Patient-Centered Outcomes Research Institute

Workshop to Advance the Use of Electronic Data for Conducting PCOR

Lessons from the Field: Sentinel Initiative

Patrick Archdeacon, MD
Medical Officer
Office of Medical Policy/CDER/FDA

Disclaimer

- The opinions and conclusions expressed in this presentation are those of the presenter and should not be interpreted as those of the FDA

FDA Amendments Act of 2007

Section 905: Active Postmarket Risk Identification and Analysis

- Establish a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with the goals of including
  - at least 25,000,000 patients by July 1, 2010
  - at least 100,000,000 patients by July 1, 2012
- Access a variety of sources, including
  - Federal health-related electronic data (such as data from the Medicare program and the health systems of the Department of Veterans Affairs)
  - Private sector health-related electronic data (such as pharmaceutical purchase data and health insurance claims data)

Sentinel Initiative

- Improving FDA's capability to identify and investigate safety issues in near real time
- Enhancing FDA's ability to evaluate safety issues not easily investigated with the passive surveillance systems currently in place
  - Expanding FDA's access to subgroups and special populations (e.g., the elderly)
  - Expanding FDA's access to longer term data
  - Expanding FDA's access to adverse events occurring commonly in the general population (e.g., myocardial infarction, fracture) that tend not to get reported to FDA through its passive reporting systems

**Will augment, not replace, existing safety monitoring systems

Sentinel Initiative: A Collaborative Effort

- Collaborating Institutions (Academic and Data Partners)
  - Private: Mini-Sentinel pilot
  - Public: Federal Partners Collaboration
- Industry
  - Observational Medical Outcomes Partnership
- All Stakeholders
  - Brookings Institution cooperative agreement on topics in active surveillance

Mini-Sentinel

www.mini-sentinel.org

Contract awarded Sept 2009 to
Harvard Pilgrim Health Care Institute

- Develop the scientific operations needed for an active medical product safety surveillance system
- Create a coordinating center with continuous access to automated healthcare data systems, which would have the following capabilities:
  - Provide a "laboratory" for developing and evaluating scientific methodologies that might later be used in a fully-operational Sentinel System.
  - Offer the Agency the opportunity to investigate safety issues in existing automated healthcare data system(s) and to learn more about some of the barriers and challenges, both internal and external.

The annotated Mini-Sentinel

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2012; **21**: 1–8
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.2343

ORIGINAL REPORT

The U.S. Food and Drug Administration's Mini-Sentinel program:

- Supplement to Pharmacoepidemiology and Drug Safety
- 34 peer reviewed articles; 297 pages
- Goals, organization, privacy policy, data systems, systematic reviews, stats/epi methods, chart retrieval/ review, protocols for drug/vaccine studies...

Mini-Sentinel goals

- Develop a consortium
- Develop policies and procedures
- Create a distributed data network
- Evaluate/develop methods in safety science
- Assess FDA-identified topics

Governance

- Planning board – principal investigators, FDA, public representative
- Operations center
- Cores: data, methods, protocols
- Policy committee
- Safety science committee
- Privacy board
- Workgroups

Governance principles/policies

- Public health practice, not research
- Minimize transfer of protected health information and proprietary data
- Public availability of "work product"
  - Tools, methods, protocols, computer programs
  - Findings
- Data partners participate voluntarily
- Maximize transparency
- Confidentiality
- Conflict of Interest

Mini-Sentinel's Evolving Common Data Model

- Administrative data
  - Enrollment
  - Demographics
  - Outpatient pharmacy dispensing
  - Utilization (encounters, diagnoses, procedures)
- EHR data
  - Height, weight, blood pressure, temperature
  - Laboratory test results (selected tests)
- Registries
  - Immunization
  - Mortality (death and cause of death)

The Mini-Sentinel Distributed Database

- Quality-checked data held by 17 partner organizations
- Populations with well-defined person-time for which medically-attended events are known
- 126 million individuals*
  - 345 million person-years of observation time (2000-2011)
  - 44 million individuals currently enrolled, accumulating new data
  - 27 million individuals have over 3 years of data

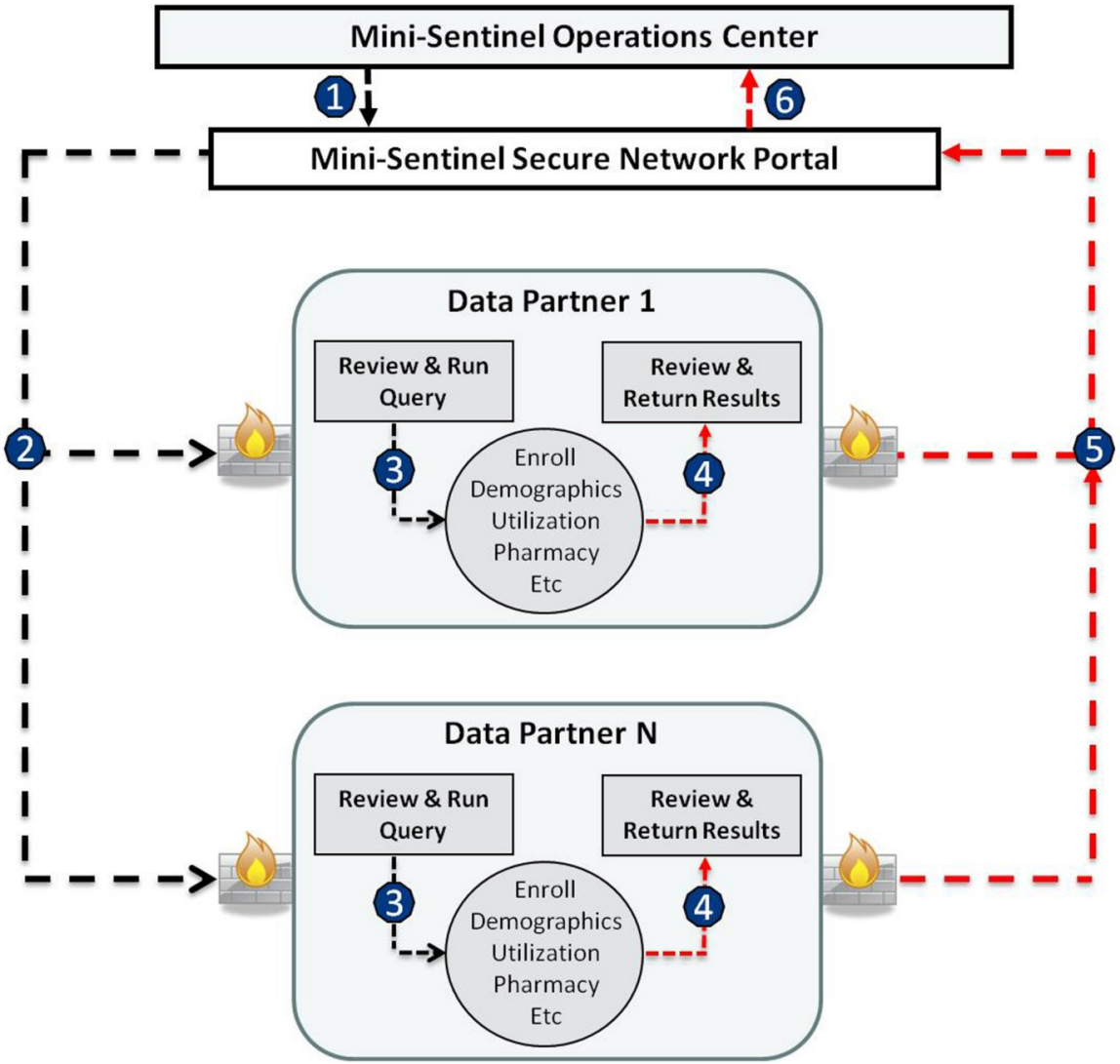
*As of 12 December 2011. The potential for double-counting exists if individuals moved between data partner health plans.

Mini-Sentinel Partner Organizations

Why a Distributed Database?

- Avoids many concerns about inappropriate use of confidential personal data
- Data Partners maintain physical control of their data
- Data Partners understand their data best
  - Valid use / interpretation requires their input
- Eliminates the need to create, secure, maintain, and manage access to a complex, central data warehouse

Mini-Sentinel Distributed Analysis



1- User creates and submits query (a computer program)

2- Data partners retrieve query

3- Data partners review and run query against their local data

4- Data partners review results

5- Data partners return summary results via secure network/portal

6 Results are aggregated

Distributed Querying Approach

Three ways to query data:

1) Pre-tabulated summary tables
2) Reusable, modular SAS programs that run against person level Mini-Sentinel Distributed Database
3) Custom SAS programs for in-depth analysis

Results of all queries performed publically posted once activity complete

Current Modular Programs

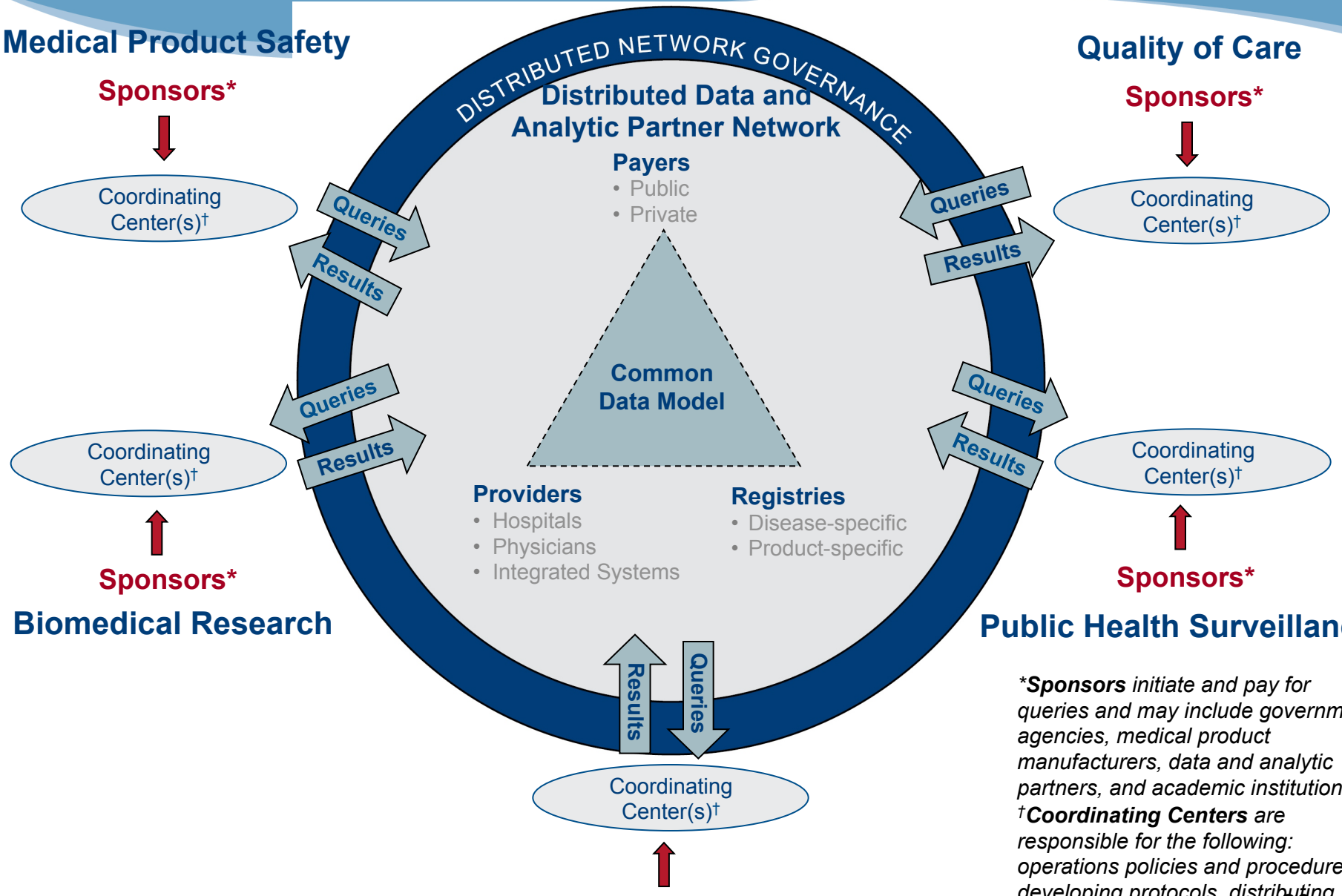
1. Drug exposure for a specific period
   - Incident and prevalent use combined
2. Drug exposure with a specific condition
   - Incident and prevalent use combined
   - Condition can precede and/or follow
3. Outcomes following first drug exposure
   - May restrict to people with pre-existing diagnoses
   - Outcomes defined by diagnoses and/or procedures
4. Concomitant exposure to multiple drugs
   - Incident and prevalent use combined
   - May restrict to people with pre-existing conditions

New Modular Program Capabilities On the Horizon…

- Modular Programs capable of perform sequential monitoring using different epidemiology designs and analysis methods to adjust for confounding:
  - Cohort study design using score-based matching (propensity score and/or disease risk score) adjustments
  - Cohort study design using regression techniques
  - Self-Controlled Cohort study design

In Progress / Future Mini-Sentinel Activities

- Expand MSDD/CDM (e.g., add additional laboratory and vital sign data)
- Continue methods development and HOI validation
- Semi-automated or automated confounding control using propensity and disease risk scores
- Evaluation of emerging safety issues and conduct of routine surveillance with NMEs
- Evaluation of emerging safety issues with drugs on market > 2 yrs



**Sponsors* initiate and pay for queries and may include government agencies, medical product manufacturers, data and analytic partners, and academic institutions.*

*†**Coordinating Centers** are responsible for the following: operations policies and procedures, developing protocols, distributing queries, and receiving and aggregating results.*

Barriers and Lessons Learned

Barriers

- Study methodologies and statistical approaches require further optimization
- Policies and governance appropriate for PHS activities may not translate to CER
- Limited resources and funding

Lessons

- Some competition is healthy, but collaboration is critical to success
- Establishing effective governance and policies is time-intensive – start early!!
- Technical barriers (methods, statistics, data) exist but do not represent the biggest challenges

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Welcome to Mini-Sentinel

Mini-Sentinel is a pilot project sponsored by the U.S. Food and Drug Administration (FDA) to inform and facilitate development of a fully operational active surveillance system, the Sentinel System, for monitoring the safety of FDA-regulated medical products.

Mini-Sentinel is one piece of the Sentinel Initiative, a multi-faceted effort by the FDA to develop a national electronic system that will complement existing methods of safety surveillance.

Mini-Sentinel Collaborators include Data and Academic Partners that provide access to health care data and ongoing scientific, technical, methodological, and organizational expertise.

New Postings

May 27, 2011

- HOI Evidence Review - ABO Incompatibility Reactions
- HOI Evidence Review - Infections Due to Blood Products, Tissue Grafts, or Organ Transplants
- HOI Evidence Review - Lymphoma