FDA’s Mini-Sentinel Program
Update for the Brookings Active
Surveillance Implementation Council

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Harvard Pilgrim Health Care Institute
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# Stages of postmarket surveillance

<table>
<thead>
<tr>
<th>Aim</th>
<th>Signal Generation</th>
<th>Signal Refinement</th>
<th>Signal Evaluation</th>
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Example:
- Active surveillance in Mini-Sentinel and VSD using coded electronic health information.
## Stages of postmarket surveillance

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### Approach

- Repeated monitoring of ~10 of AE:product pairs or one-time expedited analysis of a single pair

### Example

Active surveillance in Mini-Sentinel and VSD using coded electronic health information
Sentinel prototype

- Develop a **consortium of data partners** and other content experts
- Develop **policies and procedures**
- Create a **distributed data network** with access to electronic health data and full text records
  - Develop secure communications capability
- Evaluate extant **methods** in safety science
  - Develop new epidemiological and statistical methods as needed
- Evaluate **FDA-identified medical product-adverse event pairs of concern**
Distributed data partners
Additional partners
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 for individuals
1- Query (an executable program) is submitted by Coordinating Center to the Portal
2- Data Partners retrieve the query
3- Data partners review query and perform analysis locally by executing the distributed program
4- Data partners review results
5- Data partners return results to the Portal
Mini-Sentinel Secure Portal

User Authentication
Query Interfaces and Distribution
Query Management & Results Viewer
Data Partner Login, Settings & Auditing

Mini-Sentinel Functions
1. Governance
   -- FDA
   -- Planning Board
2. Assignment of user rights
   -- Ops Center – all rights
   -- FDA – menu-driven queries
3. Data resources and formats
   -- Mini-Sentinel Common Data Model
   -- Creation of distributed dataset via programs from Ops Center
4. Analyses performed via programs distributed by the portal
   -- Data partners control execution
5. Communication
   -- FDA, Brookings, Mini-Sentinel website, investigators’ publications

PopMedNet Services to Mini-Sentinel
1. Network creation and support
2. Documentation
3. Software development
4. Administrative leadership
5. Secure portals – FISMA compliant*

Mini-Sentinel Distributed Database

*Powered by PopMedNet; www.popmednet.org
Distributed data partners
Yearly enrollments (71M unique enrollees)
Duration of enrollment

- 3+ years: 31%
- 5+ years: 18%
Methods development

- Epidemiology methods
  - Taxonomy of study designs for different purposes
  - Literature review for algorithms to identify 20 outcomes using claims data

- Data access and validation
  - Successful test of ability to retrieve hospital records, redact identifiers, adjudicate diagnosis

- Statistical methods
  - Better adjustment for confounding
  - Case based methods
  - Regression methods for sequential analysis
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.
Next steps – active surveillance

- **Drugs**
  - Implement active surveillance protocol for acute MI related to new oral hypoglycemics
  - Evaluate new safety issues for older drugs
  - Evaluate impact of regulatory actions, e.g., restricted distribution

- **Vaccines (Post-licensure Rapid Immunization Safety Monitoring – PRISM)**
  - Active surveillance of rotavirus vaccine and intussusception
  - Active surveillance of human papilloma virus vaccine and venous thromboembolism
Next steps – data and methods

Data

- Quarterly updates of distributed data set
- Add blood pressure, height, weight, tobacco use
- Add selected laboratory test results
- Evaluate methods for obtaining EHR data
- Identify complementary immunization data sources

Methods

- Link to state immunization registries and health plans
- Test anonymous linkage between data partners
- Assess comparability of Mini-Sentinel data to national data
- Develop additional statistical methods
Laboratory tests

- Glucose
- Hemoglobin A1c
- Hemoglobin
- Creatinine
- International Normalized Ratio (INR)
- Alanine aminotransferase (ALT)
- Alkaline Phosphatase
- Total Bilirubin
- Lipase
- D-dimer
- Absolute Neutrophil Count (ANC)
Laboratory tests

- What’s a glucose?
  - Variable methods of lab data capture from different sites
  - Test characteristics (source, measurement process, clinical circumstances) are rarely neatly abstracted into discrete columns
  - Nature of the test needs to be deduced from the test name which is not always so obvious
    - Serum glucose vs whole blood glucose, vs urine glucose, CSF glucose
    - Fasting or non fasting?
    - Part of a glucose challenge test or not?
### LOINC

**Logical Observation Identifiers Names and Codes**

<table>
<thead>
<tr>
<th>LOINC</th>
<th>Component</th>
<th>Property</th>
<th>System</th>
<th>Timing</th>
<th>Scale</th>
<th>Method</th>
<th>Class</th>
<th>Type</th>
<th>Status</th>
<th>Short name</th>
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<tbody>
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<td>Imp</td>
<td>Ser/Plas</td>
<td>Pt</td>
<td>Nar</td>
<td>CHAL</td>
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<tr>
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**serum glucose**

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602 hits!
Challenges

- Develop reliable approaches to different types of:
  - Medical products
  - Outcomes
  - Patients
  - Data that are new to safety science (EHRs, inpatient settings, laboratories, ...)

- Make the system operational
  - Need for timeliness in detection and followup

- Avoid false alarms
Avoiding false alarms

- Develop a framework for evaluation
  - Based on experience of CDC Vaccine Safety Datalink

- Evaluate signals **before** dissemination
  - Steps range from simple data checks to detailed epidemiologic evaluation. Examples:
    - Search for data anomalies: errors, missing data, changes in coding practices
    - Assess temporal/geographic clustering
    - Evaluate additional control exposures/groups
    - Confirm outcomes
    - Search for confounders
Developing the Sentinel System — A National Resource for Evidence Development

Rachel E. Behrman, M.D., M.P.H., Joshua S. Benner, Pharm.D., Sc.D., Jeffrey S. Brown, Ph.D., Mark McClellan, M.D., Ph.D., Janet Woodcock, M.D., and Richard Platt, M.D.

The Food and Drug Administration (FDA) now has the capacity to “query” the electronic health information of more than 60 million people, posing specific questions in order to monitor the safety of approved medical products. This information to answer additional convening an ongoing series of discussions among stakeholders to address the near- and long-term challenges inherent in implementing the Sentinel System. In 2009, the FDA gave the Harvard Pilgrim Health Care Institute the lead role.
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