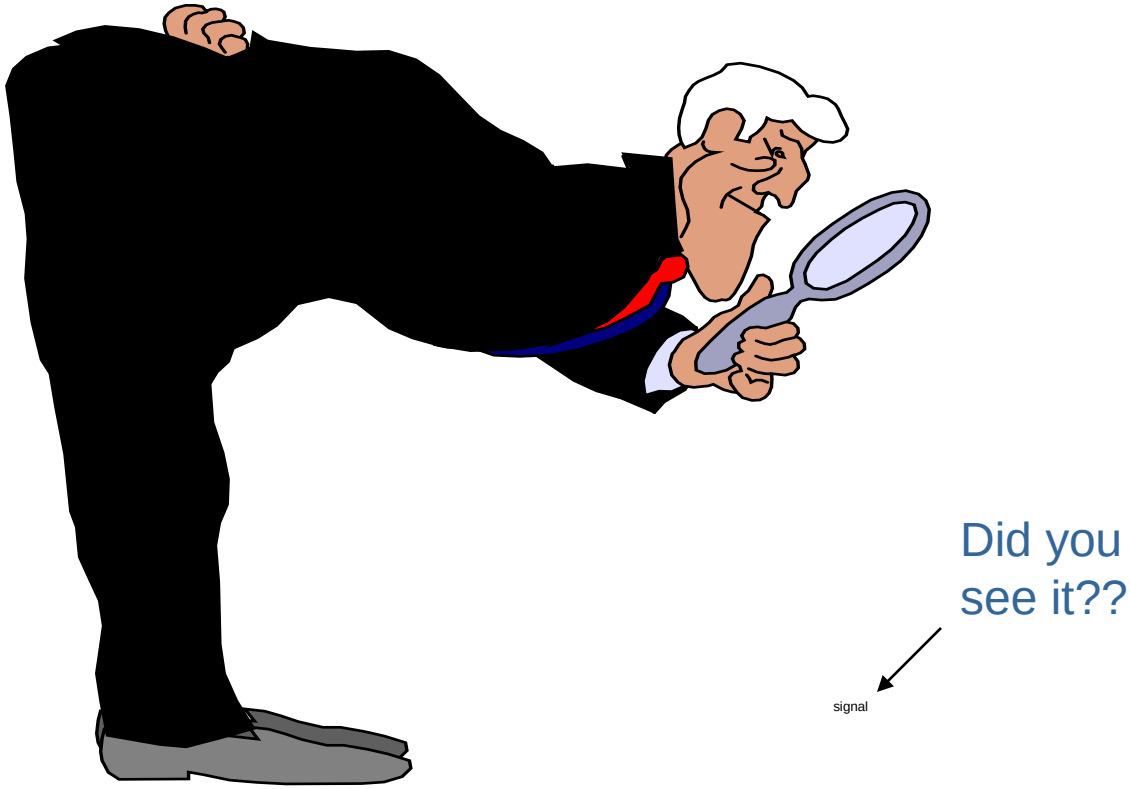
Reporting Tutorial – MedWatch*Learn*

- **Online practice portal**
  - Students/Health Professionals
  - Consumers Section
  - Learn how to fill out a MedWatch Report

www.fda.gov/medwatchlearn

Reporting Tutorial - MedWatch *Learn*

What happens to my report?



MedWatch: Safety Information *IN*

L-citrulline investigation 2014

- Late January
  - Puzzling case at medical center
- February 7
  - Pharmacist submits report
  - Mother submits report
- February 7-13
  - FDA investigation
- February 14
  - Manufacturer recall
  - MedWatch Safety Alert communication

FDA Healthcare Professionals in Action

Safety Info *Out*

Lidocaine Viscous: Drug Safety Communication - Boxed Warning Required - Should Not Be Used to Treat Teething Pain

MedWatch Safety Alert Example

ISSUE: FDA notified health professionals, their provider organizations and caregivers for infants, that prescription oral viscous lidocaine 2% solution should not be used to treat infants and children with teething pain. FDA is requiring a Boxed Warning to be added to the prescribing information (label) to highlight this information. Oral viscous lidocaine solution is not approved to treat teething pain, and use in infants and young children can cause serious harm, including death.

Topical pain relievers and medications that are rubbed on the gums are not necessary or even useful because they wash out of the baby's mouth w[illegible]hen too much viscous lidocaine is given to infants and young children or they accidentally swallow[illegible]esult in seizures, severe brain injury, and problems with the heart. Cases of overdose due to wr[illegible]idental ingestion have resulted in infants and children being hospitalized or dying.

22 case reports

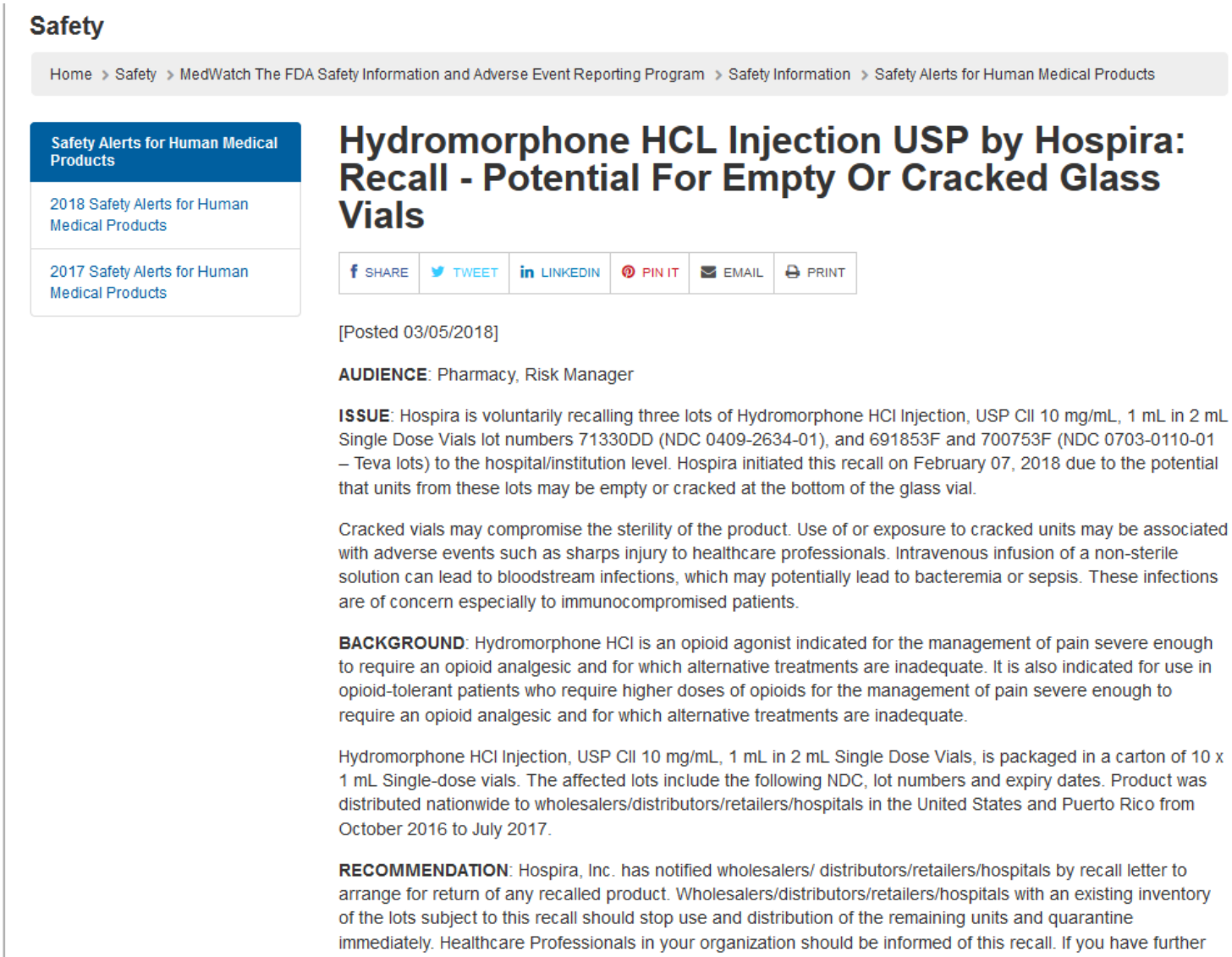
BACKGROUND: In 2014, FDA reviewed 22 case reports of serious adverse reactions, including deaths, in infants and young children 5 months to 3.5 years of age who were given oral viscous lidocaine 2 percent solution for the treatment of mouth pain, including teething and stomatitis, or who had accidental ingestions. See further details in the FDA Drug Safety Communication.

RECOMMENDATION: Health care professionals should not prescribe or recommend this product for teething pain. Parents and caregivers should follow the American Academy of Pediatrics' recommendations for treating teething pain.

- Use a teething ring chilled in the refrigerator (not frozen).
- Gently rub or massage the child's gums with your finger to relieve the symptoms.

FDA is also encouraging parents and caregivers not to use topical medications for teething pain that are available over the counter (OTC) because some of them can be harmful. FDA recommends following the American Academy of Pediatrics' recommendations to help lessen teething pain.

MedWatch: Safety Info *Out*



Safety

Home > Safety > MedWatch The FDA Safety Information and Adverse Event Reporting Program > Safety Information > Safety Alerts for Human Medical Products

Safety Alerts for Human Medical Products

2018 Safety Alerts for Human Medical Products

2017 Safety Alerts for Human Medical Products

Hydromorphone HCL Injection USP by Hospira: Recall - Potential For Empty Or Cracked Glass Vials

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT

[Posted 03/05/2018]

AUDIENCE: Pharmacy, Risk Manager

ISSUE: Hospira is voluntarily recalling three lots of Hydromorphone HCl Injection, USP CII 10 mg/mL, 1 mL in 2 mL Single Dose Vials lot numbers 71330DD (NDC 0409-2634-01), and 691853F and 700753F (NDC 0703-0110-01 – Teva lots) to the hospital/institution level. Hospira initiated this recall on February 07, 2018 due to the potential that units from these lots may be empty or cracked at the bottom of the glass vial.

Cracked vials may compromise the sterility of the product. Use of or exposure to cracked units may be associated with adverse events such as sharps injury to healthcare professionals. Intravenous infusion of a non-sterile solution can lead to bloodstream infections, which may potentially lead to bacteremia or sepsis. These infections are of concern especially to immunocompromised patients.

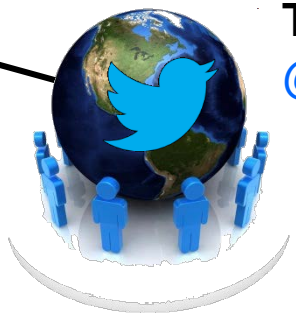
BACKGROUND: Hydromorphone HCl is an opioid agonist indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. It is also indicated for use in opioid-tolerant patients who require higher doses of opioids for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Hydromorphone HCl Injection, USP CII 10 mg/mL, 1 mL in 2 mL Single Dose Vials, is packaged in a carton of 10 x 1 mL Single-dose vials. The affected lots include the following NDC, lot numbers and expiry dates. Product was distributed nationwide to wholesalers/distributors/retailers/hospitals in the United States and Puerto Rico from October 2016 to July 2017.

RECOMMENDATION: Hospira, Inc. has notified wholesalers/ distributors/retailers/hospitals by recall letter to arrange for return of any recalled product. Wholesalers/distributors/retailers/hospitals with an existing inventory of the lots subject to this recall should stop use and distribution of the remaining units and quarantine immediately. Healthcare Professionals in your organization should be informed of this recall. If you have further

How Do I Stay Informed?

To subscribe, E-mail us at
MedWatchSafetyAlerts@fda.hhs.gov

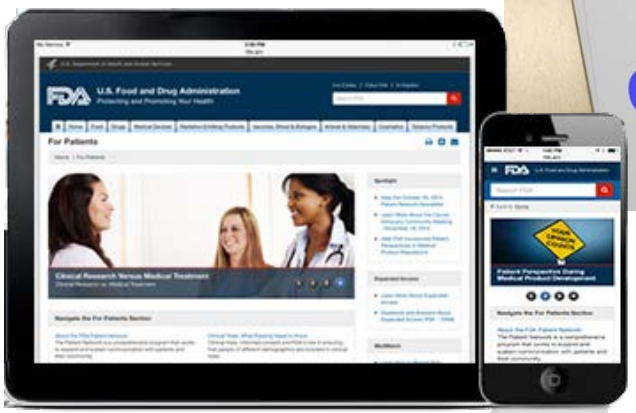


Twitter
@FDAMedWatch

www.fda.gov/medwatch

Ways to Get Involved With FDA

Sentinel Initiative




drugsafety

High doses of loperamide can cause serious cardiac events

BRENDA J. ROSE

FDA is warning that taking higher-than-recommended doses of the common OTC and prescription antidiarrheal medicine loperamide, including through abuse or misuse of the product, can cause serious cardiac events, including Torsades de pointes, cardiac arrest, ventricular tachycardia, syncope, and death. The risk of these serious cardiac events may also be increased when high doses of loperamide are taken with several kinds of medicines that interact with loperamide.

The majority of reported serious heart problems occurred in individuals who were intentionally misusing and abusing high doses of loperamide in attempts to self-treat opioid withdrawal symptoms or to achieve a feeling of euphoria.

Background

Loperamide is approved to help control symptoms of diarrhea, including traveler's diarrhea. It is sold under the OTC brand name Imodium A-D, as store brands, and as generics.

It is important not to exceed the total daily dose that is recommended on the drug label. Loperamide is approved for use in single doses of 4 mg for the first dose, followed by 2 mg after each loose stool for adults. The maximum approved total daily dose is 8 mg per day for OTC use and 16 mg per day for prescription use. Dosing for children depends on the age of the child and is not recommended for use in children younger than 2 years.

Loperamide can interact with drugs that are cytochrome (CYP) 3A4 inhibitors (e.g., itraconazole, clarithromycin, omeprazole), CYP2C8 inhibitors (e.g., gemfibrozil), and *P*-glycoprotein inhibitors (e.g., quinidine).

In the **majority** of **severe cases**, individuals **intentionally abused loperamide.**

Safety data

In the 39 years between when loperamide was first approved in 1976 and 2015, FDA received reports of 48 cases of serious heart problems associated with use of loperamide. Thirty-one of these cases resulted in hospitalizations, and 10 patients died.

More than one-half of the 48 cases were reported after 2010.

In the majority of severe cases, individuals intentionally abused loperamide. Some patients also misused loperamide by taking higher-than-recommended doses to treat their diarrhea. In the most severe cases, individuals self-treated with doses ranging from 70 mg to 1,600 mg per day, which is 4 to 100 times the recommended dose. In several cases, individuals used concomitant drugs—CYP3A4 inhibitors, CYP2C8 inhibitors, and *P*-glycoprotein inhibitors—to increase gastrointestinal absorption, decrease loperamide metabolism, and increase blood–brain barrier penetration.

In addition to reviewing the reports described above, FDA searched the medical literature and identified other cases of serious cardiac events with loperamide. Data from U.S. poison control call centers also indicate that since 2006, and particularly since 2010, calls have increased for intentional loperamide exposures, which include cases of intentional abuse, intentional misuse, suspected suicide attempt, and unknown intentional exposures.

Counseling pearls

As the members of the health care team most often available at the point of purchase, pharmacists have an opportunity to help patients and caregivers select an appropriate OTC product. Pharmacists should provide the following information when counseling patients and caregivers seeking loperamide-containing products:

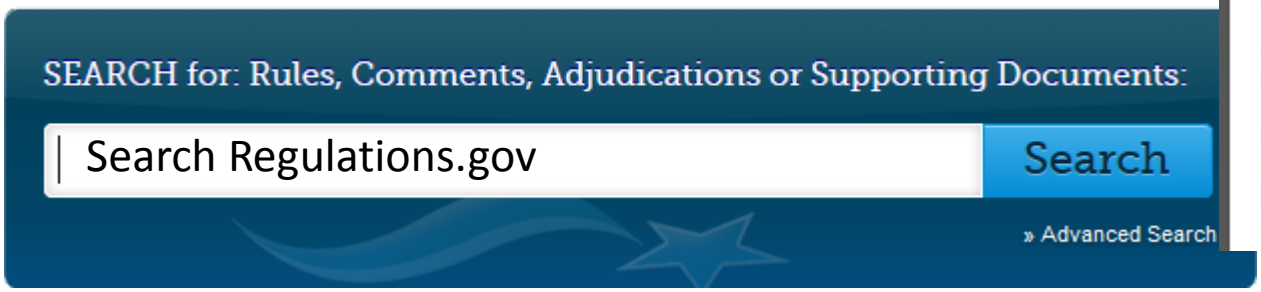
- Direct patients to take loperamide only at the dose directed by their primary care provider or according to the OTC Drug Facts label.
- Counsel patients about the cardiac risks of loperamide, and tell them not to use more than the recommended dose.
- Instruct patients to stop taking loperamide and contact their primary care provider if their diarrhea lasts more than 2 days, their symptoms get worse, or they have abdominal swelling or bulging.
- Warn patients that drug interactions with commonly used medications also increase the risk of serious cardiac adverse events.
- Refer patients with opioid use disorders for treatment. There are FDA-approved drugs to reduce opioid withdrawal symptoms.

Pharmacists are encouraged to report adverse events related to the use of these products to FDA's MedWatch Safety Information and Adverse Event Reporting Program, as follows:

- Complete and submit the report online at www.fda.gov/MedWatch/report.htm.
- Download the form or call 800-332-1088 to request a reporting form, then complete and return to the address on the preaddressed form, or submit by fax to 800-FDA-0178.

FDA will continue to evaluate this safety issue and will determine if additional FDA actions are needed.

Brenda J. Rose, PharmD, is a member of the Health Professional Liaison Program in FDA's Office of Health and Constituent Affairs. She acknowledges the help of subject matter experts in FDA's Center for Drug Evaluation and Research.



Professional Publications

Hospital Pharmacy

Hosp Pharm. 2017 February; 52(2): 153–154.
doi: 10.1310/hpj5202-153

PMCID: PM

Summaries of Safety Labeling Changes Approved by the FDA: Boxed W
Highlights October - December 2016

Brenda J. Rose, PharmD

Author information ► Copyright and License information ►

Abstract

The FDA's MedWatch program safety labeling changes for boxed warnings are compiled
and therapeutic biologics where important changes have been made to the safety infor
Drug Safety Labeling Changes (SLC) database was conducted on December 31, 2016 fo
"10/1/2016-12/31/2016", labeling section "Boxed Warning". These and other label chan
the Drug Safety Labeling Changes (SLC) database, where data are available to the pub
and searchable formats. (Drug Safety Labeling Changes are available at: http://www.
/scripts/cder/safetylabelingchanges/?source=govdelivery&utm_medium=email&utm
Boxed warnings are ordinarily used to highlight either: adverse reactions so seriou
potential benefit from the drug that it is essential that it be considered in assessin
of using the drug; OR serious adverse reactions that can be prevented/reduced i
appropriate use of the drug; OR FDA approved the drug with restrictions to ensu
concluded that the drug can be safely used only if distribution or use is restricte

NEWS

Summaries of safety labeling changes approved by FDA—boxed warnings highlights, July–September 2016

As part of FDA's MedWatch program, changes to the boxed warnings in the labeling of drugs and therapeutic biologics are compiled quarterly. These and other labeling changes are searchable in the Drug Safety Labeling Changes (SLC) database,[1] where data are available to the public in downloadable and searchable formats. Boxed warnings are ordinarily used to highlight (1) an adverse reaction so serious in proportion to the potential benefit from the drug that it is essential that the reaction be considered in assessing the risks and benefits of using the drug, (2) serious adverse reactions that can be prevented or reduced in frequency or severity by appropriate use of the drug, and (3) situations in which FDA approved a drug with restrictions to ensure safe use because FDA concluded that the drug can be safely used only if distribution or use is restricted. The following changes to boxed warnings were identified in an October 10 search of the Drug Safety Labeling Changes (SLC) database over the date range July 1, 2016, through September 30, 2016.

Class of Systemic Fluoroquinolone Antibacterial Drugs, includes Avelox (moxifloxacin hydrochloride), Avelox in 0.8% sodium chloride solution for I.v. use (moxifloxacin hydrochloride), Cipro (ciprofloxacin; ciprofloxacin hydrochloride), Cipro IV in 5% dextrose injection (ciprofloxacin), Cipro XR (ciprofloxacin), Factive (gemifloxacin mesylate), Levaquin (levofloxacin), moxifloxacin hydrochloride, and Noroxin (norfloxacin); refer to www.accessdata.fda.gov/scripts/cder/safetylabelingchanges for specific new drug application

Edited Boxed Warnings (class template)

Updated Quinolone Boxed Warning

WARNING: SERIOUS ADVERSE REACTIONS INCLUDING TENDINITIS, TENDON RUPTURE, PERIPHERAL NEUROPATHY, CENTRAL NERVOUS SYSTEM EFFECTS AND EXACERBATION OF MYASTHENIA GRAVIS

- Fluoroquinolones, including [Product], have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together including:
  - Tendinitis and tendon rupture
  - Peripheral neuropathy
  - Central nervous system effects
- Discontinue [Product] immediately and avoid the use of fluoroquinolones, including [Product], in patients who experience any of these serious adverse reactions. Fluoroquinolones, including [Product], may exacerbate muscle weakness in patients with myasthenia gravis. Avoid [Product] in patients with known history of myasthenia gravis.
- Because fluoroquinolones, including [Product], have been associated with serious adverse reactions, reserve [Product] for use in patients who have no alternative treatment options for the following indications:

(for Avelox, Avelox in 0.8% sodium chloride solution for I.v. use, moxifloxacin hydrochloride, and Cipro IV)
- Acute bacterial sinusitis
- Acute bacterial exacerbation of chronic bronchitis

(for Cipro)
- Acute exacerbation of chronic bronchitis
- Acute uncomplicated cystitis
- Acute sinusitis

(for Cipro XR and Noroxin)
- Uncomplicated urinary tract infections

(for Factive)
- Acute bacterial exacerbation of chronic bronchitis

(for Levaquin)
- Uncomplicated urinary tract infection
- Acute bacterial exacerbation of chronic bronchitis
- Acute bacterial sinusitis

Krystexxa (pegloticase)
Added Section to Boxed Warning

Updated Krystexxa Boxed Warning

WARNING: ANAPHYLAXIS AND INFUSION REACTIONS; G6PD DEFICIENCY ASSOCIATED HEMOLYSIS AND METHEMOGLOBINEMIA *(Title Updated)*

Addition of:

Screen patients at risk for G6PD deficiency prior to starting Krystexxa. Hemolysis and methemoglobinemia have been reported with Krystexxa in patients with G6PD deficiency. Do not administer Krystexxa to patients with G6PD deficiency.

FDA Case Studies

U.S. FOOD & DRUG ADMINISTRATION

FDA CASE STUDY

FDA MedWatch Adverse Event Reporting Curriculum Case Study

DRUGS, DEVICES, & BIOLOGICS: Health professionals encounter adverse events with medical products and learn about reporting to FDA MedWatch

This fictionalized case study is part of an educational series published by the U.S. Food and Drug Administration.

A Patch of a Different Color

Dr. Jim Bean was excited as he reached examination room 4, where his last patient of the day was waiting for him. The family practice physician would be on a plane heading to Miami for a national medical conference later that evening. Old colleagues he hadn't seen since his residency, workshops and presentations on the latest advances in medicine and, most importantly, the remaining continuing education credits he needed for his licensure were a few short hours away. Pulling a chart out of the file holder on the wooden door, Jim knocked and let himself in after the voice on the other side said he could enter.

"Hello, Chris! How are you today?" Jim asked, shaking the young man's hand before sitting on a low stool in a corner of the room. Jim had joined the family practice of six physicians 2 years earlier. He had just finished his residency at the time, and Chris had become one of his first regular patients.

"I'm doing well, Dr. Bean," Chris smiled.

"That's what I like to hear." Jim said as he looked down at Chris' charts. The 24-year-old had been successfully treated for years with medication for Attention Deficit Hyperactivity Disorder (ADHD). In the 2 years that Jim had been treating Chris, he had switched his patient from oral ADHD medications to a patch worn on the skin. He noted the last prescription date in charts and said, "I'll need to refill your prescription. Let's get you checked out first and then I'll have the nurses send the prescription to your pharmacy before you leave."

After a routine checkup, Jim turned his attention to Chris' patch. Peeling it off, he noticed that some of Chris's skin at the application site was discolored. "Chris," he said, eyebrows pinched with concern, "I'm noticing some depigmentation underneath your patch that wasn't here the last time I saw you. Can you tell me when this first started happening?"

"I'm not sure," Chris replied. He took a few moments to think. "I noticed my skin was getting lighter there, but didn't think anything of it since I tend to put the patch in the same place and that area isn't exposed much to light."

U.S. FOOD & DRUG ADMINISTRATION

FDA MedWatch Adverse Event Reporting Curriculum Case Study: Instructor's Guide

DRUGS, DEVICES, & BIOLOGICS: Health professionals encounter adverse events with medical products and learn about reporting to FDA MedWatch

LEARNING OBJECTIVES

- Identify how to receive safety information from the FDA.
- Identify how to submit a quality medical product problem report to FDA.
- Explain how reports are used by FDA to investigate medical product problems and are translated into safety actions such as recalls or safety communications.
- Review the definitions of drug, device, and biologic.

TOPICS

Adverse event reporting; MedWatch; Forms 3500, 3500B, 3500A; Drugs; Devices; Biologics

ASSUMPTIONS

This case study is based on the assumption that the target audience is undergraduate students or health professionals who have little experience with adverse event reporting.

SUGGESTED APPROACH

1. Preparing Students: Students are expected to read the case study prior to the training session.

2. Engaging Students: The training session should consist of a discussion of the case study and completion of a MedWatch form.

3. Immersing Students: The training session should emphasize group discussion of the two examples in the case study. Students should be encouraged to review an additional case study on MedWatchLearn after class.

STUDENT ACTIVITIES

Before Class

Review the following materials before class:

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

2. Print hard copies of Form 3500B and Form 3500 and bring them to class. http://www.fda.gov/Safety/MedWatch/HowToReport/DownloadForms/default.htm

Answer the following questions before class:

1. How are reporting forms 3500, 3500B, and 3500A different?

Answer:

- Form FDA 3500, Voluntary Reporting: For use by health care professionals, consumers, and patients.
- Form FDA 3500B, Voluntary Reporting for Consumers: A consumer-friendly version of the 3500 reporting form.
- Form FDA 3500A Mandatory Reporting: For use by IND reporters, manufacturers, distributors, importers, and user facilities personnel.

2. True or False: Vaccine product problems should be reported to MedWatch.

Answer: **False.** Vaccine product problems should be reported to the Vaccine Adverse Event Reporting System (VAERS), not MedWatch. VAERS is a national vaccine safety surveillance program co-sponsored by FDA and the Centers for Disease Control and Prevention (CDC).

3. Good case reports include the following elements:

a. Description of the adverse events or disease experience, including time to the beginning of signs or symptoms
b. Clinical course of the event and patient outcomes (e.g., hospitalization or death)
c. Relevant therapeutic measures and laboratory data at baseline, during therapy, and subsequent to therapy, including blood levels, as appropriate
d. All of the above

Answer: **d.** All of the above

1

U.S. FOOD & DRUG ADMINISTRATION

FDA CASE STUDY

FDA Drug Information Curriculum Case Study

Useful FDA Drug Information for Clinicians: Practicing clinicians seek available information on a new drug before making a treatment decision

This fictionalized case study is part of an educational series published by the U.S. Food and Drug Administration.

A Rounding Team and One Patient

If they listened closely, the patients in the cardiology wing of Sun Valley hospital could hear them. Several pairs of rubber-soled shoes slapped the ground in quick patterns as they tried to keep up with the long stride of Dr. Michael Carosel, attending physician and director of the cardiology department. In his wake, the steady and practiced steps of his chief resident, Dr. Andrea Nash, barely made a sound as she followed with ease. Behind her, the newest crop of residents and interns beginning their four-week rotation program worked hard to keep pace in what many nurses at the community hospital jokingly called "Carosel's Running of the Interns."

However, no one complained. Dr. Carosel was well-respected in the California medical community. A practitioner of medicine for over 20 years, he had served as the Director of Cardiology at Sun Valley for the past 11 years. In that time, he had managed to employ Andrea, one fellow, and two residents. The four were among the brightest talents in cardiology in the country.

Quick sighs of relief once the march

"Okay, everyone," Dr. Carosel began, "our patient of the day is named Simone, a 52-year-old female who was admitted two days ago after experiencing severe chest pain. This is not her first myocardial infarction (heart attack)," he continued. "She was

U.S. FOOD & DRUG ADMINISTRATION

FDA Drug Information Curriculum Case Study: Instructor's Guide

FDA Useful Drug Information for Clinicians: Practicing clinicians seek available information on a new drug before making a treatment decision

LEARNING OBJECTIVES

- Identify an online resource for FDA's drug review materials found at: www.fda.gov.
- Determine if a drug or biologic marketed in the U.S. has been discussed at an FDA advisory committee meeting.
- Gain an understanding of the FDA advisory committee's evaluation of a product's benefits and risks.
- Explain the characteristics of a new molecular entity (NME).
- Gain an understanding of risk evaluation and mitigation strategies (REMS) and their role.

TOPICS

FDA Drug Information Resources; Drugs@FDA; Risk Evaluation and Mitigation Strategy (REMS); FDA CardioBeat; FDA Drug Shortages Program

ASSUMPTIONS

This case study is based on the assumption that the target audience is undergraduate students or health professionals who are unfamiliar with FDA drug information resources.

SUGGESTED APPROACH

1. Preparing Students: Students are expected to read the case study prior to the training session.

2. Engaging Students: The training session should consist of a discussion of the case study.

3. Immersing Students: The training session should emphasize group discussion of the case study. Students should be encouraged to use their mobile devices to access the drug resources apps mentioned in the case study and navigate to the FDA websites referenced in class.

STUDENT ACTIVITIES

Before Class

Review the following websites:

1. Drugs@FDA
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

2. FDA Advisory Committee http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/default.htm

3. REMS@FDA
http://www.accessdata.fda.gov/scripts/cder/rems/index.cfm

4. Drug Shortages Program
http://www.fda.gov/Drugs/DrugSafety/DrugShortages/

Answer the following questions before class:

1. What is Drugs@FDA?

Answer: Drugs@FDA is a searchable database of drug product labels and approval-related documents, including reviews, approval letters, and current and archived labels.

2. True or False: Advisory Committee members are FDA employees.

Answer: **False**. Advisory committees are made up of outside experts that provide FDA with independent opinions and recommendations on applications to market new drugs and on FDA policies. The marketing applications they review include data about the safety and effectiveness of human drugs. The committees receive summary information about the drug applications and copies of FDA's review of the application documents. Based on this information, advisory

1

http://www.fda.gov/ForHealthProfessionals/LearningActivities/default.htm

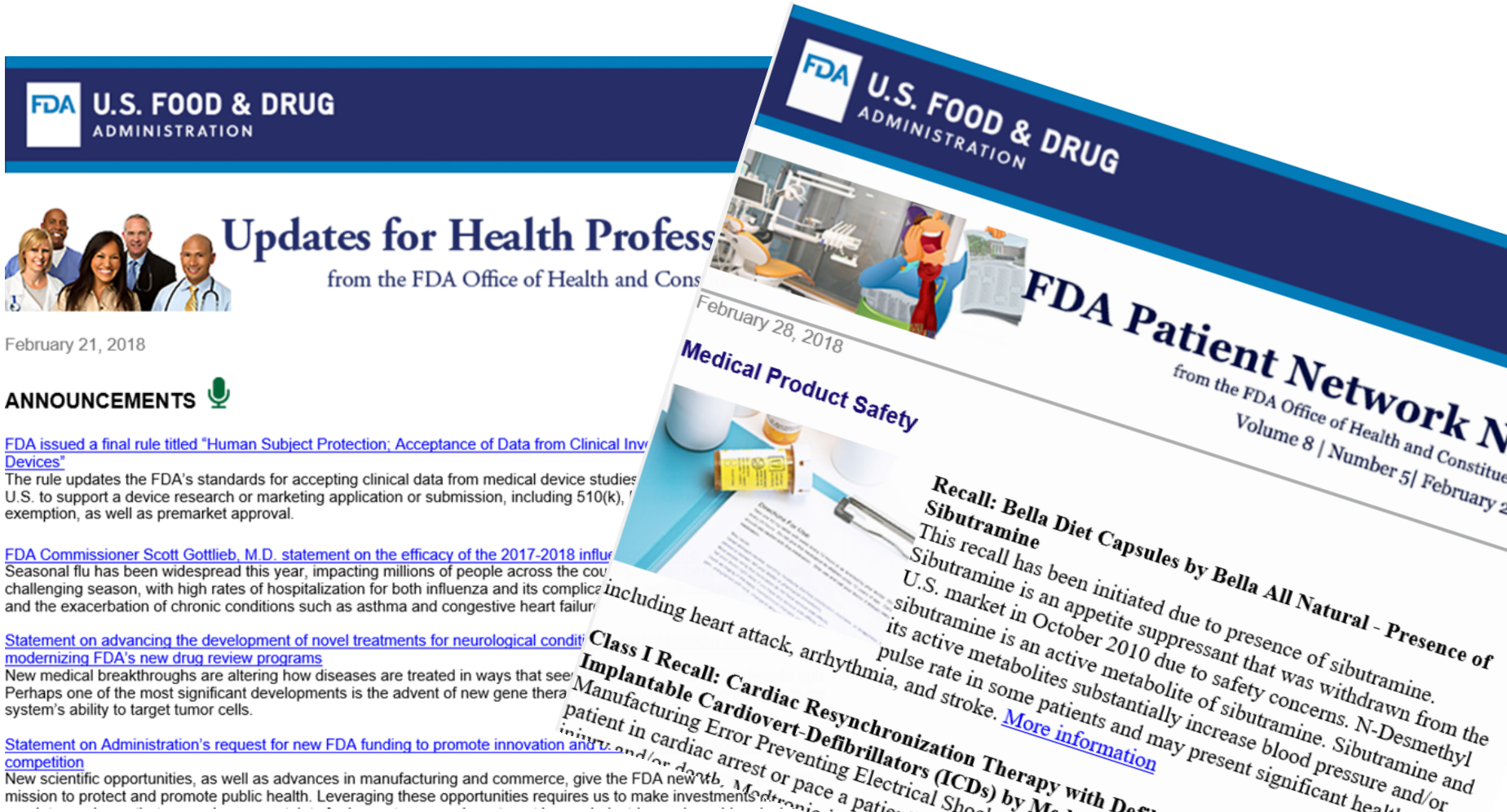
Information for Health Professionals

- Healthcare Professional Network
  - Bi-weekly Email Newsletter
  - MedWatch
  - Webinars and Education
  - Disease Specific Email Updates

Information for Patients

- FDA Patient Network
  - Bi-weekly Email Newsletter
  - Website
  - Webinars & In-person Meeting's
  - Disease Specific Email Updates
  - Twitter

FDA Health Professional and FDA Patient Network Newsletter

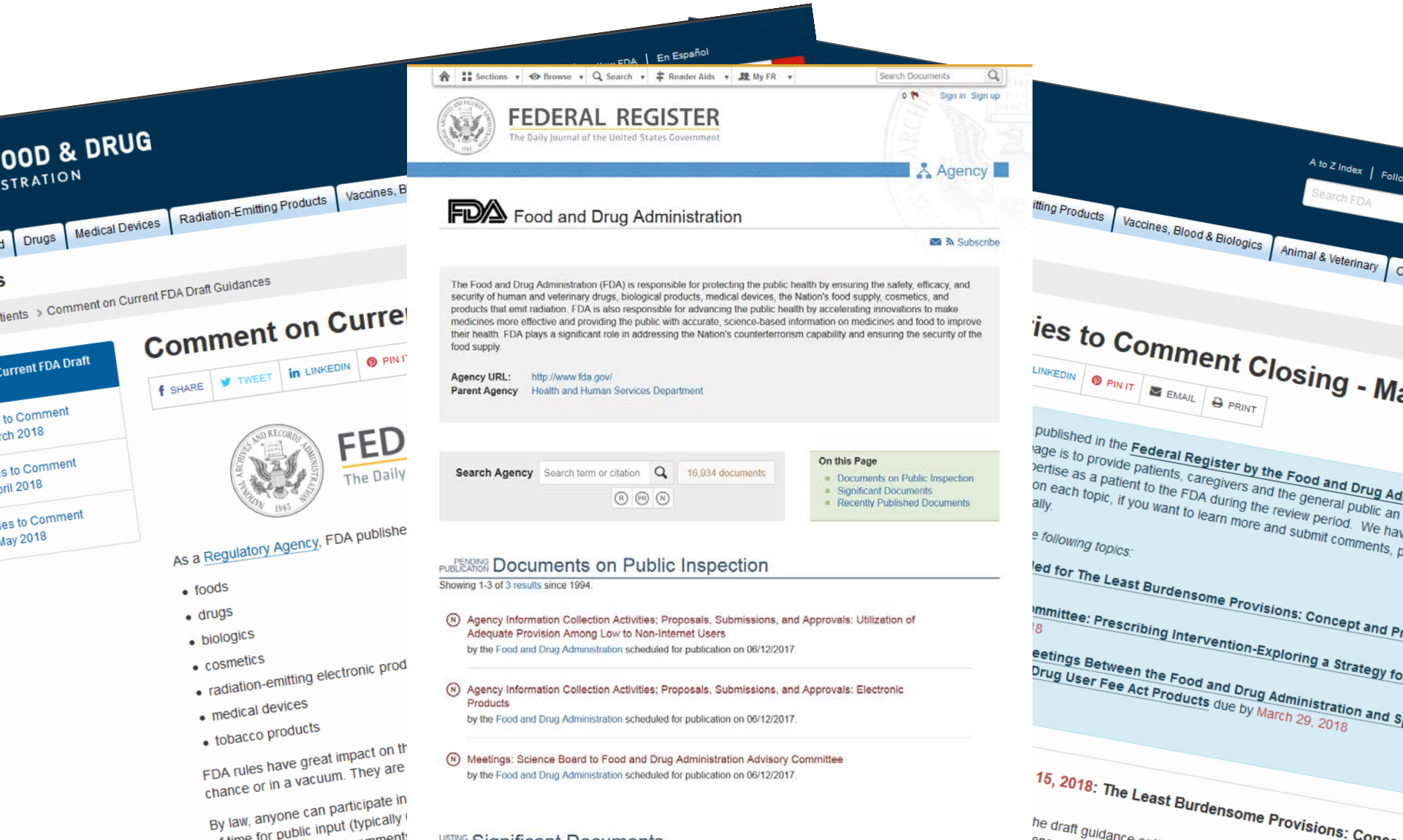


www.FDA.gov/ForPatients

FDA Patient Representative Program

- Began in 1990s
- Patients having an active role on FDA Advisory Committees and consultations with review divisions
- Patient voice represented in important discussions about regulatory decision-making
- Presence at the table
- 200 Patient Representatives, over 300 diseases/conditions

Submit Comments Through the Federal Register



Participate in an FDA Sponsored Public Meeting

Information for Health Professionals and Patients

Home > For Patients > Clinical Trials: What Patients Need to Know

Clinical Trials: What Patients Need to Know

SHARE | TWEET | LINKEDIN | PIN IT | EMAIL | PRINT

en español

Learn more about clinical trials and find a trial that might be right for you. Clinical trials are voluntary research studies conducted in people and designed to answer specific questions about the safety or effectiveness of drugs, vaccines, other therapies, or new ways of using existing treatments. It is important to remember that the FDA does not conduct Clinical Trials.

Clinical Trials: What Patients Need to Know
- What Patients Need to Know About Institutional Review Boards
- Glossary of Terms
- Clinical Research Versus Medical Treatment
- What Are the Different Types of Clinical Research?
- Informed Consent for Clinical Trials

Resources for You
- NIH Clinical Research Trials and You
- Good Clinical Practice
- Interactive Patient Education Tutorial On Clinical Trials
- Protecting America's Health Through Human Drugs
- Protection of Human Subjects of Research
- Get to Know ClinicalTrials.GOV (webinar)

Search for a Clinical Trial

Enter a word or phrase, such as the name of a medical condition or intervention.
Example: Cancer AND Los Angeles or expanded access AND compassionate use

Search

Learn More About Clinical Trials

- Clinical Research Versus Medical Treatment
  Understand the differences between clinical research and medical treatment and what those difference for you. Find answers to your questions about clinical trials, such as why they are done, who should c participating, and issues to consider before joining a trial.
- What are the Different Types of Clinical Research
  Understand the different types of research and the four clinical trial phases, such as their purpose and how many people participate in each of the phases.
- Informed Consent for Clinical Trials
  Understand what informed consent is and the questions you need to know before signing informed consent.
- Diversity in Clinical Trial Participation
  It is important to test drugs and medical products in the people they are meant to help. Learn about FDASIA 907 and how FDA works to make sure that people of different ages, races, ethnic groups, and genders are included in clinical trials.
- What is an Institutional Review Board
  Understand what Institutional Review Boards are, who is on them and who they protect.

Home > For Patients > Clinical Trials: What Patients Need to Know > Informed Consent for Clinical Trials

Informed Consent for Clinical Trials

Informed Consent for Clinical Trials

SHARE | TWEET | LINKEDIN | PIN IT | EMAIL | PRINT

en español

On this page you will find information on:

- What is Informed Consent
- Before enrolling in a clinical trial, the following information must be given to each potential research subject
- When Appropriate, one or more of the following elements of information must also be provided in the informed consent document
- A potential research subject must have an opportunity to
- Informed consent may not include language that

To many, the term *informed consent* is mistakenly viewed as the same as getting a research participant's signature on the consent form. FDA believes that obtaining research participant's verbal or written informed consent is only part of the process. Informed consent invo providing a potential participant with:

- adequate information to allow for an informed decision about participation in the clinical investigation.
- facilitating the potential participant's understanding of the information.
- an appropriate amount of time to ask questions and to discuss with family and friends the research protoc and whether you should participate.
- obtaining the potential participant's voluntary agreement to participate.
- continuing to provide information as the clinical investigation progresses or as the subject or situation requires.

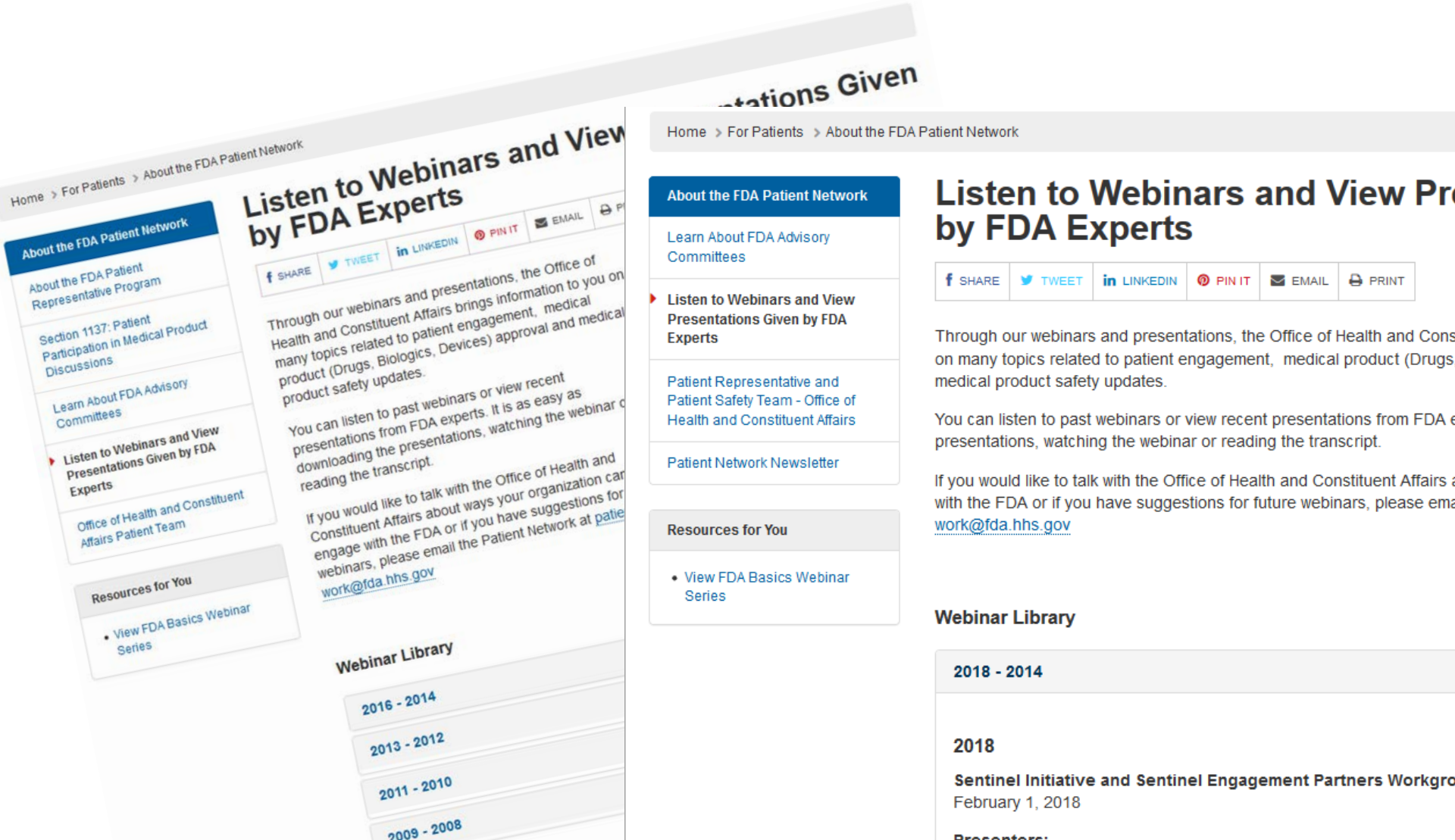
To be effective, the process must provide sufficient opportunity for the participant to consider whether to participate. (21 CFR 50.20.) FDA considers this to include allowing sufficient time for participants to consider the information and providing time and opportunity for the participant to ask questions and have those questions answered. The investigator (or other study staff who are conducting the informed consent interview) and the participant should exchange information and discuss the contents of the informed consent document. This process must occur under circumstances that minimize the possibility of coercion or undue influence. (21 CFR 50.20.)

What is Informed Consent?

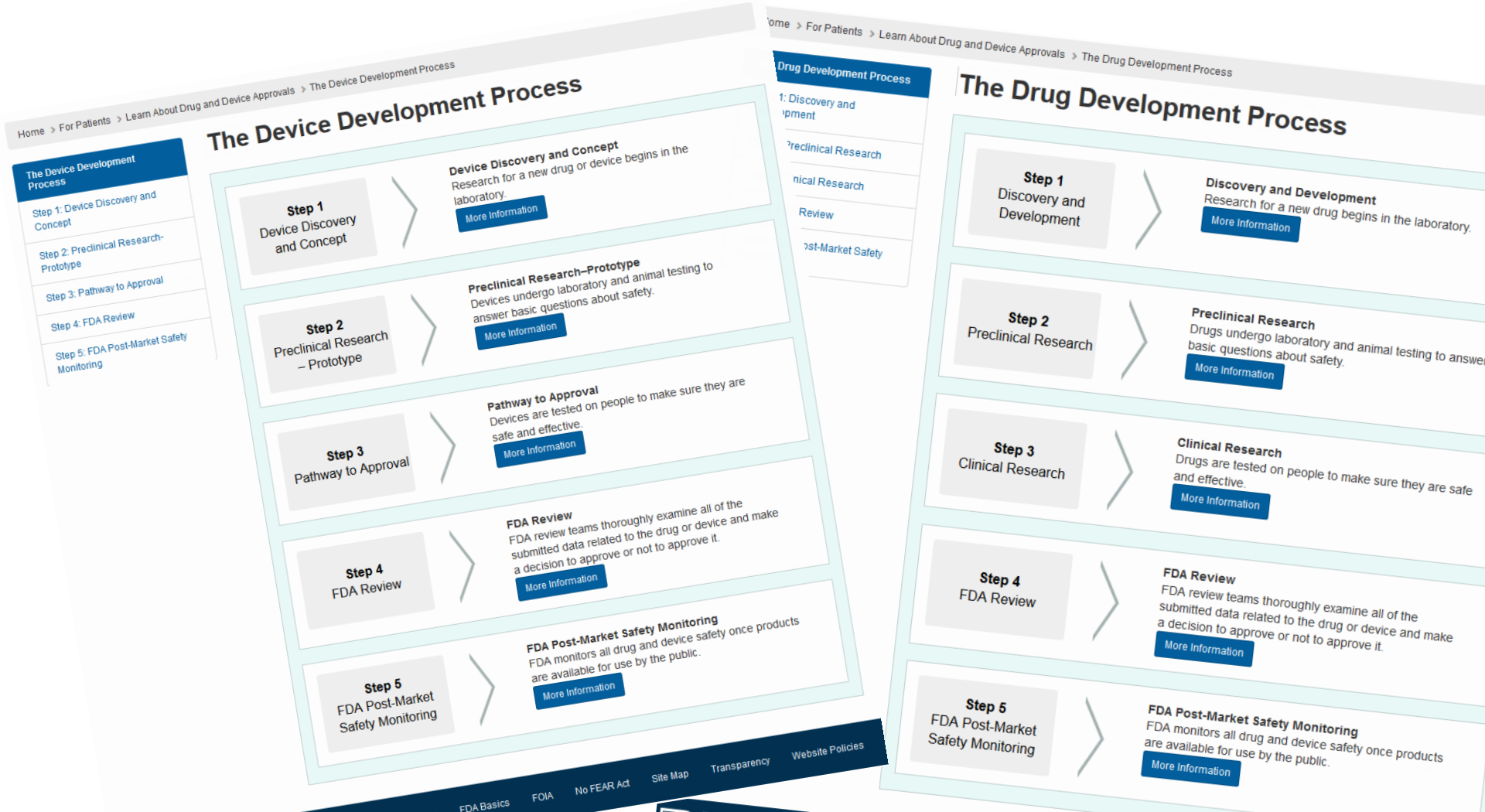
As new medical products are being developed, no one knows for sure how safe or effective they will find. Clinical trials are used to answer questions about the safety and effectiveness of

Information for Health Professionals and Patients

Watch Webinars Led by FDA Experts



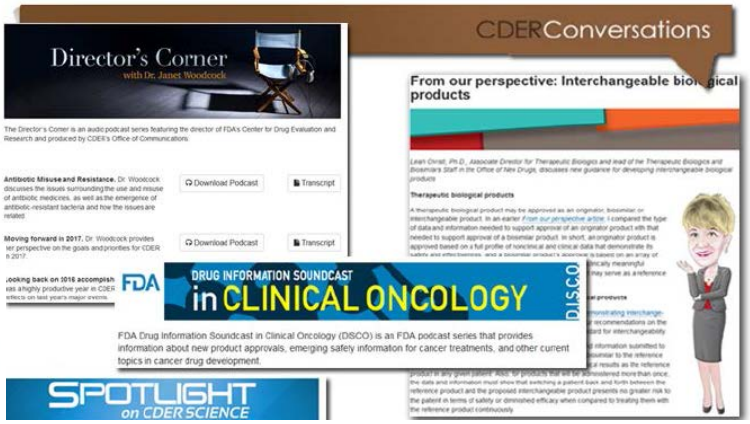
Learn How Medical Products are Developed and Approved



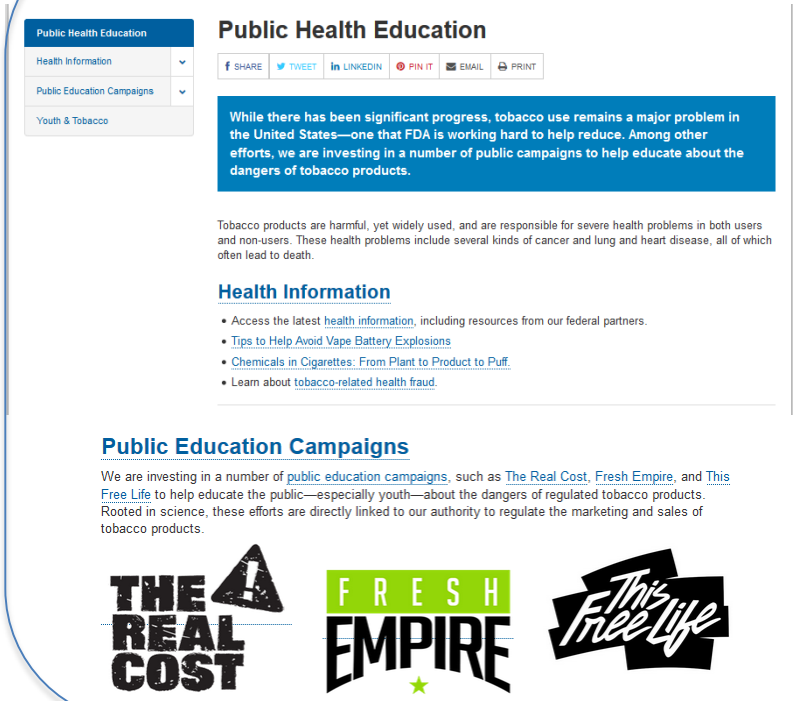
Disease Specific Email Updates

FDA Facebook and Twitter

Center for Drug Evaluation and Research



Center for Tobacco Products



Public Health Education

Health Information

Public Education Campaigns

Youth & Tobacco

Public Health Education

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT

While there has been significant progress, tobacco use remains a major problem in the United States—one that FDA is working hard to help reduce. Among other efforts, we are investing in a number of public campaigns to help educate about the dangers of tobacco products.

Tobacco products are harmful, yet widely used, and are responsible for severe health problems in both users and non-users. These health problems include several kinds of cancer and lung and heart disease, all of which often lead to death.

Health Information

- Access the latest health information, including resources from our federal partners.
- Tips to Help Avoid Vape Battery Explosions
- Chemicals in Cigarettes: From Plant to Product to Puff.
- Learn about tobacco-related health fraud.

Public Education Campaigns

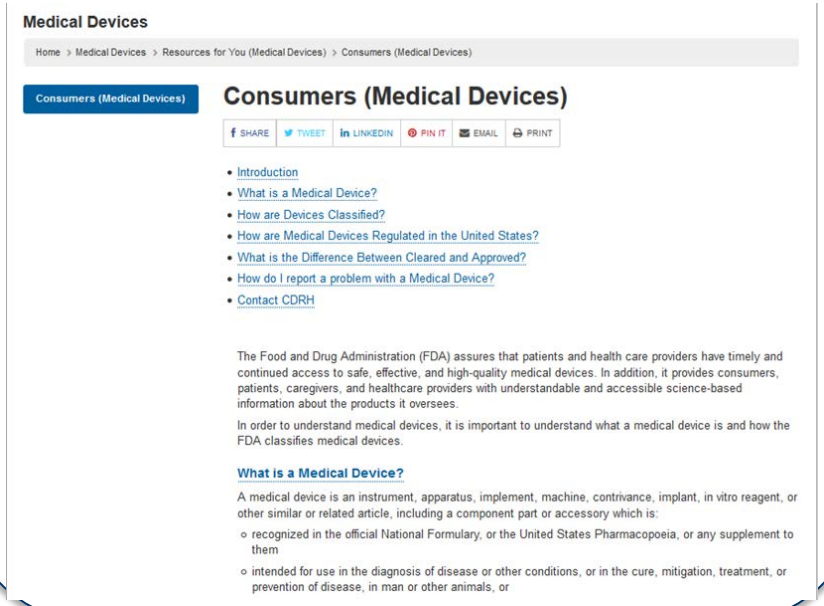
We are investing in a number of public education campaigns, such as The Real Cost, Fresh Empire, and This Free Life to help educate the public—especially youth—about the dangers of regulated tobacco products. Rooted in science, these efforts are directly linked to our authority to regulate the marketing and sales of tobacco products.

THE REAL COST

FRESH EMPIRE

This Free Life

Center for Devices and Radiological Health



Medical Devices

Home > Medical Devices > Resources for You (Medical Devices) > Consumers (Medical Devices)

Consumers (Medical Devices)

Consumers (Medical Devices)

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT

- Introduction
- What is a Medical Device?
- How are Devices Classified?
- How are Medical Devices Regulated in the United States?
- What is the Difference Between Cleared and Approved?
- How do I report a problem with a Medical Device?
- Contact CDRH

The Food and Drug Administration (FDA) assures that patients and health care providers have timely and continued access to safe, effective, and high-quality medical devices. In addition, it provides consumers, patients, caregivers, and healthcare providers with understandable and accessible science-based information about the products it oversees.

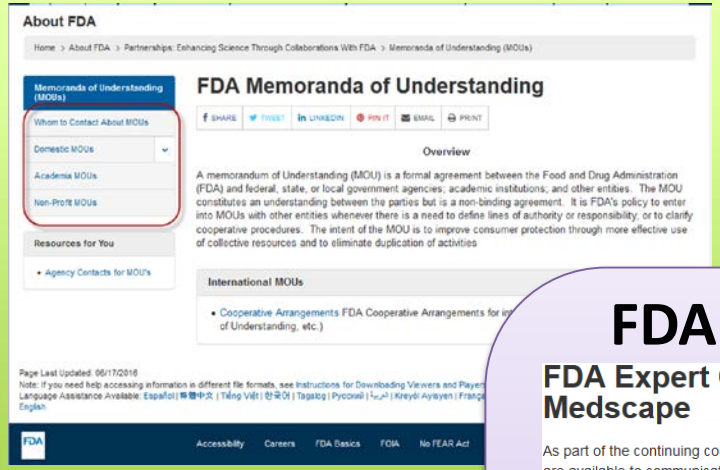
In order to understand medical devices, it is important to understand what a medical device is and how the FDA classifies medical devices.

What is a Medical Device?

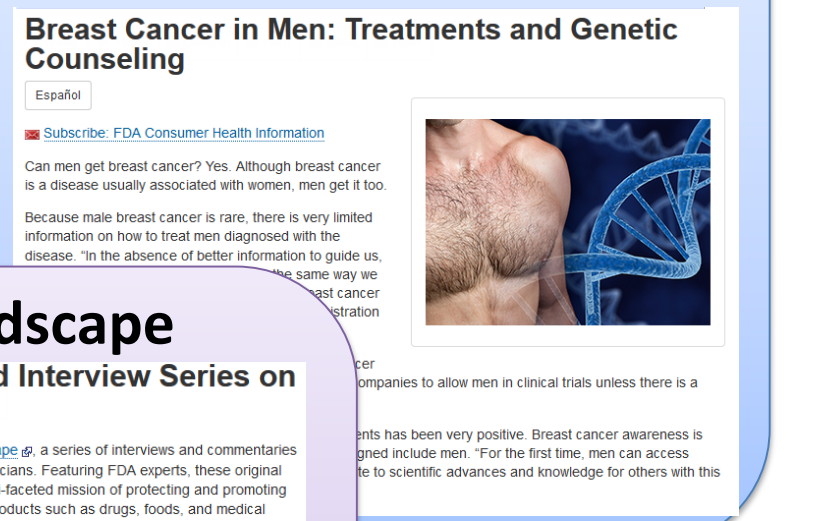
A medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part or accessory which is:

- recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them
- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or

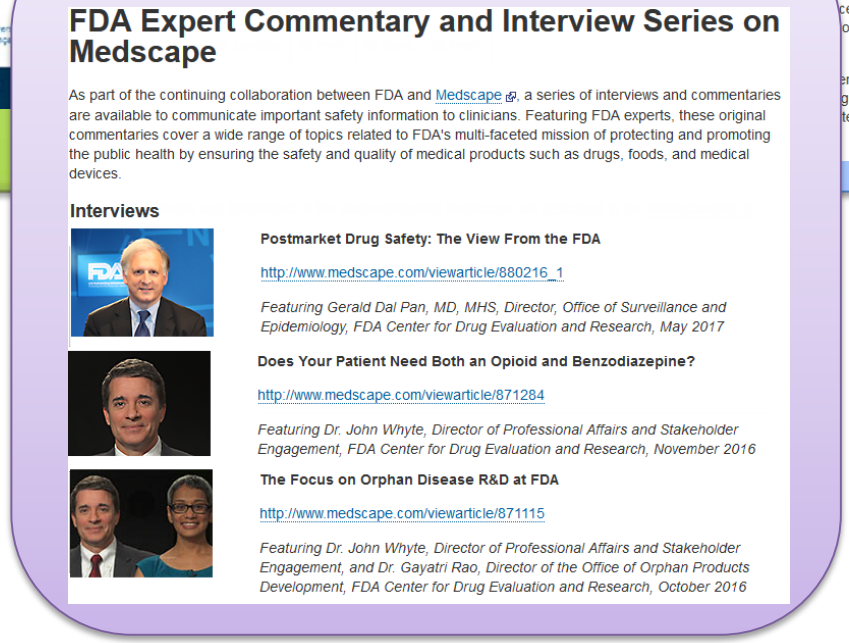
Memoranda of Understanding



FDA Consumer Updates



FDA and Medscape



Why is the Patient/Health Professional Voice Important?

- Provide insight on issues, problems, and/or questions that are important to patients and health professionals
- Both patients and health professionals have a vested interest in improving health
- Varied perspectives, both in terms of associated risk tolerance and perceived potential benefit
- The human element (judgment vs. empirical data)

What Value Might Be Added by Community Engagement?

- Faster recruitment and improved retention in trials
- Reducing the time for product development
- Cutting cost of drug development
- Help develop meaningful endpoints and measurements

- Medical products that better reflect outcome and quality of life measures most important to patients

Challenges to meaningful engagement

- **Understanding of trial design** (meaningful endpoints and data, measuring outcome, control arms)
- **Understanding the regulatory framework**, standards, and requirements (level of evidence)
- **Legal and practical limitations** facing sponsors (promotion v. education and engagement)
- **Division** within patient communities and healthcare professional organizations
- **Different objectives** or agendas among organizations
- **Disagreement** on meaningful measurement

Testing Your Knowledge!

What is FDA's Public Health Mission?

Ensure the _____, _____, and _____of human and animal drugs, biological products and medical devices

a. Safety, effectiveness and security
b. Accuracy, effectiveness, and purity
c. Timelines, reliability and security

Who can report adverse events to the MedWatch Program?

a. Healthcare professionals
b. Patients
c. Consumers
d. Industry/Pharmaceutical Companies
e. All of the above

How can MedWatch reports result in improved product safety?

a. By updating the product label.
b. Requiring a medication guide.
c. Requesting a product to be removed form the market.
d. a and b
e. All of the above

How can you be involved in the FDA decision making process?

a. Attend an FDA Advisory Committee meeting.
b. Attend a protest at the FDA.
c. Participate in webinars and workshops hosted by FDA experts.
d. a and c
e. All of the above

Which is *Not* Regulated by the FDA

a. Tamper-resistant packaging for over-the-counter (OTC) drugs
b. Child-proof packaging for OTC drugs
c. Plastic containers for soft drinks
d. Valentine heart box containing chocolates
e. Tube containing medical ointment

Thank you

steve.morin@fda.hhs.gov


FDA
U.S. FOOD & DRUG
ADMINISTRATION