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

CSRC/DIA Think Tank
June 3, 2016

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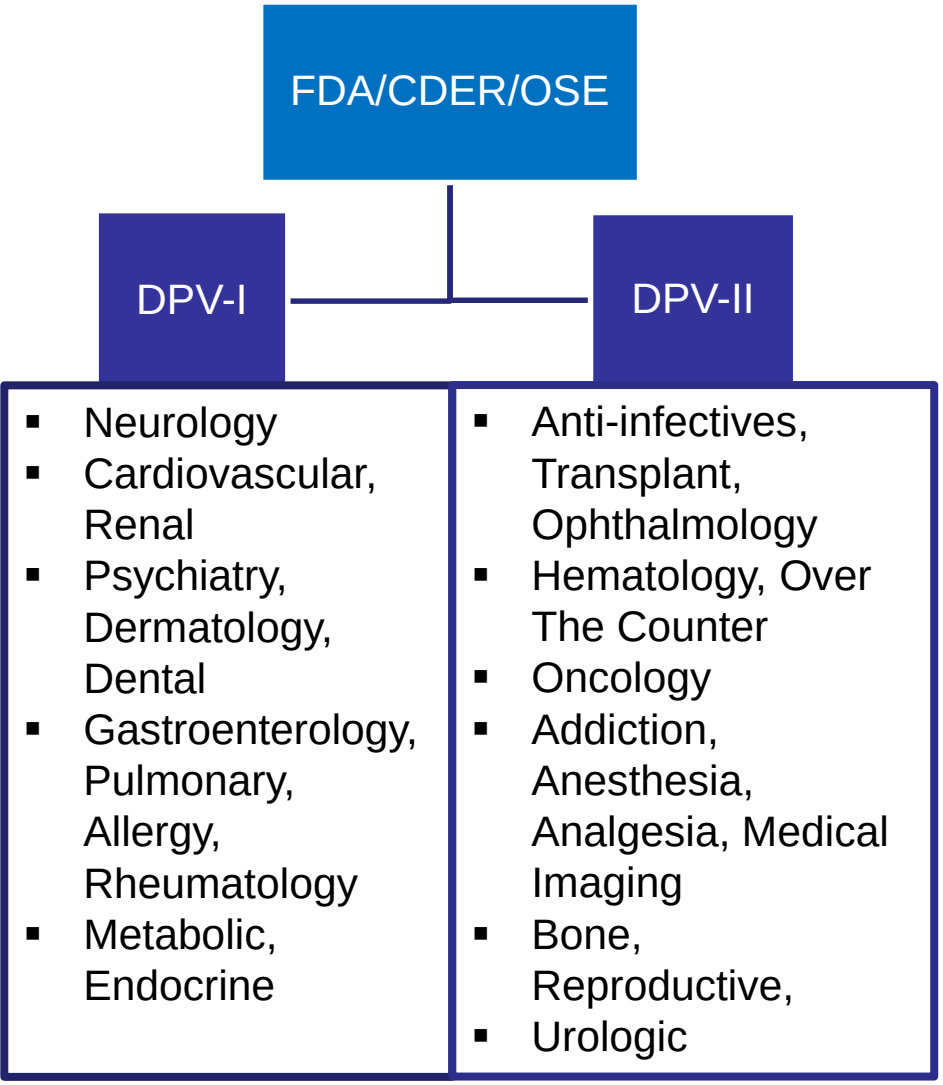
Divisions of Pharmacovigilance (DPV) Overview



Advance public health by detecting safety signals from multiple data sources

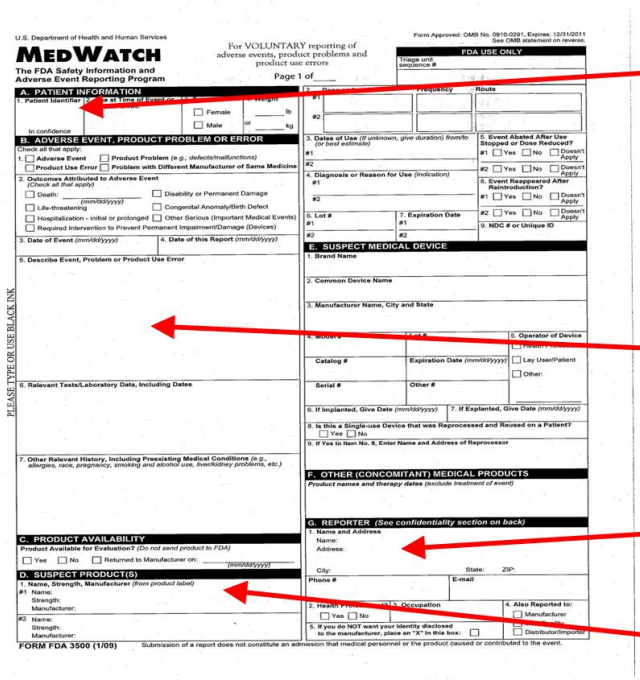
Evaluate the safety of drug and therapeutic biologic products

Recommend appropriate regulatory actions,

Communicate relevant safety information

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



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 FAERS Database

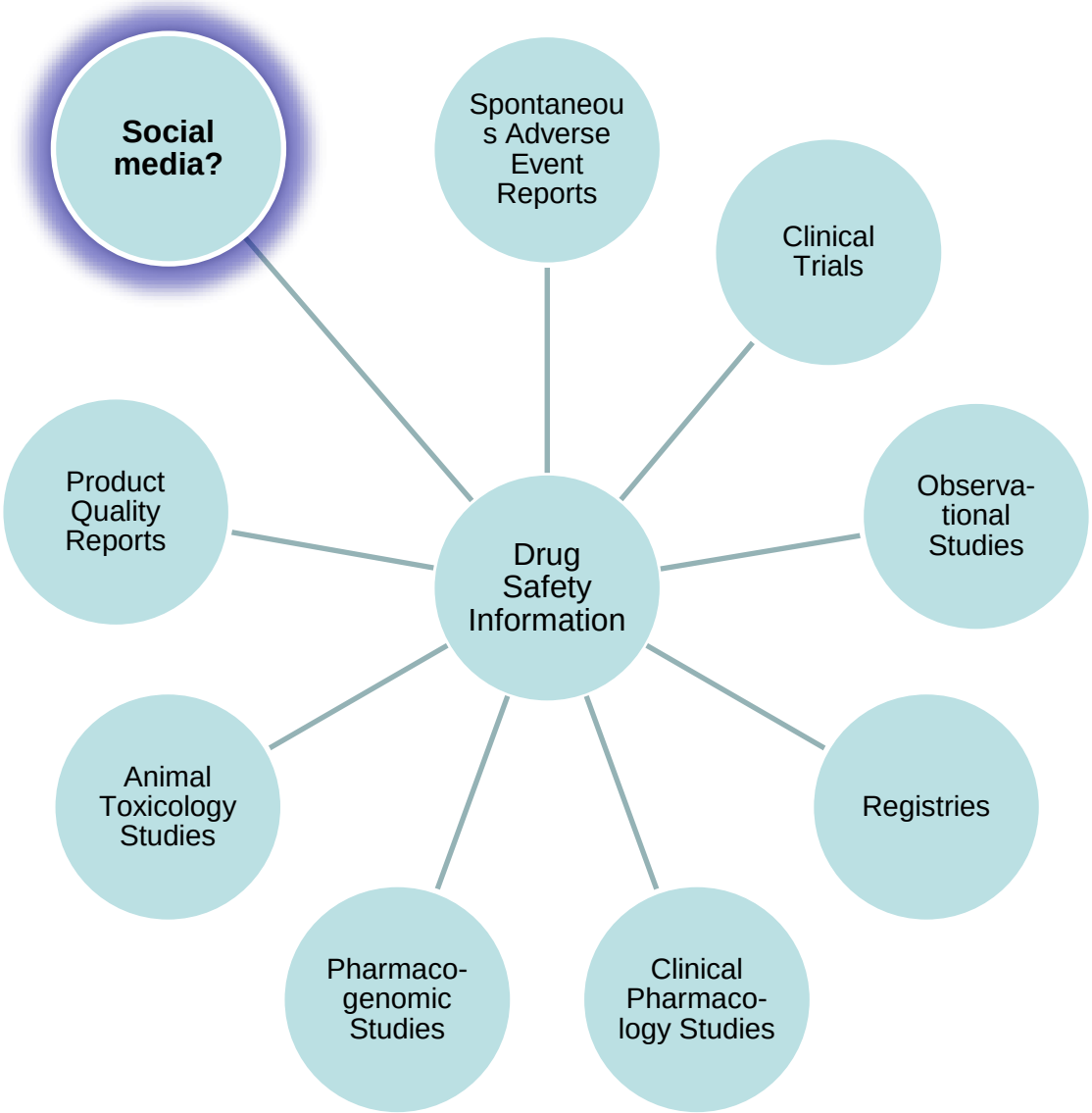
More Useful For

- 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