Overview of Infrastructure and Strategies for Post-Market Safety Assessment

Shari Targum, MD, FACC, FACP
Team Leader
Division of Cardiovascular and Renal Products
CDER/FDA

Disclosures

No financial arrangements to disclose.

The views presented are my own.

Background

Traditional post-marketing safety:

- Spontaneous reports from patients or health care professionals,
- Published case reports,
- Postmarketing clinical studies
  - Randomized controlled trials
  - Observational studies

Adverse Event Spontaneous Reporting Systems

- Industry required to report adverse events reported to them
- US Pharmacovigilance: Voluntary reporting
  - Under-reporting of adverse events
  - Effective for unusual drug-related adverse events
  - Not very effective for increased frequency of common events.

- Withdrawal of Vioxx (2004): led to widespread interest in postmarketing safety process

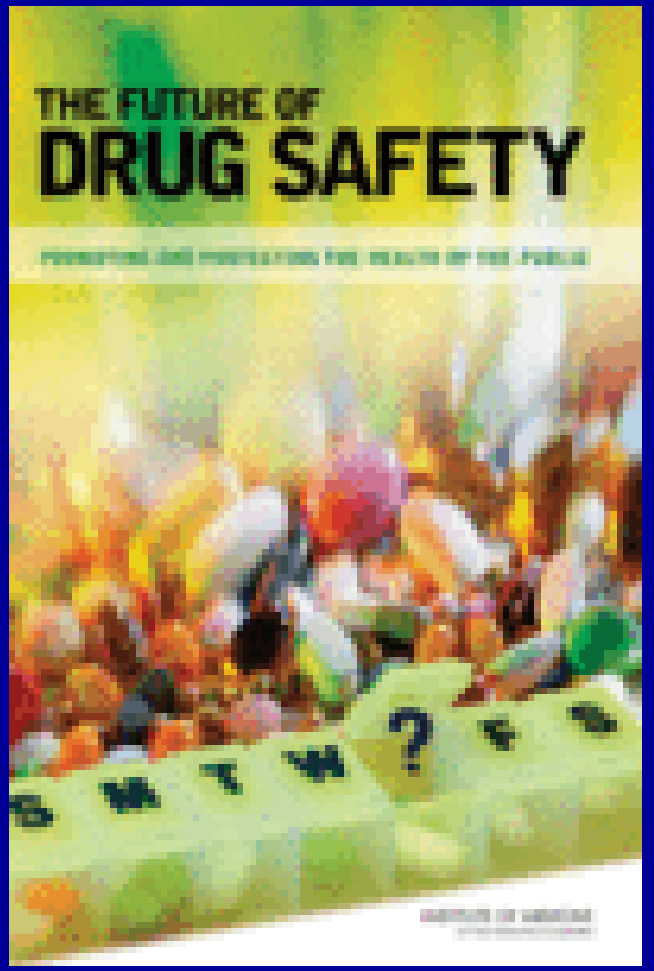
Drug Safety Oversight Board (2005):
provide oversight and advice to CDER Director on the management of emerging drug safety issues.

But this was only the beginning….

US Government Accountability Office (GAO) report: “Drug Safety: Improvement Needed in FDA’s Postmarket Decision-Making and Oversight Process” (March, 2006)

Institute of Medicine report (2006)

- “Future of Drug Safety—Promoting and protecting the Health of the Public” (2006).
- Recommended that CDER build internal epidemiologic and informatics capacity in order to improve postmarket assessment of drugs;



FDA Response to the IOM Report (Jan. 2007)

- Identify risk management tools and programs;
- Obtain access to types of data other than spontaneous reports
  - Expand capability to conduct targeted surveillance;
  - Look at effects of classes of drugs;
  - Signal detection.

FDA/CDER actions

- Process improvement team
- Deputy Director for Safety within each review division;
- Postmarketing safety tracking system;
- Regular joint meetings between Office of New Drugs/Office of Surveillance and Epidemiology:

Food and Drug Administration Amendments Act (2007)

- Gave FDA new resources and authority to
  - Require sponsors to make post-approval safety labeling changes;
  - Require sponsors to develop and comply with risk evaluation and mitigation strategies (REMS);
  - Require postmarketing studies (PMR);
  - Called upon FDA to set up new electronic surveillance system, using electronic data sources, for adverse events.

New Tools,
New Collaborations

Sentinel Initiative

- Launched in May, 2008
- Enable FDA to actively query electronic health record systems, claims databases and registries to evaluate safety issues
- Goal is a long-term, sustainable, linked system

How does Sentinel complement what we are doing?

- Safety issues can be identified and evaluated in near real-time
- Sentinel expands the capacity for evaluating safety issues
  - Improved access to subgroups, special populations
  - Improved precision of risk estimates due to expanded number of populations available for study
- Active surveillance can identify an increased risk of common AEs (e.g., MI, fracture) that health care providers may not suspect are related to medical products

Courtesy of J. Racoosin, MD, MPH

Some Challenges

- Protecting privacy—data security
- Data quality
- Database management
- Standards
- Methods

Work in progress--Currently working on the “how and what”—expect evolution over time.

Observational Medical Outcomes Partnership (OMOP)

- Public-private partnership
- Funded and managed through the Foundation for the National Institutes of Health
  - Utilizing electronic health records and health insurance claims
  - Develop and test various analytical methods for ability to detect and evaluate drug safety issues over time.

In the Future

- Development of more tools—need to understand capabilities and limitations
- Advances in analytic methods
- Understanding the data—
  - Time dependencies
  - Cumulative exposure
  - Interaction with other medications

- Risk Characterization
  - Better predictive toxicology, mechanistic understanding of safety
  - Modeling
  - Understand cumulative risk and interactions
- Risk stratification
  - Genomics
    - SAE consortium (www.saeconsortium.org)
  - Demographics
  - Underlying condition

Risk Management

- Does monitoring improve patient safety?
- Can risk be mitigated?

Risk Communication

- How and what to communicate
- How to handle uncertainty to better inform decision-making

Safety Science is a Changing Field

- New approaches might complement traditional methods of safety evaluation
- Utilize new technology/methods
  - Opportunities for research
- Partnerships
- Understand strengths and limitations
- Arrive at a “more complete picture”

Thank you.

shari.targum@fda.hhs.gov