



Post-marketing Drug Safety Surveillance: Pharmacovigilance in FDA/CDER

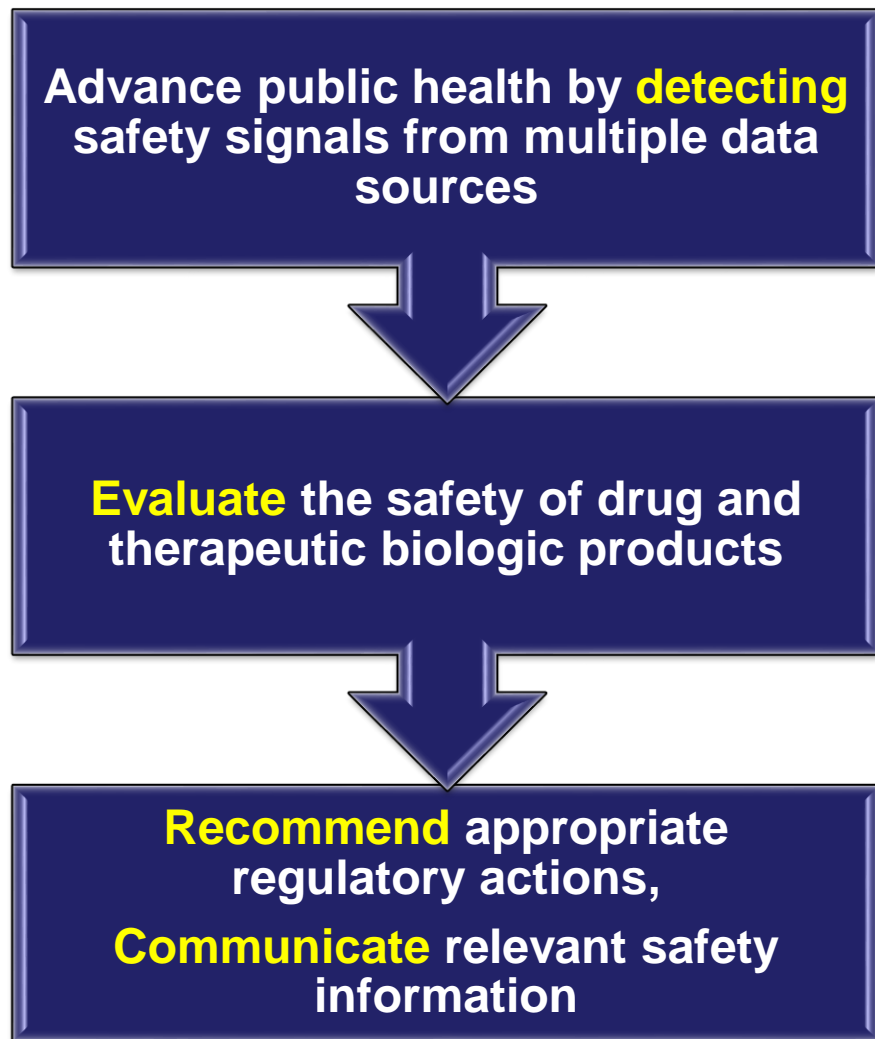
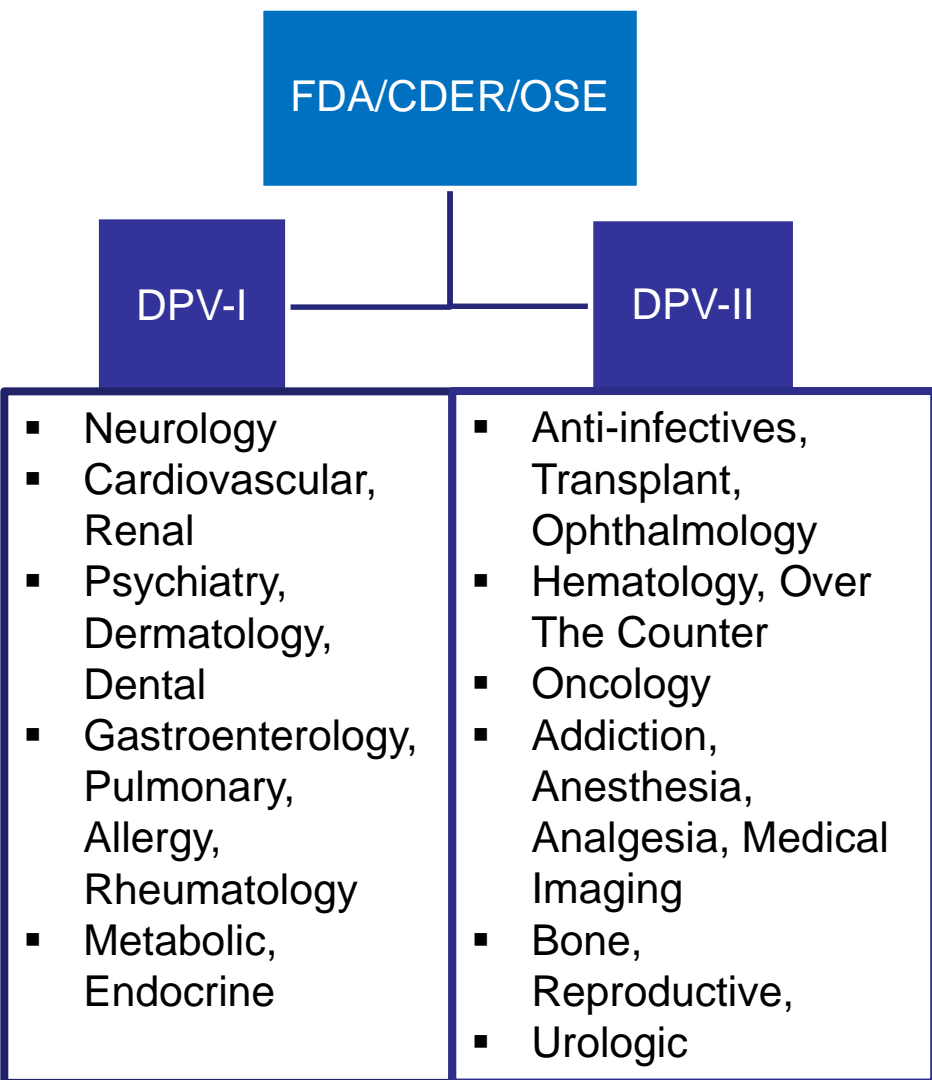
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The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect FDA policy and should not be attributed to or considered binding on the U.S. Food and Drug Administration (FDA).

Divisions of Pharmacovigilance (DPV) Overview





Sources of Possible Safety Signals

- Routine Pharmacovigilance
 - FDA Adverse Event Reporting System (FAERS) containing Individual Case Safety Reports (ICSRs)
 - Hands-on review of ICSRs
 - Data mining
- Manufacturers' Periodic Safety Update Reports
- Study results
- Medical literature
- Media
- New Drug Application (NDA) safety database
- Outside inquiry
- Foreign Regulatory Agencies
- Others

MEDWATCH
The FDA Safety Information and Adverse Event Reporting Program

Form Approved OMB No. 0918-0041 Expires 12/31/2011 See OMB statement on device

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

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A. PATIENT INFORMATION

1. Patient Identifier (Required for all reports) (Do not send to FDA)

2. Adverse Event, Product Problem or Error

3. Date of Event (mm/dd/yyyy) 4. Date of this Report (mm/dd/yyyy)

5. Describe Event, Problem or Product Use Error

6. Suspect Medical Device

7. Other Relevant History, including Preexisting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, investigational products, etc.)

8. Suspect Product(s)

9. Reporter (See confidentiality section on back)

10. Also Reported to:

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

Uninterpretable vs Interpretable ICSR

- Male
- Sotalol on 2/11
- QT prolongation, ?
Date
- Reported by patient's
wife
- Male, 59, diabetes, hypertension, hyperlipidemia, normal echo and baseline QTc 420 ms. On simvastatin, insulin.
- Metoprolol → Sotalol 2/11 (HTN, new AF)
- “Blacked out” on 3/17
- ER evaluation:
 - BP 130/82, HR 52, “both lower than usual”
 - Dehydration
 - Creatinine 2.5
 - QT markedly prolonged 520 ms
 - ECG non-sustained polymorphic VT
- Treatment: hydration, discontinuation of Sotalol, resolved QT and non-sustained VT



What Information Does Good Quality ICSRs Contain for Adequate Assessment of Safety Signals?

- Description of adverse event
- Suspected and concomitant product therapy details (e.g., dose, dates of therapy)
- Patient characteristics (e.g., age, sex), baseline medical condition, co-morbid condition, family history, other risk factors
- Documentation of the diagnosis
- Clinical course and outcomes
- Relevant therapeutic measures and laboratory data
- **Dechallenge and rechallenge information**
- Reporter contact information
- Any other relevant information

Guidance for Industry - Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment, March 2005

The image shows a screenshot of the FDA MedWatch Consumer Voluntary Reporting form (FD-3500B). The form is titled "MEDWATCH Consumer Voluntary Reporting (FORM FDA 3500B)". It includes sections for "About the Problem" and "Product Information". The "About the Problem" section asks for details about the adverse event, including whether it was a new health problem, if it was a problem with a product, and if it was a problem with a medical device. The "Product Information" section asks for details about the product, including the name, strength, and manufacturer. The form also includes a section for "Reporter Information" and a section for "Comments".



The FAERS Database

More Useful For

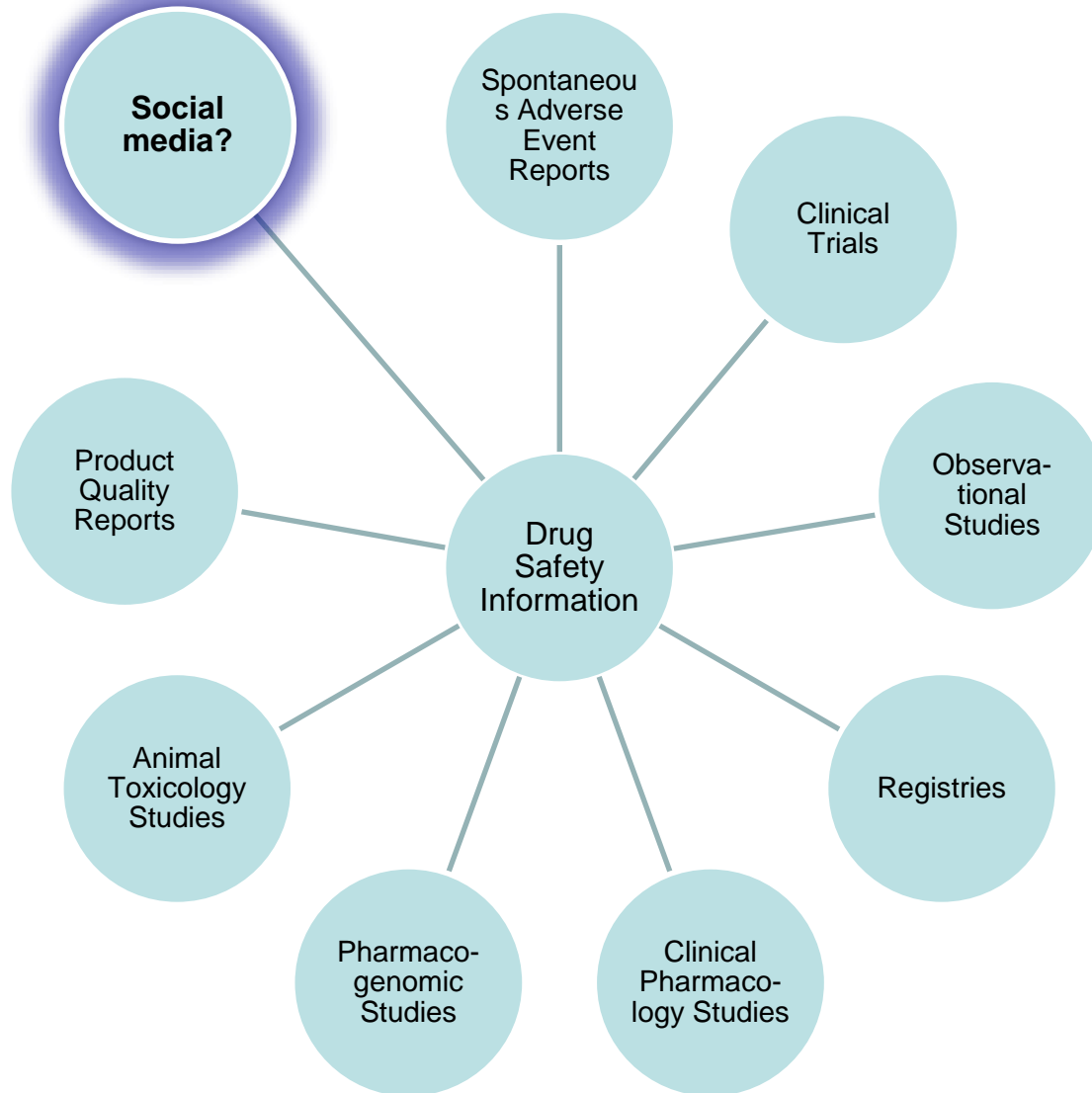
- Detecting Adverse Events
 - That are serious and unlabeled
 - With low or rare background rate
- Identifying
 - Potential risk factors
 - Trends or clinically significant emerging safety concerns

Less Useful For

- Detecting Adverse Events
 - Related to worsening of pre-existing disease
 - Related to disease manifestations for which drug is indicated for
 - Events with long latency



Sources of Drug Safety Information





What FDA Has Said On Reporting From Internet Sources

March 2001 Draft Guidance on Postmarketing Reporting:

*“Adverse experience information that is submitted to an applicant via the Internet (e.g., e-mail) **should be reported to the FDA if the applicant has knowledge of the four basic elements for an individual case safety report.** Applicants should review any Internet sites sponsored by them for adverse experience information, but are not responsible for reviewing any Internet sites that are not sponsored by them. However, if an applicant becomes aware of an adverse experience on an Internet site that it does not sponsor, the applicant should review the adverse experience and determine if it should be reported to the FDA.”*



How Does FDA Handle Adverse Event (AE) Reports From Social Media?

- For purposes of reporting by companies to FDA, AE reports from social media should be treated as spontaneous reports
 - Spontaneous reports are unsolicited communications from individuals (e.g., health care professional, consumer) to a company or regulatory authority that describes a suspected adverse experience
- They are reviewed like any other spontaneous report
 - FDA applies the same review process for all reports, regardless of source or product type




How to Report to FDA MedWatch

- How to Report:
 - Online
(www.fda.gov/medwatch)
 - Download the form
 - Mail
 - Fax 1-800-332-0178
- For questions about the form:
 - 1-800-332-1088



Your FDA gateway for clinically important safety information and reporting serious problems with human medical products.

 Report a Problem

 Safety Information

 Stay Informed



FDA Guidances for Industry That Discusses Minimum Data Set

- **August 1997 Guidance for Industry: Postmarketing Adverse Experience Reporting for Human Drug and Licensed Biological Products: Clarification of What to Report,**
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071981.pdf>
- **March 2001 Draft Guidance for Industry: Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines,**
(<http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm092257.pdf>)
- **July 2009 Guidance to Industry: Postmarketing Adverse Event Reporting for Nonprescription Human Drug Products Marketed without an Approved Application,**
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM171672.pdf>¹²