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

Richard Platt, MD, MSc
Harvard Pilgrim Health Care Institute
and Harvard Medical School

June 1, 2011

Stages of postmarket surveillance

	Signal Generation	Signal Refinement	Signal Evaluation
Aim = Identify excess risk	All (suspected and unanticipated) adverse events (AEs), all products	**Specific AE:product pairs of concern**	A highly suspected AE:product pair

Stages of postmarket surveillance

Aim = Identify excess risk	All (suspected and unanticipated) adverse events (AEs), all products	**Specific AE:product pairs of concern**	A highly suspected AE:product pair
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

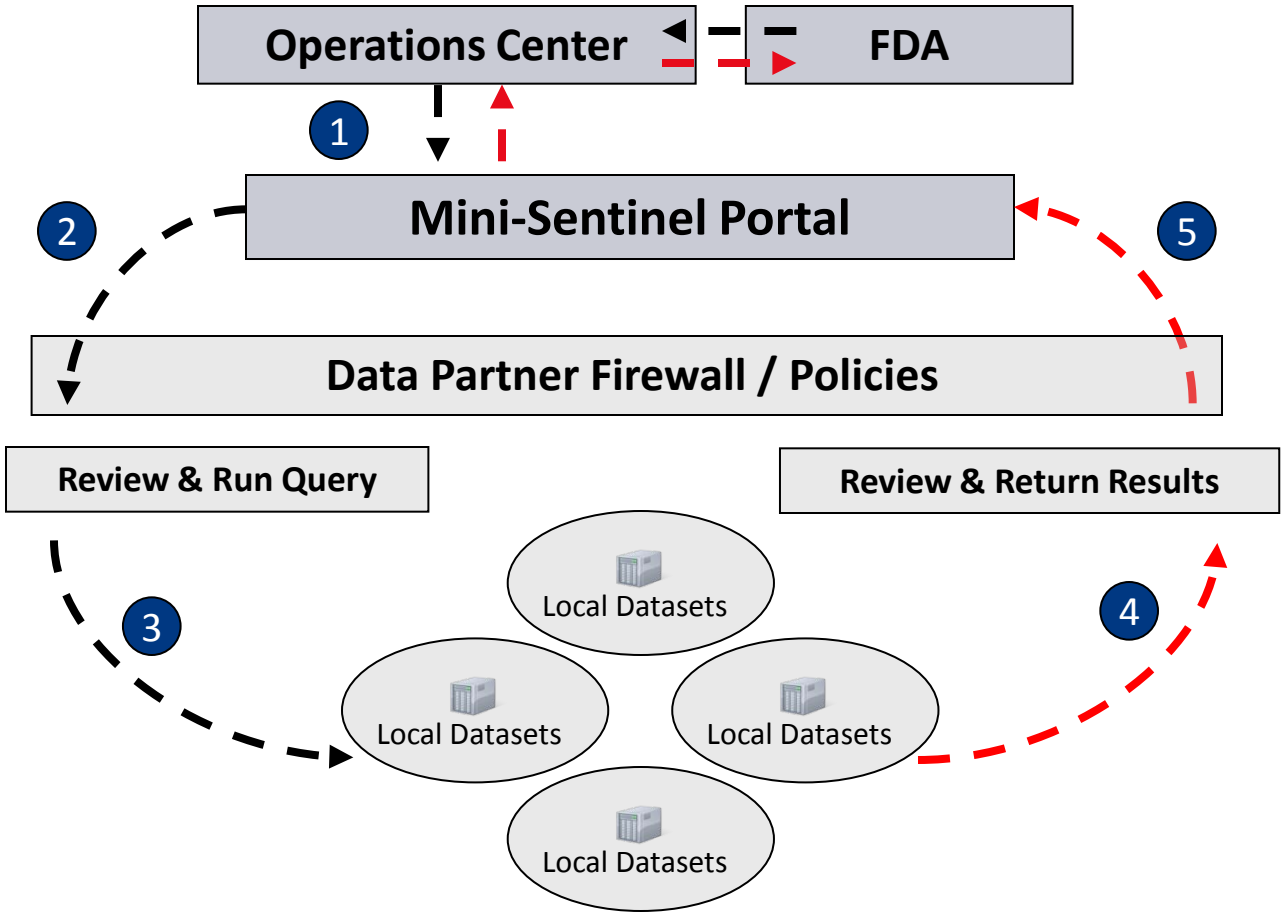
Distributed data partners

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

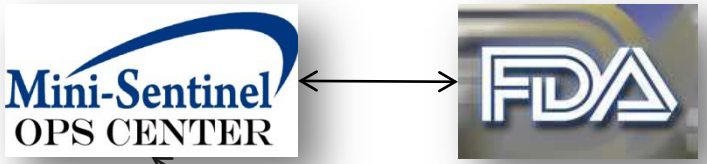
Mini-Sentinel distributed data network



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

FDA Mini-Sentinel Distributed Data Network

- Portal control
- Executable programs
- Menu driven queries



Mini-Sentinel Secure Portal

User Authentication

Query Interfaces and Distribution

Query Management & Results Viewer

Data Partner Login, Settings & Auditing

1. Kaiser Permanente

A KP N Cal

D KP HI

B KP S Cal

E KP GA

C KP NW

F KP CO

2. Aetna

3. Fallon

4. Group Health

5. Harvard Pilgrim

6. Health Partners

7. Henry Ford Hlth System

8. Humana

9. Lovelace Clinic

10. Marshfield Clinic

11. TN Medicaid (Vanderbilt)

12.WellPoint (HealthCore)

Subnetwork

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

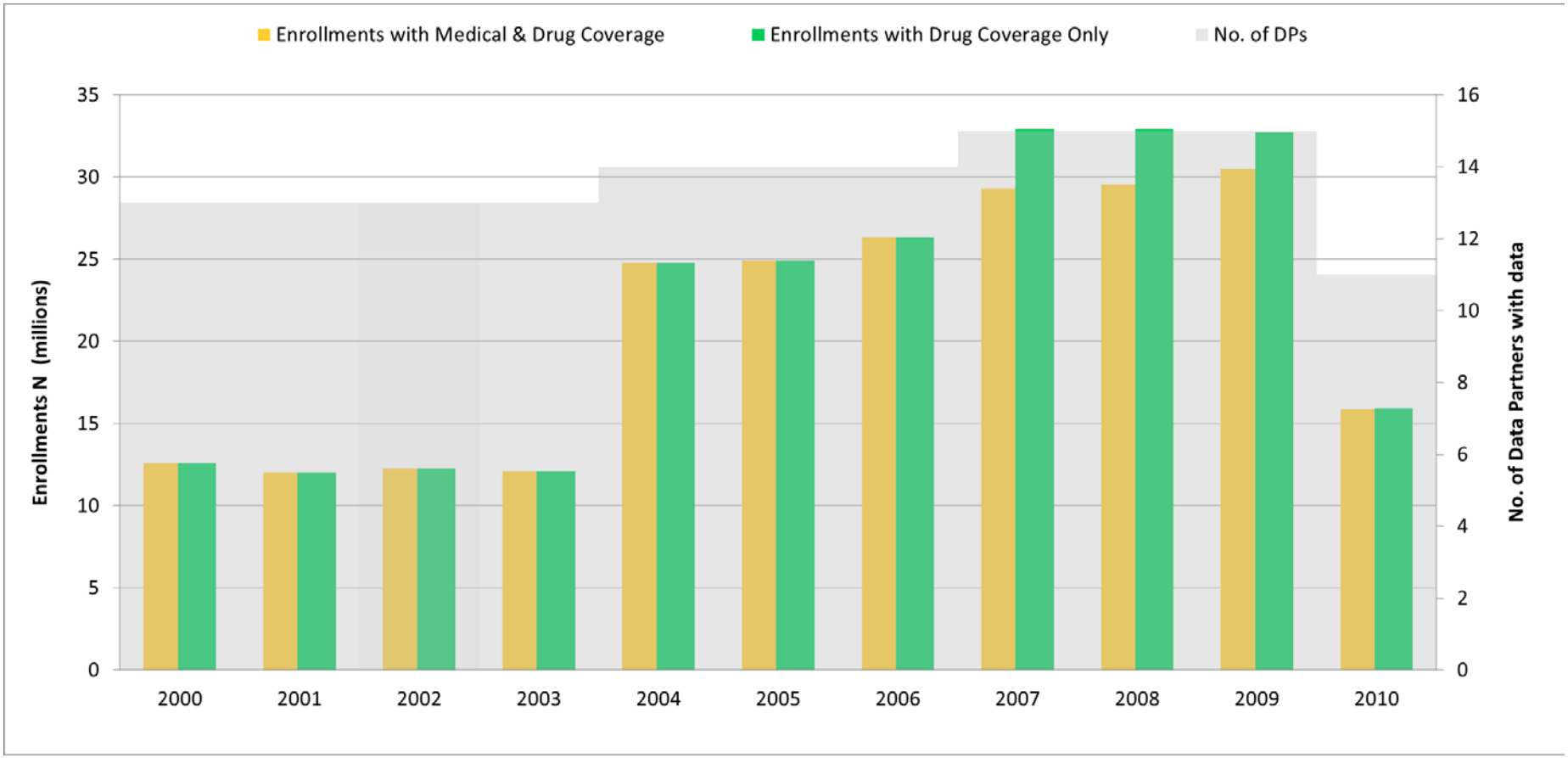
1. **Network creation and support**
2. **Documentation**
3. **Software development**
4. **Administrative leadership**
5. **Secure portals – FISMA compliant***

Mini-Sentinel Distributed Database

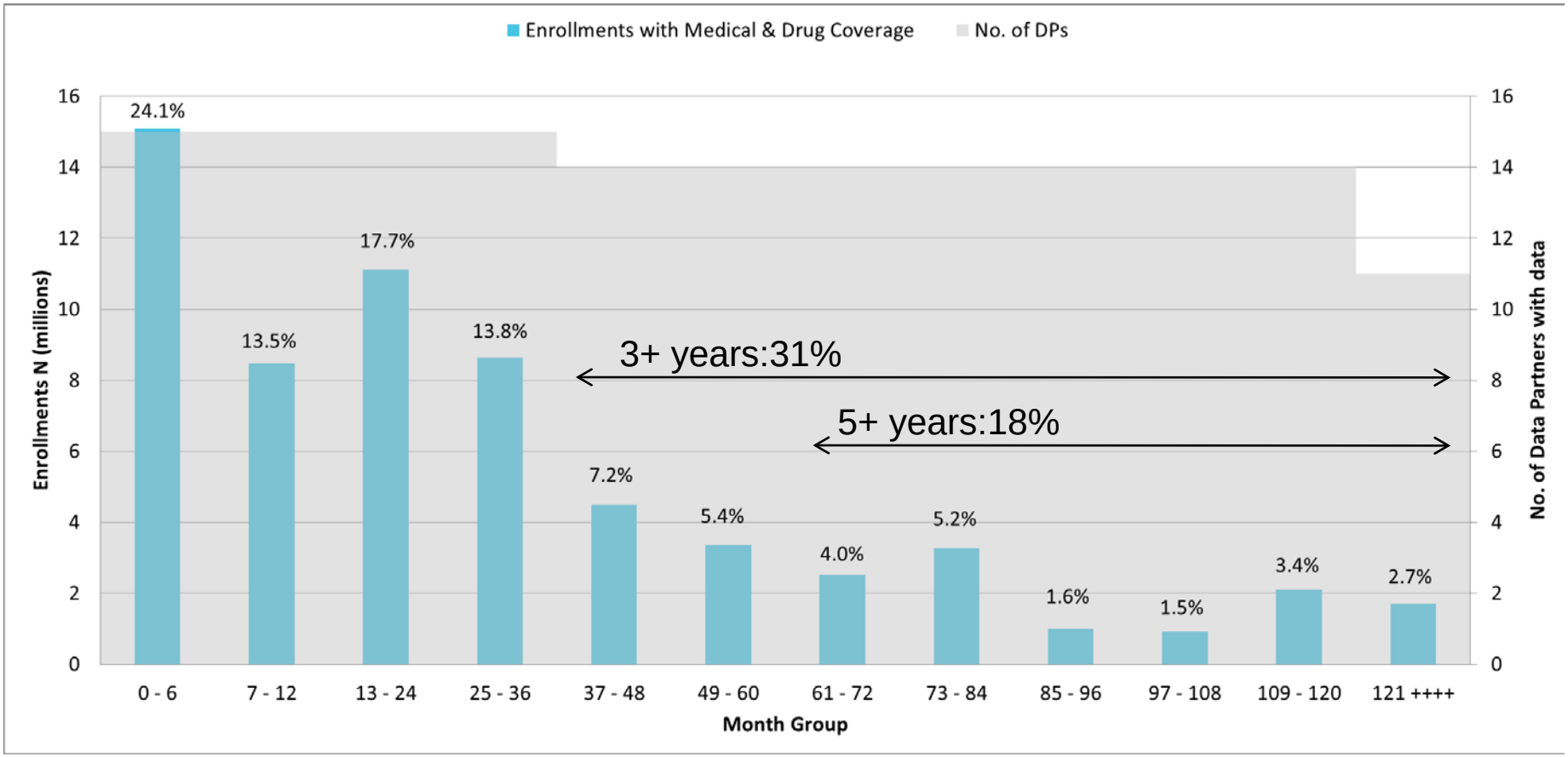
*Powered by PopMedNet; www.popmednet.org

Distributed data partners

Yearly enrollments (71M unique enrollees)



Duration of enrollment



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

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

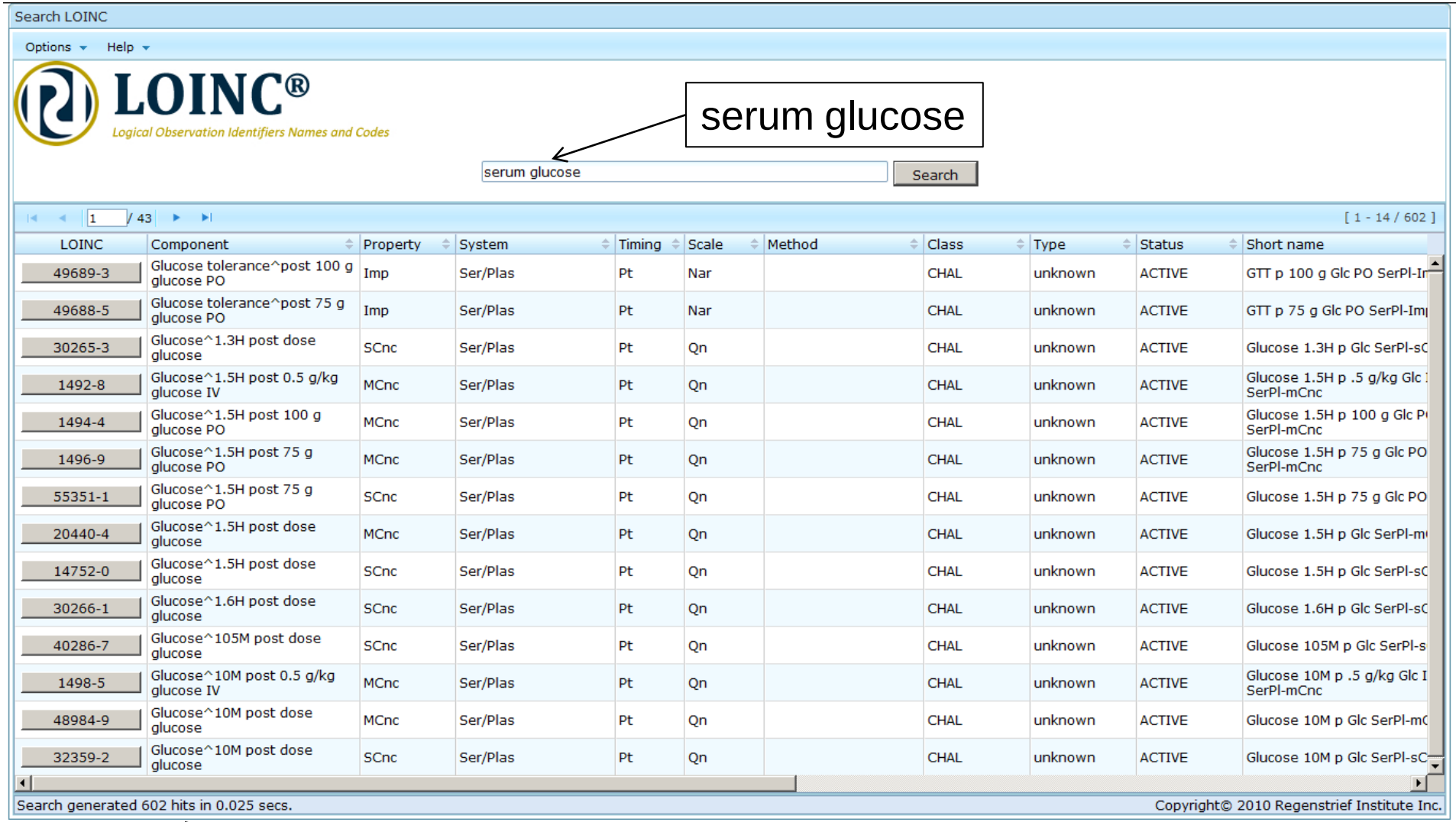
- Data
  - Quarterly updates of distributed data set
  - Add blood pressure, height, weight, tobacco use
  - Add selected laboratory test results
  - Evaluate methods for obtaining EHR data
  - Identify complementary immunization data sources
- Methods
  - Link to state immunization registries and health 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?


Search LOINC
Options
Help
LOINC®
Logical Observation Identifiers Names and Codes
serum glucose
serum glucose
Search
1 / 43
[1 - 14 / 602]
LOINC | Component | Property | System | Timing | Scale | Method | Class | Type | Status | Short name
49689-3 | Glucose tolerance^post 100 g glucose PO | Imp | Ser/Plas | Pt | Nar | | CHAL | unknown | ACTIVE | GTT p 100 g Glc PO SerPl-Ir
49688-5 | Glucose tolerance^post 75 g glucose PO | Imp | Ser/Plas | Pt | Nar | | CHAL | unknown | ACTIVE | GTT p 75 g Glc PO SerPl-Imp
30265-3 | Glucose^1.3H post dose glucose | SCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 1.3H p Glc SerPl-sC
1492-8 | Glucose^1.5H post 0.5 g/kg glucose IV | MCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 1.5H p .5 g/kg Glc I SerPl-mCnc
1494-4 | Glucose^1.5H post 100 g glucose PO | MCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 1.5H p 100 g Glc P SerPl-mCnc
1496-9 | Glucose^1.5H post 75 g glucose PO | MCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 1.5H p 75 g Glc PO SerPl-mCnc
55351-1 | Glucose^1.5H post 75 g glucose PO | SCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 1.5H p 75 g Glc PO
20440-4 | Glucose^1.5H post dose glucose | MCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 1.5H p Glc SerPl-m
14752-0 | Glucose^1.5H post dose glucose | SCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 1.5H p Glc SerPl-sC
30266-1 | Glucose^1.6H post dose glucose | SCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 1.6H p Glc SerPl-sC
40286-7 | Glucose^105M post dose glucose | SCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 105M p Glc SerPl-s
1498-5 | Glucose^10M post 0.5 g/kg glucose IV | MCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 10M p .5 g/kg Glc I SerPl-mCnc
48984-9 | Glucose^10M post dose glucose | MCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 10M p Glc SerPl-mC
32359-2 | Glucose^10M post dose glucose | SCnc | Ser/Plas | Pt | Qn | | CHAL | unknown | ACTIVE | Glucose 10M p Glc SerPl-sC
Search generated 602 hits in 0.025 secs.
Copyright© 2010 Regenstrief Institute Inc.

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

The NEW ENGLAND JOURNAL of MEDICINE

February 10, 2011. Volume 364: 498-9

Perspective

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.[3] In 2009, the FDA gave the Harvard Pilgrim Health Care Institute the lead role

HugeDomains.com
Shop for over 200,000 Premium Domains

Questions? We're here to help! Call today:
1-303-893-0552

Home | Categories | FAQs | About Us | Contact Us | Shopping Cart

Get your domain name today, we make it easy

Search: Enter Keyword or Phrase [Search]

MiniSentinel.com is for sale (Mini Sentinel)

Click here to buy MiniSentinel.com for **$1,995**

Create a blog, promote your business, or build a site for your personal use.
Your web address is memorable and uniquely your own.

Buy Now

Only $1,995
Call us for more information: 1-303-893-0552

Shop with confidence - return any domain within 30 days

30 Day Satisfaction Guarantee! Learn More

HugeDomains.com
Shop for over 250,000 Premium Domains

Questions? We're here to help! Call today:
1-303-893-0552

Home | Categories | FAQs | About Us | Contact Us | Shopping Cart

Get your domain name today, we make it easy

Search: Enter Keyword or Phrase [Search]

MiniSentinel.com is for sale (Mini Sentinel)

Click here to buy MiniSentinel.com for **$2,395**

Create a blog, promote your business, or build a site for your personal use.
Your web address is memorable and uniquely your own.

Buy Now

Only $2,395
Call us for more information: 1-303-893-0552

Shop with confidence - return any domain within 30 days

30 Day Satisfaction Guarantee! Learn More

Thank you