



FDA's Adverse Event Surveillance Systems and MedWatch

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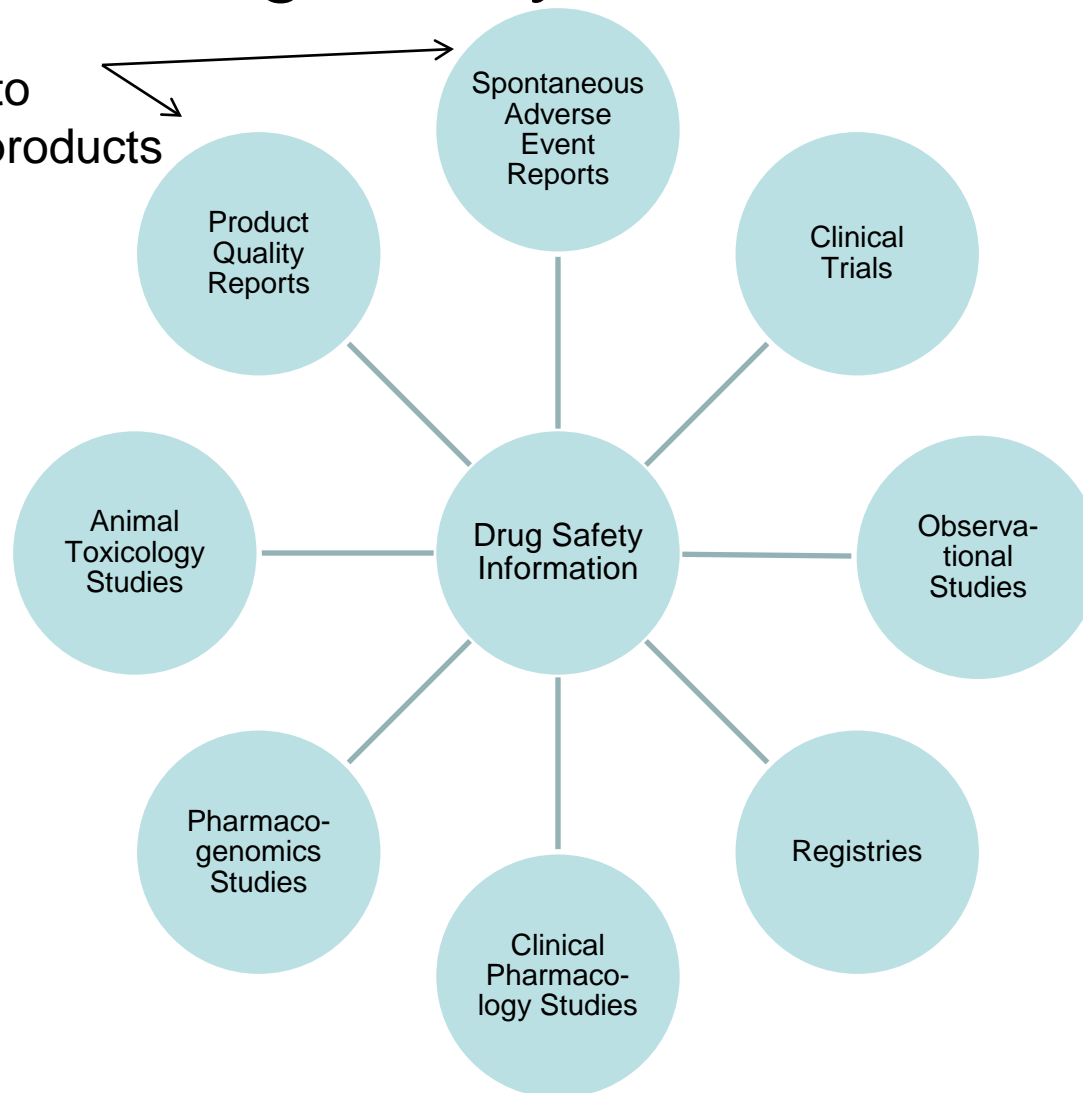
50-State Meeting
21 March 2014

Purpose of Postmarketing Safety Reporting

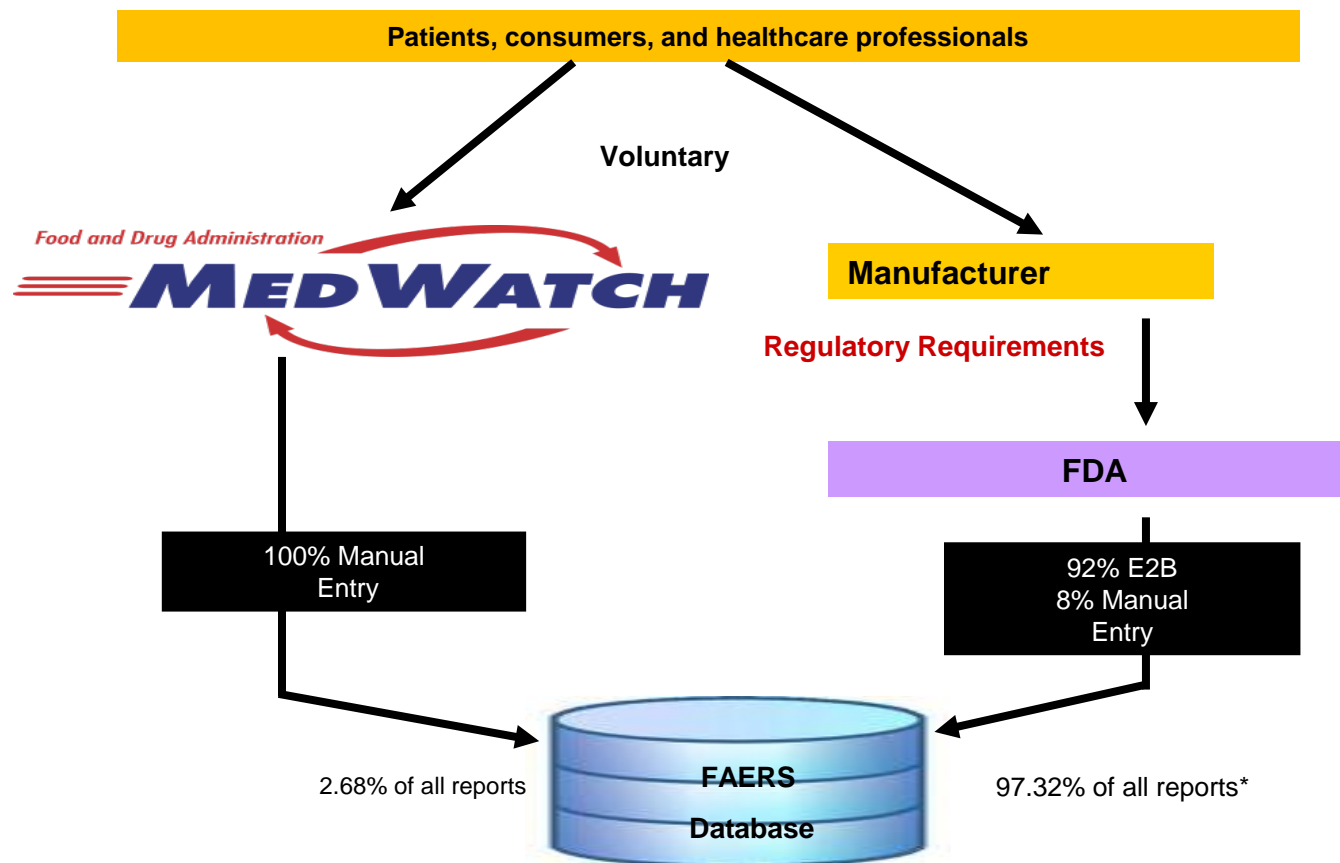
- To learn about new risks
- To learn more about known risks
- To learn about medication errors
- To learn how patterns of use may contribute to unsafe use
- To learn about product quality problems

Sources of Drug Safety Information

Most relevant to
compounded products



How Adverse Event Reports Get to FDA



*only includes 2013 up to 12/9/2013

Reporting Adverse Events to FDA

Industry ICH E2B electronic standard

MedWatch form 3500A

Public MedWatch 3500

MedWatch 3500B



ICH E2B Standard

- Internationally harmonized standard
- For use by industry
- About 90% of adverse event reports are through the ICH E2B standard
- May not be suitable for firms with low reports volumes
 - FDA is exploring alternative ways for manufacturers to submit reports electronically

Guidance for Industry

E2BM Data Elements for Transmission Of Individual Case Safety Reports

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)
April 2002

ICH
Revision 1

MedWatch Form 3500

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: 12/31/2011
See OMB statement on reverse.

Page 1 of _____

FDA USE ONLY

Trace unit sequence # _____

A. PATIENT INFORMATION

1. Patient Identifier # _____ 2. Age (Time of Event or Date of Birth) _____ 3. Sex Female Male _____ lb or _____ kg 4. Weight _____

B. ADVERSE EVENT, PRODUCT PROBLEM, OR ERROR

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: _____

E. SUSPECT MEDICAL DEVICE

1. Brand Name _____

2. Common Device Name _____

3. Manufacturer Name, City and State _____

4. Model # _____ Lot # _____ 5. Operator of Device Health Professional Lay User/Patient Other _____

Catalog # _____ Expiration Date (mm/dd/yyyy) _____

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 Professional? Yes No 3. Occupation _____

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 (1/09) Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

- MedWatch Form 3500
 - Designed for use by the public
 - Not consumer friendly
 - Best for healthcare professionals
- Four main elements
 - Patient
 - Product
 - Event
 - Reporter



MedWatch Form 3500A

Reset Form

Form Approved OMB No. 0910-0291, Expires 6/30/2016
See OMB statement on reverse.

U.S. Department of Health and Human Services
Food and Drug Administration
MEDWATCH
FORM FDA 3500A (2/13)

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

IR Report # _____
U/Importer Report # _____
FDA Use Only

Page 1 of _____

A. PATIENT INFORMATION			
1. Patient Identifier #	2. Age at Time of Event	3. Sex <input type="checkbox"/> Male <input type="checkbox"/> Female	4. Weight <input type="checkbox"/> lbs <input type="checkbox"/> kg
5. Date of Birth: _____			
6. Adverse Event or Product Problem			
1. Adverse Event <input type="checkbox"/> or Product Problem (e.g., defects/manufacture)			
2. Outcome Attributed to Adverse Event (Check all that apply)			
<input type="checkbox"/> Death (INDICATE) <input type="checkbox"/> Disability or Permanent Damage <input type="checkbox"/> Life-threatening <input type="checkbox"/> Congenital Anomaly/Birth Defect <input type="checkbox"/> Hospitalization - Initial or prolonged <input type="checkbox"/> Other Serious (Important Medical Events) <input type="checkbox"/> Required Intervention to Prevent Permanent Impairment/Damage (Device)			
3. Date of Event (mm/dd/yyyy)			
4. Date of This Report (mm/dd/yyyy)			
5. Describe Event or Problem			
(Continue on page 3)			
D. SUSPECT MEDICAL DEVICE			
1. Brand Name			
2. Common Device Name		2b. Procedure	
3. Manufacturer Name, City and State			
4. Model #	Lot #	5. Operator of Device	
6. Catalog #	Expiration Date (mm/dd/yyyy)	<input type="checkbox"/> Health Professional <input type="checkbox"/> Lay User/Patient	
7. Serial #	Unique Identifier (UDI) #	Other: _____	
8. If implanted, Give Date (mm/dd/yyyy)			
9. If Explained, Give Date (mm/dd/yyyy)			
10. In this a Single-use Device that was Reprocessed and Reused on a Patient?			
<input type="checkbox"/> Yes <input type="checkbox"/> No			
11. If Yes to Item No. 8, Enter Name and Address of Reprocessor			
12. Device Available for Evaluation? (Do not send to FDA)			
<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Returned to Manufacturer on: _____			
13. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)			
(Continue on page 3)			
E. INITIAL REPORTER			
1. Name and Address			
Phone # _____ Email Address _____			
(Continue on page 3)			
2. Health Professional? <input type="checkbox"/> Yes <input type="checkbox"/> No			
3. Occupation _____			
4. Initial Reporter Also Sent Report to FDA <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk.			

PLEASE TYPE OR USE BLACK INK

Reset Form

MEDWATCH FORM FDA 3500A (2/13) (continued)		Page 2 of _____	
I. EVENT BY USER FACILITY (INDICATE)			
1. Check One <input type="checkbox"/> User Facility <input type="checkbox"/> Importer		2. U/Importer Report Number	
3. User Facility or Importer Name/Address			
4. Contact Person		5. Phone Number	
6. Date User Facility or Importer Reported Awareness of Event (mm/dd/yyyy)		7. Type of Report <input type="checkbox"/> Initial <input type="checkbox"/> Follow-up	
8. Date of This Report (mm/dd/yyyy)		9. Date of Event (mm/dd/yyyy)	
10. Approximate Age of Onset		11. Event Problem Codes (Refer to coding manual)	
12. Report Sent to FDA? <input type="checkbox"/> Yes <input type="checkbox"/> No		13. Location Where Event Occurred <input type="checkbox"/> Hospital <input type="checkbox"/> Outpatient Diagnostic Facility <input type="checkbox"/> Home <input type="checkbox"/> Nursing Home <input type="checkbox"/> Ambulatory Surgical Facility <input type="checkbox"/> Other: _____	
14. Report Sent to Manufacturer? <input type="checkbox"/> Yes <input type="checkbox"/> No		15. Report Sent to Manufacturer on: _____	
16. Manufacturer Name/Address			
G. ALL MANUFACTURERS			
1. Contact (Other (not manufacturing site for device))		2. Phone Number	
Name _____			
Address _____			
Email Address _____			
3. Date Received by Manufacturer (mm/dd/yyyy)		4. U/IR Facility <input type="checkbox"/> Hospital <input type="checkbox"/> Outpatient Diagnostic Facility <input type="checkbox"/> Home <input type="checkbox"/> Nursing Home <input type="checkbox"/> Ambulatory Surgical Facility <input type="checkbox"/> Other: _____	
5. If Impl. Give Protocol #		6. If Explained, Give Date (mm/dd/yyyy)	
7. Type of Report <input type="checkbox"/> Initial <input type="checkbox"/> Follow-up		8. Adverse Event Terms	
9. Manufacturer Report Number		10. Adverse Event Terms	
<p>This section applies only to manufacturers of the Premises Regulation Act of 1986. The public reporting burden for this collection of information has been estimated to average 66 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: Washington Headquarters Office, Paperwork Reduction Project (0910-0291), Washington, DC 20543-4148.</p>			

Reset Form Delete Page

(CONTINUATION PAGE)
For use by user-facilities,
importers, distributors, and manufacturers
for MANDATORY reporting
Page 3 of _____

MEDWATCH FORM FDA 3500A (2/13) (continued)	
5.5. Describe Event or Problem (continued)	
5.6. Relevant Tests/Laboratory Data, Including Dates (continued)	
5.7. Other Relevant History, including Preexisting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.) (continued)	
Concomitant Medical Products and Therapy Dates (Exclude treatment of event) (For continuation of C. 10 and/or D. 11, please distinguish)	
Other Remarks	



MedWatch Form 3500A

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

MEDWATCH
FORM FDA 3500A (2/13)

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

Form Approved OMB No. 0910-0201 Expires 03/30/2016 See OMB statement on front.

Page 1 of 2

A. PATIENT INFORMATION

1. Patient Identifier (Last, First, Middle Initial, Sex, Weight)

2. Age at Time of Event (Date of Birth)

B. ADVERSE EVENT OR PROBLEM

1. Adverse Event (and/or Outcome) Attributed to Adverse Event (check all that apply)

2. Describe Event or Problem

C. SUSPECT PRODUCT(S)

1. Name (give active strength & reference)

D. USER FACILITY (IF APPLICABLE)

1. User Facility or Importer Name/Address

E. Suspect Product

1. Report sent to FDA? (Yes/No)

2. Report sent to manufacturer? (Yes/No)

3. Manufacturer Name/Address

F. ALL MANUFACTURERS

1. Contact Office (and Manufacturing Site) Name, Address, Email Address

2. Date Received by Manufacturer

3. FDA OIG Protocol #

4. Type of Report (check all that apply)

5. Manufacturer report number

G. Relevant Test/Laboratory Data, including Dates

H. Other Relevant History, including Preexisting Medical Conditions

I. Concomitant Medical Products and Therapy Dates

J. Other Remarks

Submission of a report does not personnel, user facility, importer caused or contributed to the event

This section applies only to reporters in the public reporting burden for this collection of information, including the time for reviewing instructions, gathering and maintaining the data needed to complete the collection of information, sending comments regarding the collection of information, including suggestions for improving the collection of information.

- Designed for use by industry
- Lots of fields not present on other MedWatch forms
- Some fields are exclusively for devices



Consumer MedWatch Form

<p>DEPARTMENT OF HEALTH AND HUMAN SERVICES Food and Drug Administration</p> <p>MEDWATCH Consumer Voluntary Reporting (FORM FDA 3500B)</p>	<p>Form Approved: OMB No. 0910-0291 Expiration Date: 6/30/2015 (See PRA Statement on preceding general information page.)</p>

Section A – About the Problem	
<p>What kind of problem was it? (Check all that apply)</p> <p><input type="checkbox"/> Were hurt or had a bad side effect (including new or worsening symptoms)</p> <p><input type="checkbox"/> Used a product incorrectly which could have or led to a problem</p> <p><input type="checkbox"/> Noticed a problem with the quality of the product</p> <p><input type="checkbox"/> Had problems after switching from one product maker to another maker</p>	<p>Did any of the following happen? (Check all that apply)</p> <p><input type="checkbox"/> Hospitalization – admitted or stayed longer</p> <p><input type="checkbox"/> Required help to prevent permanent harm (for medical devices only)</p> <p><input type="checkbox"/> Disability or health problem</p> <p><input type="checkbox"/> Birth defect</p> <p><input type="checkbox"/> Life-threatening</p> <p><input type="checkbox"/> Death (include date): _____</p> <p><input type="checkbox"/> Other serious/important medical incident (Please describe below)</p> <p>_____</p> <p>_____</p>
<p>Date the problem occurred (mm/dd/yyyy)</p> <p>_____</p>	
<p>Tell us what happened and how it happened. (Include as many details as possible)</p> <p>_____</p> <p>_____</p> <p style="text-align: right;">Continue to Page</p>	
<p>List any relevant tests or laboratory data if you know them. (Include dates)</p> <p>_____</p> <p>_____</p> <p style="text-align: right;">Continue to Page</p>	
<p>For a problem with a product, including</p> <ul style="list-style-type: none"> prescription or over-the-counter medicine biologics, such as human cells and tissues used for transplantation (for example, tendons, ligaments, and bone) and gene therapies nutrition products, such as vitamins and minerals, herbal remedies, infant formulas, and medical foods cosmetics or make-up products foods (including beverages and ingredients added to foods) <p style="text-align: right;"> Go to Section B</p>	
<p>For a problem with a medical device, including</p> <ul style="list-style-type: none"> 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 <p style="text-align: right;"> Go to Section C (Skip Section B)</p>	

- MedWatch Form 3500B
- Introduced mid-2013
- User-friendly format for non-health care professionals
- Includes 4 minimum elements
 - Patient
 - Product
 - Event
 - Reporter
- Captures other information included on the 3500, but asks for it in a more consumer-friendly way.

Updating the MedWatch Forms

- MedWatch form has expiration dates
 - Require periodic renewal
- FDA staff determine if and how the MedWatch form needs to be changed
 - Program needs drive the changes
- Changes require extensive review

ilities,
manufacturers
porting

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Form Approved: OMB No. 0910-0291, Expires: 6/30/2015
See OMB statement on reverse.

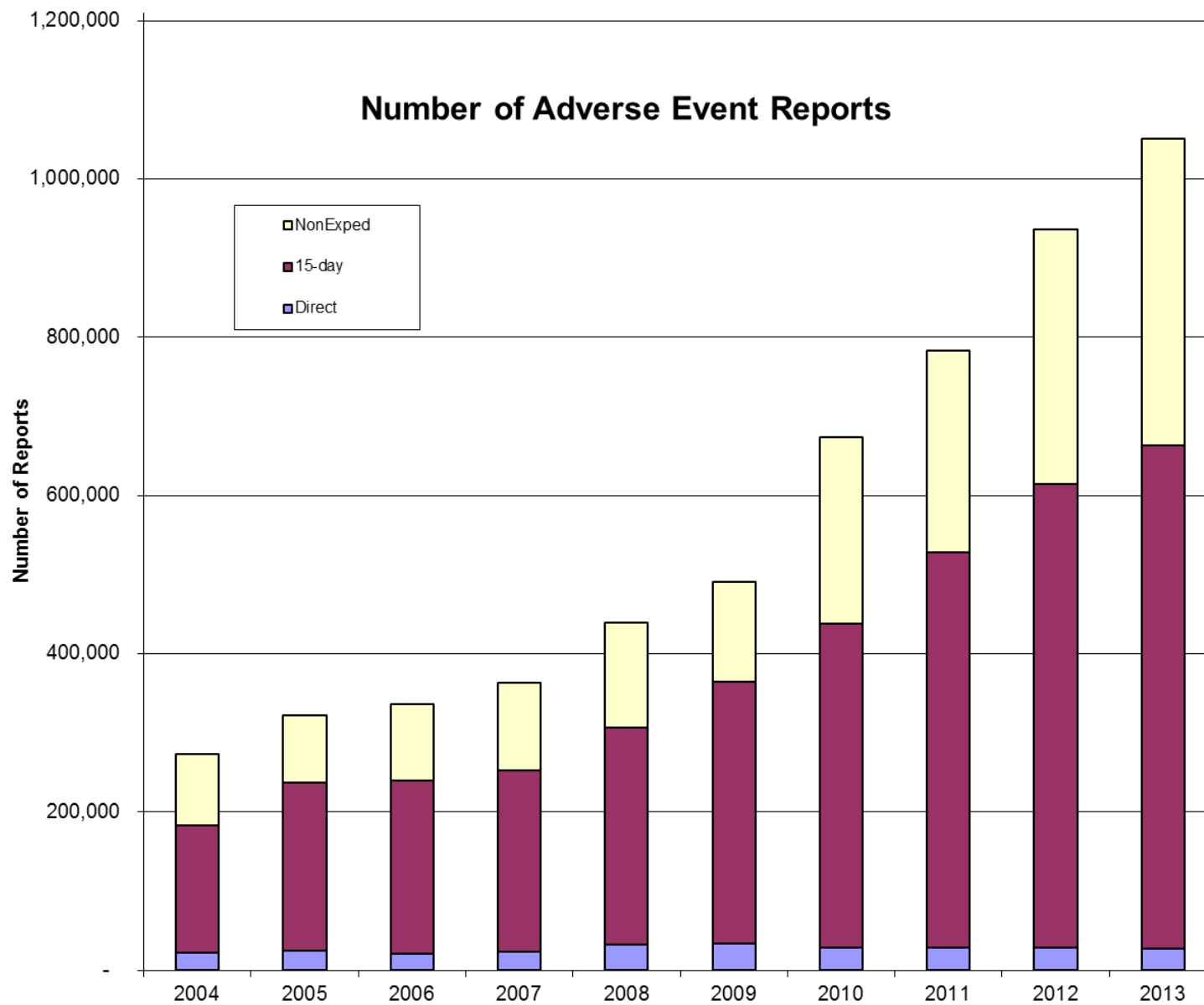
Mfr Report #	
UF/Importer Report #	
FDA Use Only	

Qualities of a Good Case Report

- What makes a good case report?
 - Description of the event
 - Suspected product(s) and concomitant treatment details
 - Patient characteristics, medical history, treatment history
 - Documentation of the diagnosis
 - Clinical course and outcomes
 - Treatment and lab values at baseline, during therapy, and after therapy
 - Response to dechallenge and rechallenge
 - Any other relevant information
- This takes time

FDA Adverse Event Reporting System (FAERS)

- Computerized database
 - Informatic structure adheres to ICH standards
- Contains human drug and therapeutic biologic reports
- Adverse events, medication errors, and indications are coded to terms in Medical Dictionary for Regulatory Activities (MedDRA)
- Products are coded using the FAERS Product Dictionary
- Public extract is released quarterly





Adverse Event Data are Incorporated into Product Labels

Table. Results From Quarterly Reports From January 2008 to December 2010

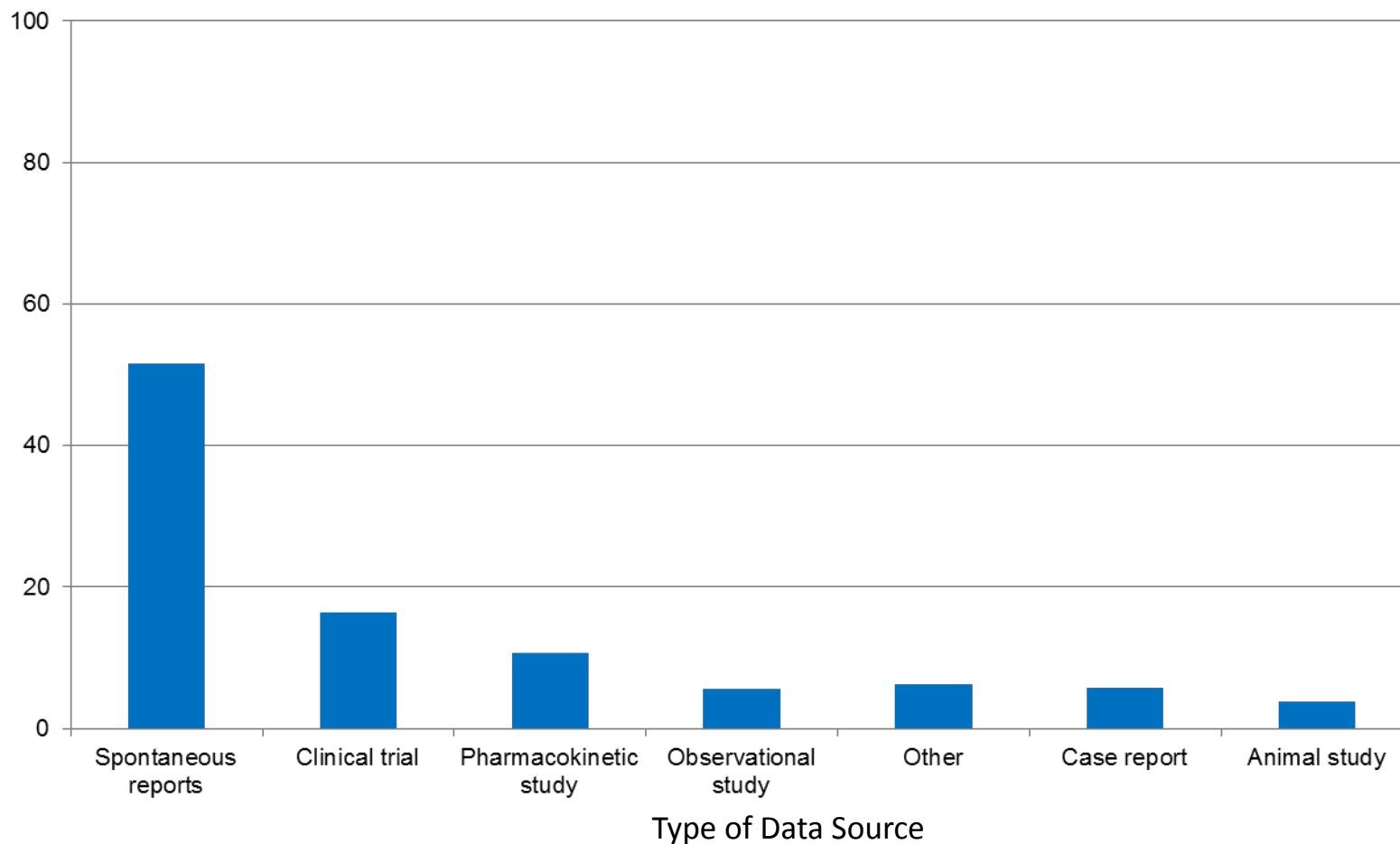
Result	Quarterly Reports, Year, No. (%)			Total
	2008	2009	2010	
Potential safety signals, No.	60	45	48	153
Label changes	30 (50)	28 (62)	16 (33)	74 (48)^b
Subgroups ^a				
Warnings and Precautions	16 (53)	19 (68)	11 (69)	46 (62)
Adverse Reactions	11 (37)	5 (18)	7 (44)	23 (31)
Drug Interactions	2 (7)	1 (4)	0	3 (4)
Dosage and Administration	1 (3)	1 (4)	0	2 (3)
Boxed Warning	6 (20)	2 (7)	1 (6)	9 (12)
Contraindications	0	1 (4)	1 (6)	2 (2)
Use in Specific Populations	0	0	1 (6)	1 (1)
REMS	2 (7)	2 (7)	0	4 (5)
Withdrawn from market	0	0	1 (6)	1 (1)

Abbreviation: REMS, Risk Evaluation Mitigation Strategy.

^aCalculated from the number of actual label changes.

^bThe calculated 48% total label changes includes the 1 drug withdrawn from the market and those drugs with newly implemented REMS.

Percentage of safety-related label changes in the United States by data source - 2010



Public Data Extracts – What data are released?

- ~200,000 reports each quarter
- Over 50 data elements as reported from each case in the following area's:

Key Areas	Type of data
Demographics	E.g. age, weight
Drug characteristics	E.g. drug name, dose, strength
Indication	MedDRA code of the indication for which the patient was treated
Outcome	E.g. hospitalization, death, life threatening
Reaction	MedDRA code for the drug reaction
Report Sources file	Health Professional, Study, Literature, Consumer etc.
Therapy Dates	E.g. start and end of drug therapy

Public Data Extract – What data are not released?

- Personal Identifiable Information (PII)
 - Data should not make it possible to identify individual patients
- “Narrative” - As it may contain, names, initials, phone number or other personal identifying information (PII)
 - “Narrative” is where the reporter describes the drug reaction in their own words
- Patient’s address or the state
 - We do release the country the event occurred or reported in
- Death date
- Dates like the onset date and the drug therapy dates are released but not dates like reaction dates which may, in some cases, imply a death date

Data Element - State

- 3 data elements related to state
 - **Reporter State**
 - Captured if reported by the reporter
 - **Sender Organization State** (Mfr.'s regulatory group send the AE)
 - Captured as part of the mandatory AE report
 - **Product Manufacturer State** (where product manufactured)
 - Only in reports submitted by industry
 - None of the state information is released as part of Public Data Extract

Compounded Product in FAERS

- Central Triage Unit identifies compounded products only from direct reports
 - “Compounded” is captured in the database
- Compounded products are coded to its active ingredient(s)
 - Discern from the report or by searching the web
 - No unique prefix or suffix identifying the ingredient as compounded
- “Compounded” identifier can be used as a search parameter



Questions?