Beyond VAERS: How the FDA continues to improve vaccine safety surveillance

FDA Webinar

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Safety surveillance

- CBER monitors the safety of vaccines and biologic products throughout the lifecycle
- Rapidly detect and assess potential safety issues
- Communicate FDA's work and findings with the public
- Respond to public concern
- Advance methods for monitoring safety

Purpose of Post-Marketing Safety Monitoring

- Limitations to pre-licensure clinical trials
  - Limited numbers of study participants
  - Study exclusion criteria limit generalizability
- Knowledge of risk evolves over time
- Passive, spontaneous reporting systems have limitations and must be supplemented with population based surveillance and studies
- Public confidence in safety and its acceptance of biological products, especially vaccines, crucial to the success of public health campaigns and disease prevention

Vaccine Adverse Event Reporting System (VAERS)

- Established in 1991
- Passive reporting from patients, public, health care providers, manufacturers
- Advantages/limitations of passive surveillance
- Methods of analysis
- Signal detection and hypothesis generating
- Very rarely conclusive results

VAERS

Vaccine Adverse Event Reporting System

- Co-administered by FDA and CDC
- Reporting by paper or electronic formats
- Standard form
- Contractor codes and enters data; MedDRA codes (uses, limitations)
- Able to search through data
- Serious AE reports are reviewed daily by medical officers to detect unexpected events

Passive safety surveillance

- **STRENGTHS:**
  - Open-ended for hypothesis generation
  - Potential detection of new or rare adverse events
  - Timeliness
  - Geographic diversity
  - Capability to monitor production lots
- **LIMITATIONS:**
  - Missing and inaccurate data
  - Under-reporting
  - Absence of controls and denominators
  - Inability to assess causation
  - Low likelihood of detection for long latency events

Vision for continued improvement of passive surveillance data

- Immediate and continuous access to accurate and automated data to optimize signal detection, in addition to medical officer review
- Transparent communication of findings
- Public access to data with adequate training or resources to instruct how to accurately analyze the data

Beyond VAERS

- Active surveillance and epidemiologic studies
- Benefits: more potential for signal detection/strengthening, and hypothesis testing
- CDC collaboration [Vaccine Safety Datalink (VSD), and Clinical Investigation and Safety Assessment (CISA)]
- New FDA regulations improve resources, projects, and regulatory responsibilities
- Sentinel Initiative
- FDA Analytic Epidemiology Branch
- Federal and international partners
- Post marketing commitments and requirements for manufacturers

FDA Amendments Act (FDAAA)

- Enacted in 2007
- Improve FDA's ability to monitor safety of medical products throughout their lifecycle
- FDAAA gives FDA authority to:
  - Require postmarketing studies and clinical trials
  - Requires sponsors to make safety related labeling changes
  - Require sponsors to develop and comply with risk evaluation and mitigation strategies (REMS)
- FDAAA also requires FDA to develop a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with at least 25,000,000 patients by 2010 and 100,000,000 by 2012

Safety throughout the Lifecycle

- In response to FDAAA, OBE began a “Safety throughout the Lifecycle” strategic initiative:
  - **Expand and improve utilization of health care data to increase the power, speed and quality of product safety monitoring after licensure**
  - Enhance use of statistical, epidemiological, and risk assessment and modeling methods for evaluation of safety throughout the lifecycle
  - Implement FDAAA and formalize safety review process throughout the lifecycle and integrate new safety activities into the Managed Review Process
  - Enhance role of Safety Teams in safety signal response, safety communications, and policy
  - Enhance safety communications

Analytic Epidemiology Branch

- New CBER/OBE unit as of 2008
- Dedicated to enhancing and expanding active, population based surveillance and studies, hypothesis testing, and methodology development
- “Adaptive toolbox” to rapidly and effectively respond to safety “signals”

Genomics for Safety Assessment

- New Genomics Evaluation Team for Safety (GETS) to focus on identifying possible human genetic contributions to adverse reactions
- Goal: improve biologic product safety

Federal Partners

- Centers for Medicare and Medicaid (CMS) approximately: primarily 35 million elderly
- Department of Defense (DoD)
- Veterans' Administration (VA)
- Indian Health Services (IHS)
- Electronic health records, claims data, population based, potential for real-time surveillance

Post-licensure Rapid Immunization Safety Monitoring (PRISM) system (Harvard Pilgrim)

- Active surveillance system to link vaccination and subsequent health outcomes data from state vaccine registries and large health plans in several states
- Funded by FDA for H1N1 vaccine safety surveillance
- Currently managed by NVPO with FDA and CDC participation
- Plan to move under “mini-sentinel” to develop capacity for general vaccine safety monitoring

Global Collaboration

- International Conference on Harmonization
- Pharmaceutical Inspection Cooperation/Scheme
- Information sharing arrangements with various regulatory authorities and WHO and engagement in priority areas
- Brighton collaboration for standardized case definitions of adverse events following immunization
- CIOMS vaccine safety working group
- Partnering with WHO and NGOs to explore additional means of providing global regulatory assistance/capacity building

Impact of H1N1

- All of the “newer” surveillance programs were already being developed
- H1N1 highlighted and accelerated the processes
- Federal and international partners
- Health care datasets
- NVAC Vaccine Safety Risk Assessment Working Group
  - Considered 1976 history of H1N1 vaccine and GBS
  - http://www.cdc.gov/mmwr/preview/mmwrhtml/mm58e1204a1.htm
  - Strong collaboration and public communication
  - National Vaccine Program Office played crucial role in coordinating efforts

Summary

- FDA Amendment Act places increasing emphasis on “Safety throughout the Lifecycle”
- New tools and databases allow us to move from reliance on passive surveillance to population-based systems
- Exploring genomics and new methodologies to improve safety surveillance
- Working towards integrated approach of safety monitoring throughout product lifecycle

Summary

- FDAAA and other initiatives help FDA to continue developing capacity to monitor the safety of products
- FDA and other partners continue to expand and develop safety surveillance and analytical studies to ensure the safety of biologic products and the health of the public

Questions?

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  - www.fda.gov/BiologicsBloodVaccines/default.htm
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