FDA's Adverse Event Surveillance Systems and MedWatch

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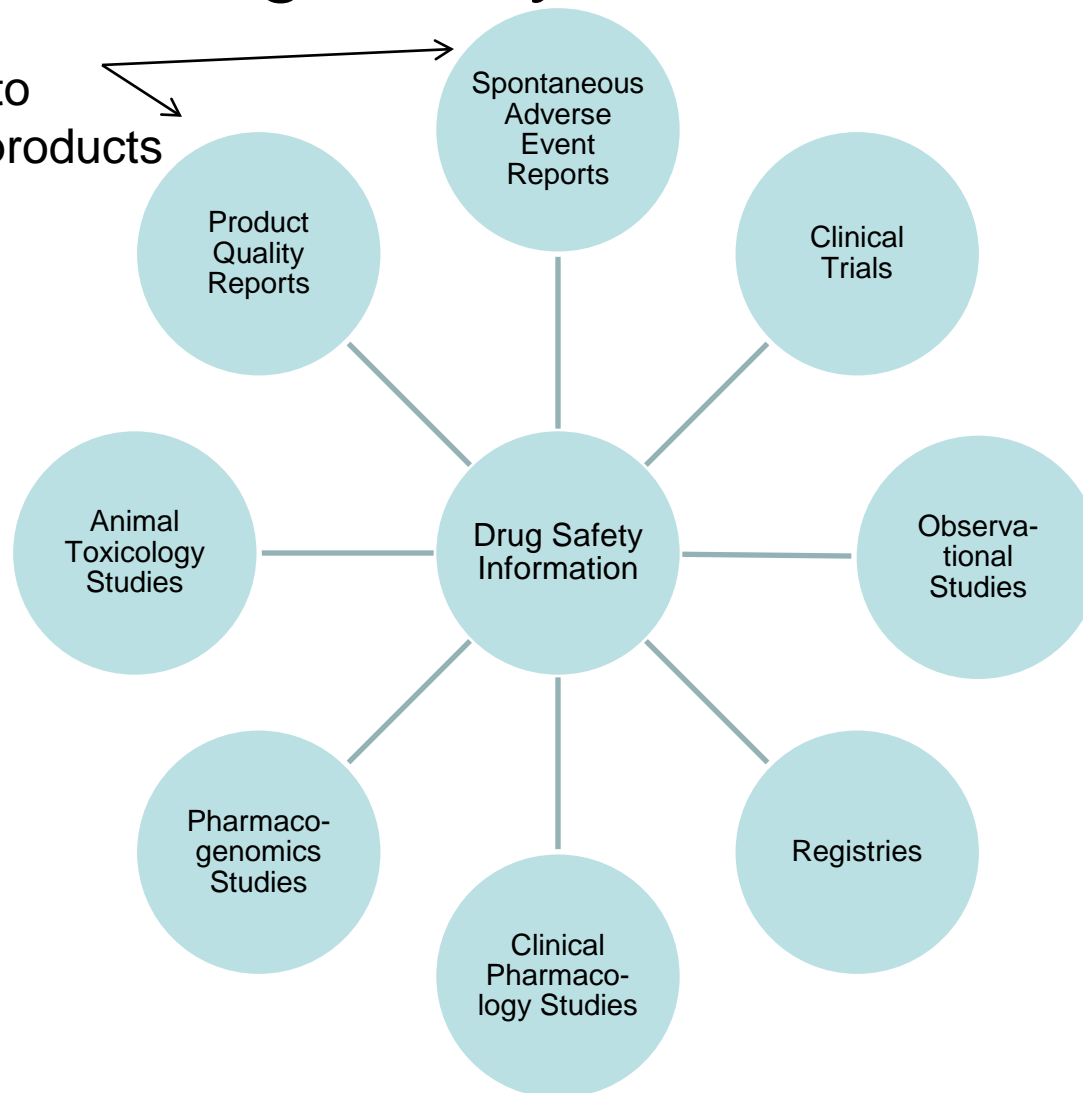
50-State Meeting

21 March 2014

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Purpose of Postmarketing Safety Reporting
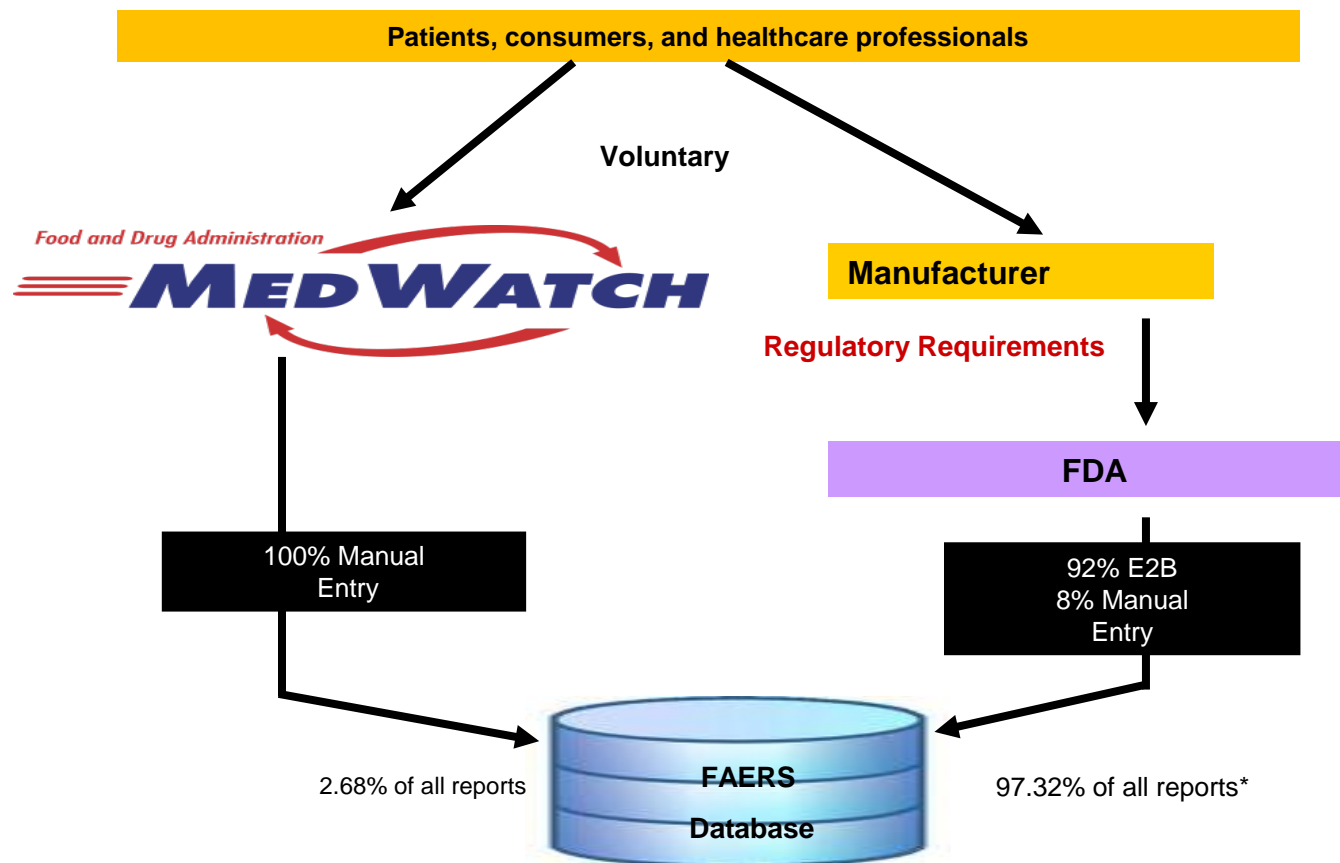
To learn about new risks

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

Spontaneous Adverse Event Reports

Product Quality Reports

Clinical Trials

Animal Toxicology Studies

Drug Safety Information

Observational Studies

Pharmaco-genomics Studies

Clinical Pharmaco-logy Studies

Registries

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

- 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

MedWatch Form 3500A

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

Consumer MedWatch Form

- 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

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

lities,
manufacturers
porting

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

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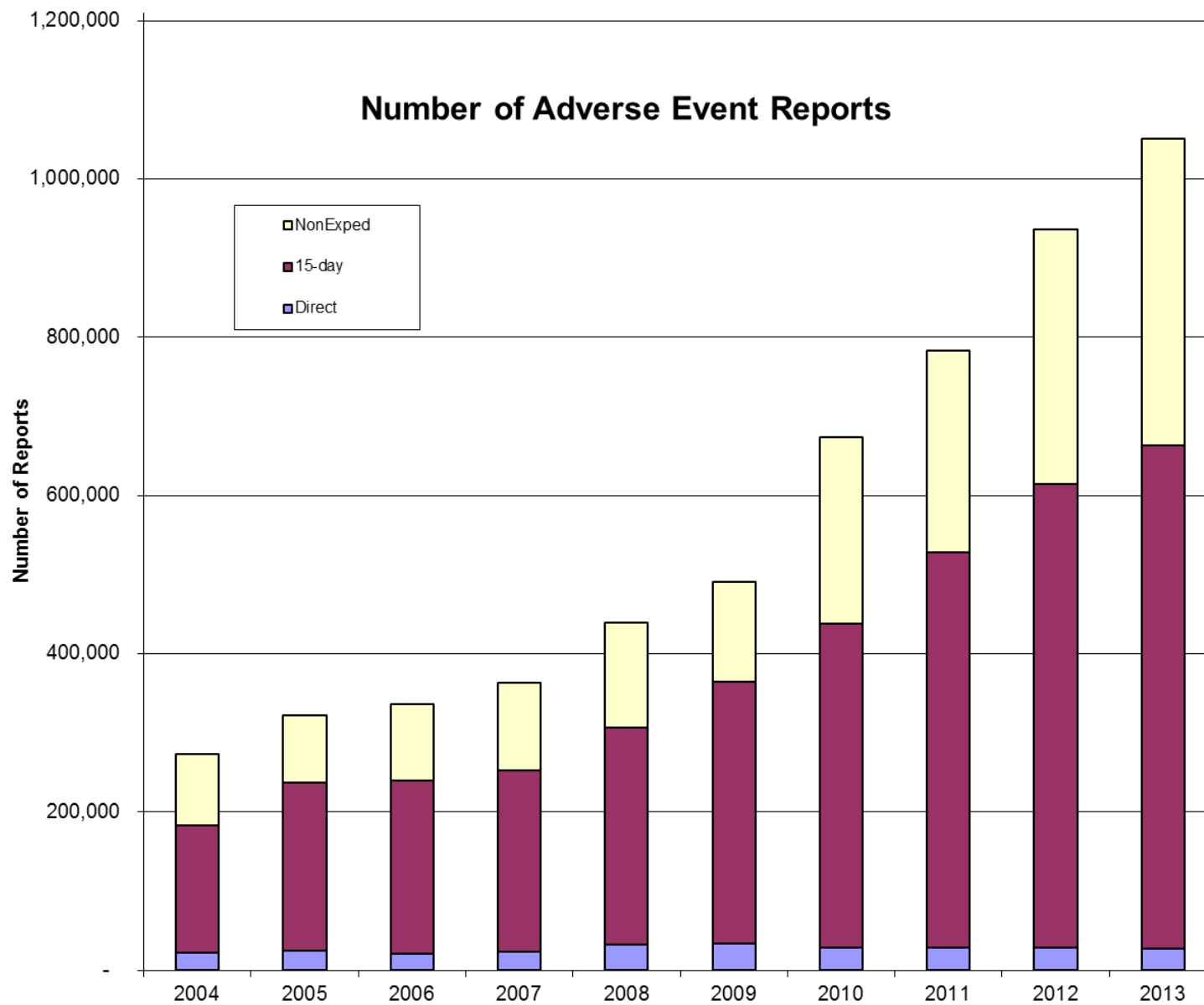
Adverse Event Data are Incorporated into Product Labels

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.
[a] Calculated from the number of actual label changes.
[b] The calculated 48% total label changes includes the 1 drug withdrawn from the market and those drugs with newly implemented REMS.

Powers, A. et al. Arch Intern Med 2012;172:72-73.

ARCHIVES OF INTERNAL MEDICINE

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

Type of Data Source
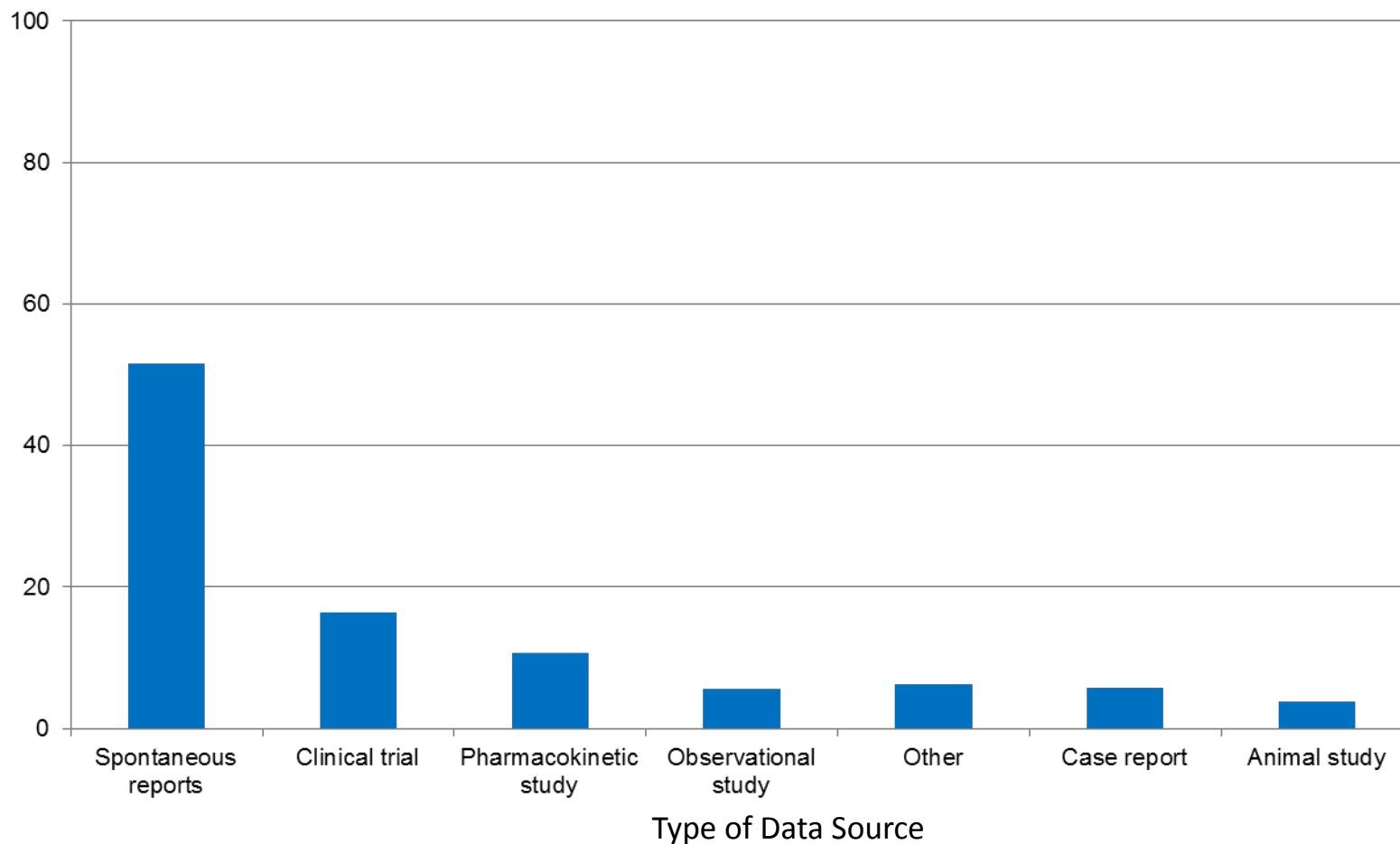
Public Data Extracts – What data are released?

- ~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 –
<u>What data are not released?</u>

- 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

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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

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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?