



Infrastructure and Methodology for Active Postmarket Risk Identification: An Update of the Sentinel Initiative

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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: A Collaborative Effort

- **Collaborating Institutions** (Academic and Data Partners)
 - Private: **Mini-Sentinel pilot (PRISM)**
 - 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.

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)

CDM Tables & Data Elements

Enrollment
PatID
Enc_Start
Enc_End
Med_Cov
Drug_Cov

Demographic
PatID
Birth_Date
Sex
Hispanic
Race

Dispensing
PatID
RxDate
NDC
RxSup
RxAmt

Encounter
PatID
EncounterID
Adate
Ddate
Provider
Facility_Location
EncType
Facility_Code
Discharge_Disposition
Discharge_Status
DRG
DRG_Type
Admitting_Source

Diagnosis
PatID
EncounterID
Adate
Provider
EncType
Dx
Dx_Codetype
OrigDX
PDX

Procedure
PatID
EncounterID
Adate
Provider
EncType
PX
PX_Codetype
OrigPX

Death
PatID
DeathDt
DtImpute
Source
Confidence

Cause of Death
patID
COD
CodeType
CauseType
Source
Confidence

Clinical Data: Selected Lab Tests and Vital Signs

LabTests

Alkaline Phosphatase (ALP)
 Alanine Aminotransferase (SGPT)
 Total Bilirubin
 Glucose
 Glycosylated hemoglobin (HbA1c)
 Creatinine
 Hemoglobin
 International Normalized Ratio (INR)
 Fibrin d-dimer
 Lipase
 Absolute Neutrophil count (ANC)

Lab DD

MRN
 Test_Type
 LOINC
 Stat
 Pt_Loc
 Result_Loc
 LOCAL_CD
 PX
 Codetype
 Order_ID
 Order_dt
 Lab_dt
 Lab_tm
 Result_dt
 Result_tm
 Result_C
 Result_unit
 Normal_low_C
 Modifier_low
 Normal_high_C
 Modifier_high
 Order_dept
 Facility_code

Vital Signs

Weight
 Height
 Systolic Blood Pressure
 Diastolic Blood Pressure
 Smoking Status

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



IMPLEMENTING OTHER ORGANIZATIONS

HealthCore® WELLPOINT



KAISER PERMANENTE®

hmo
research
network

Aetna®

Humana
Pharmacy Solutions®

VANDERBILT
SCHOOL OF MEDICINE

OUTCOME™

OPTUM™

Penn
Medicine



Cincinnati
Children's
change the outcome®

DukeMedicine

CRITICAL PATH
INSTITUTE
Improving the Path for Innovative Therapies

UAB PARTNERS™
HEALTHCARE

AHIP
America's Health
Insurance Plans

UIC

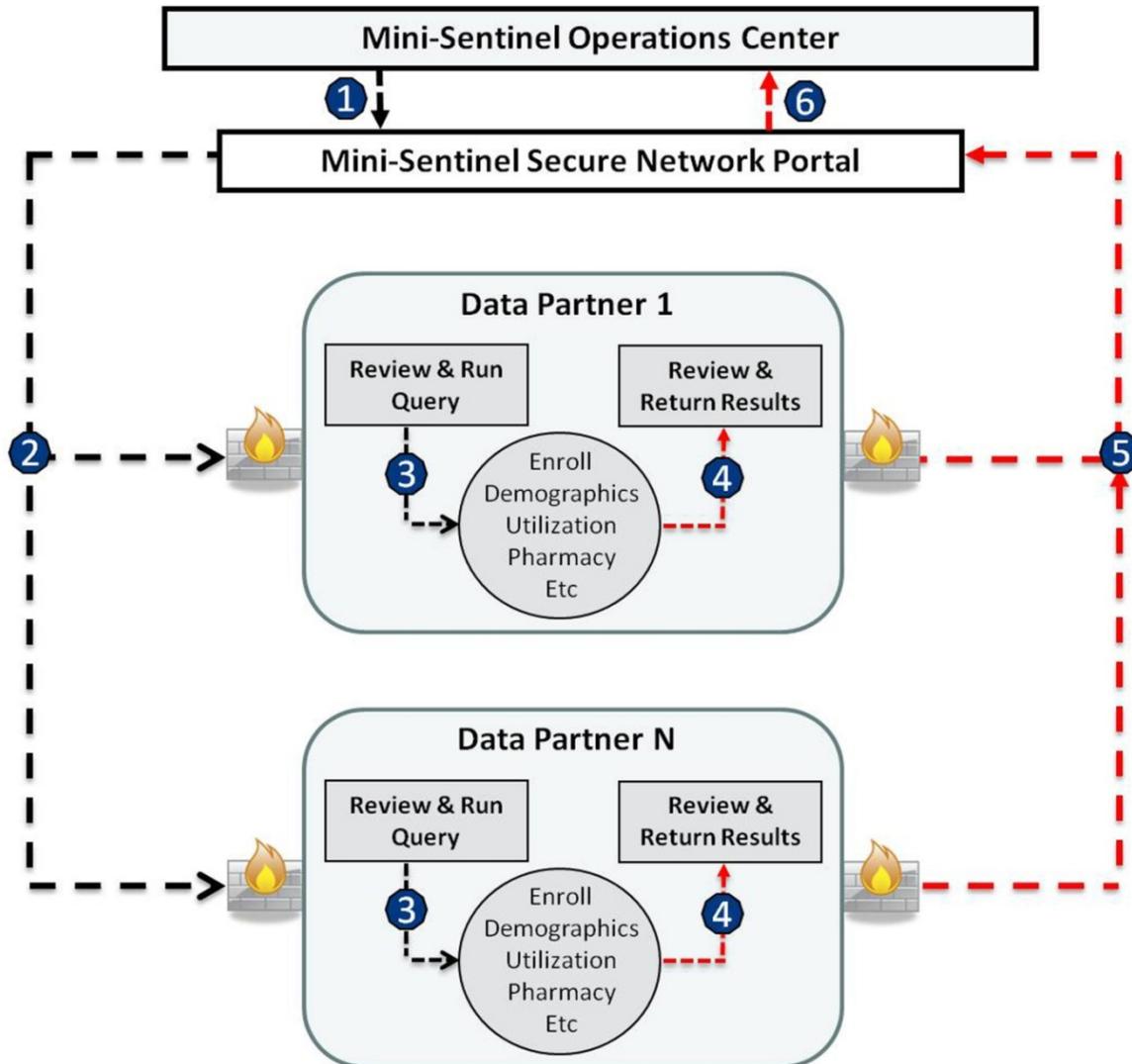
THE UNIVERSITY OF IOWA
COLLEGE OF PUBLIC HEALTH

RUTGERS
Institute for Health

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
- Create linkages across disparate data sources (e.g., registries)
- Continue methods development (e.g., automated confounding control using propensity and disease risk scores)
- Refine and clarify data use policies
- Evaluation of emerging safety issues and conduct of routine surveillance with NMEs



Medical Product Safety

Sponsors*



Coordinating Center(s)[†]

Coordinating Center(s)[†]



Sponsors*

Biomedical Research

Quality of Care

Sponsors*



Coordinating Center(s)[†]

Coordinating Center(s)[†]



Sponsors*

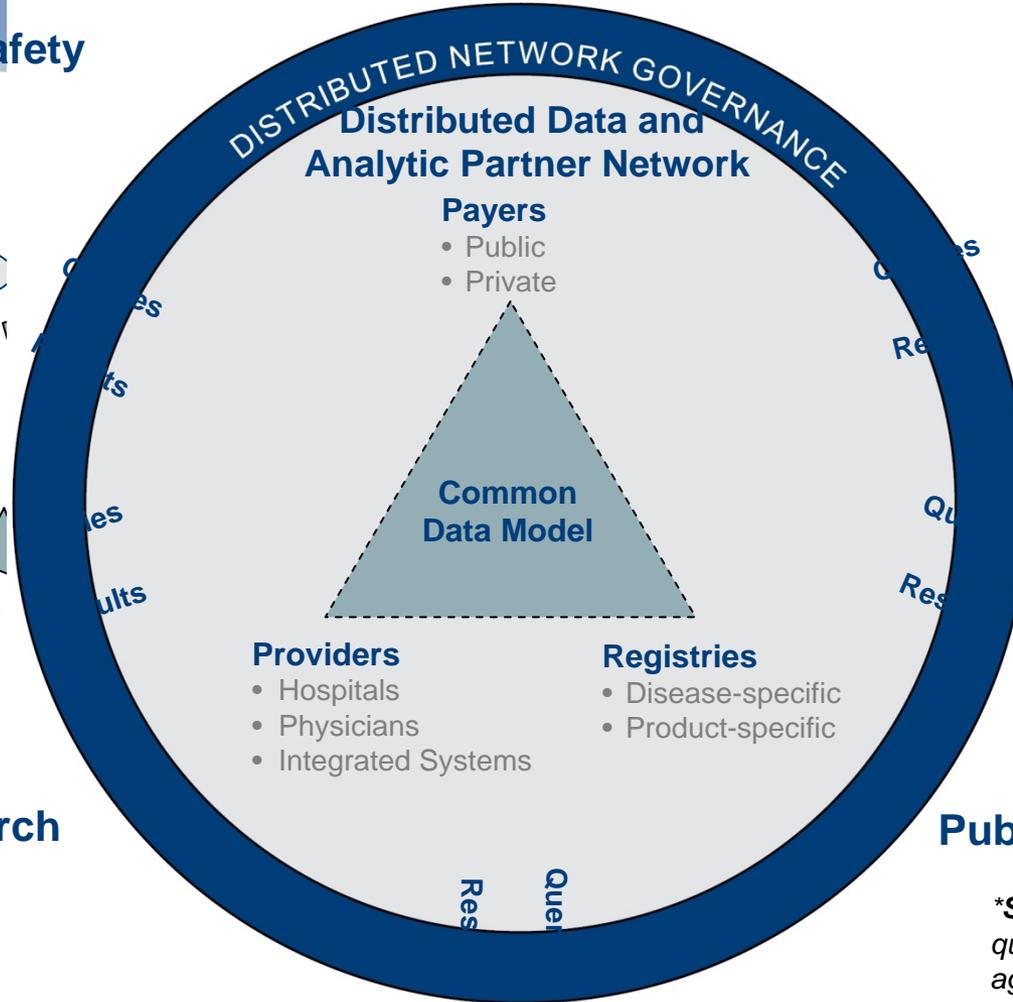
Public Health Surveillance

Comparative Effectiveness Research

Sponsors*



Coordinating Center(s)[†]



**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.*

Lessons Learned in Mini-Sentinel

- Understanding the limits of active postmarket risk identification systems is as important as recognizing their potential
- A mature Sentinel System will likely require a variety of tools to have the capacity to address a range of issues
- Realizing the vision of Sentinel as a national resource will require cooperation and communication

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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](#)

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