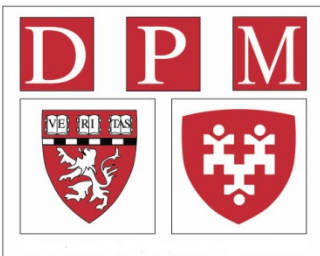


Distributed Systems for Sharing Clinical Research Information

Richard Platt
Harvard Pilgrim Health Care Institute
Harvard Medical School
October 4, 2012



Barriers and threats to data sharing

- Privacy
- Proprietary concerns
- Cost and complexity of creating a shared resource
- Inadvertent disclosure

Barriers and threats to data sharing

- Privacy
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- Inadvertent disclosure
- **Invitation to litigation**

UNITED STATES COURT OF FEDERAL CLAIMS
OFFICE OF SPECIAL MASTERS

-----X

[REDACTED]

On their own right and as best friends of their son

[REDACTED]

No. [REDACTED]
Patricia E.
Campbell-Smith
Special Master

Petitioners,

v.

SECRETARY OF HEALTH AND
HUMAN SERVICES,

Respondent.

-----X

MOTION FOR AUTHORITY TO ISSUE SUBPOENAE

MOTION TO COMPEL ACCESS TO
THE VACCINE SAFTY DATA LINK

Platt's 2nd law of collaboration

- Don't take possession of someone else's data that a third party might subpoena



Query Health: Distributed Population Queries

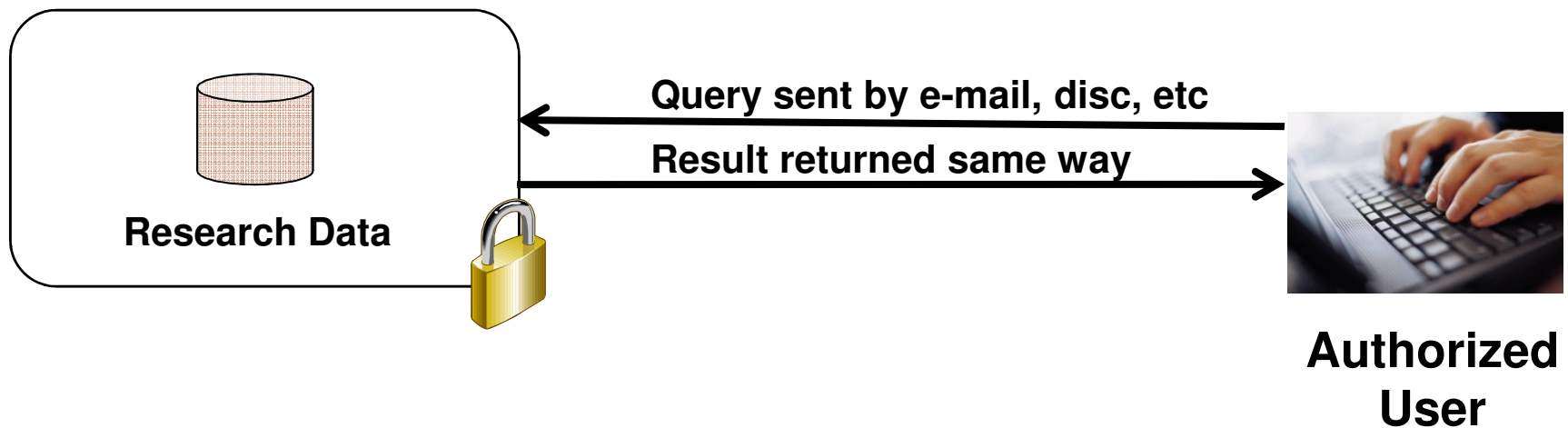


“Send questions to the data!”

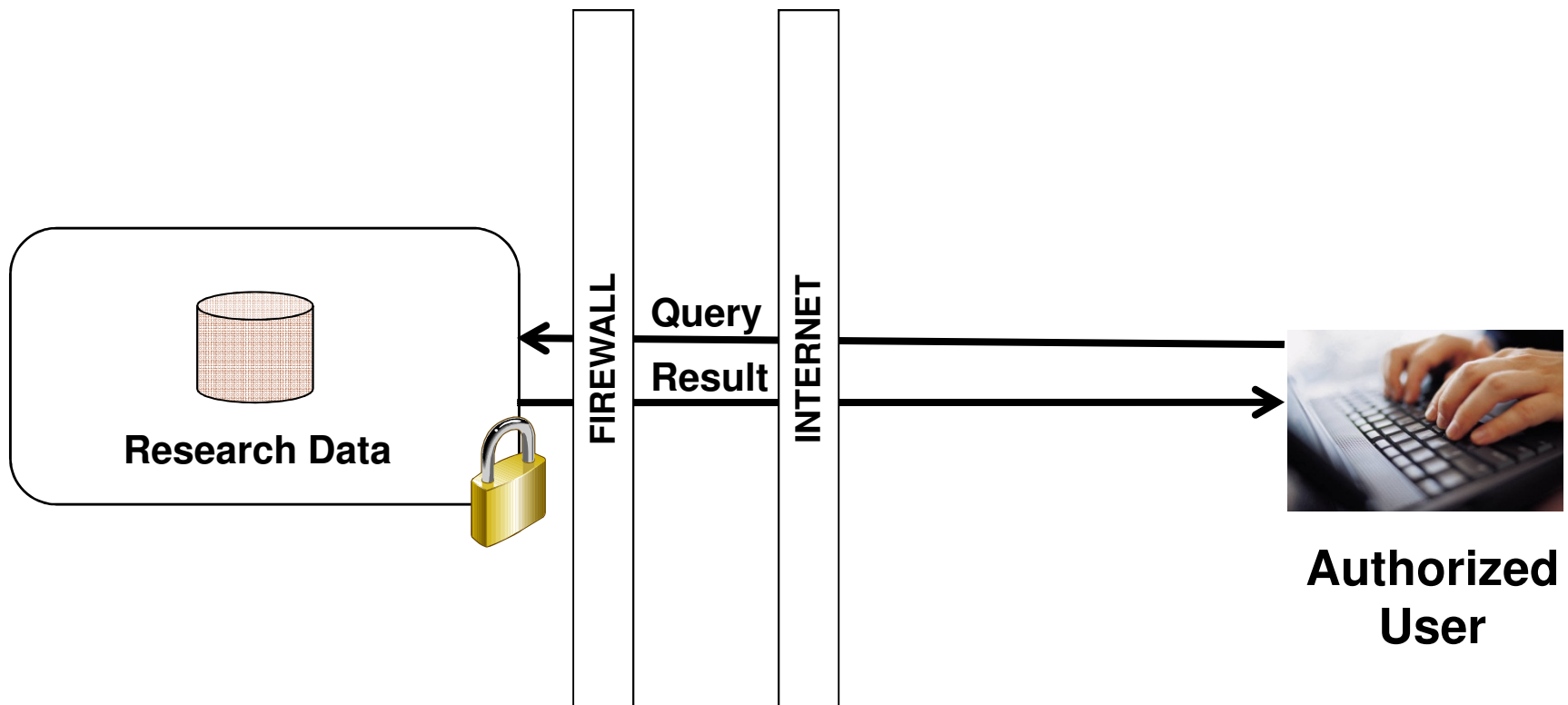
What is a question (query)?

- An analysis program that can execute on a remote data set

Analysis from a distance

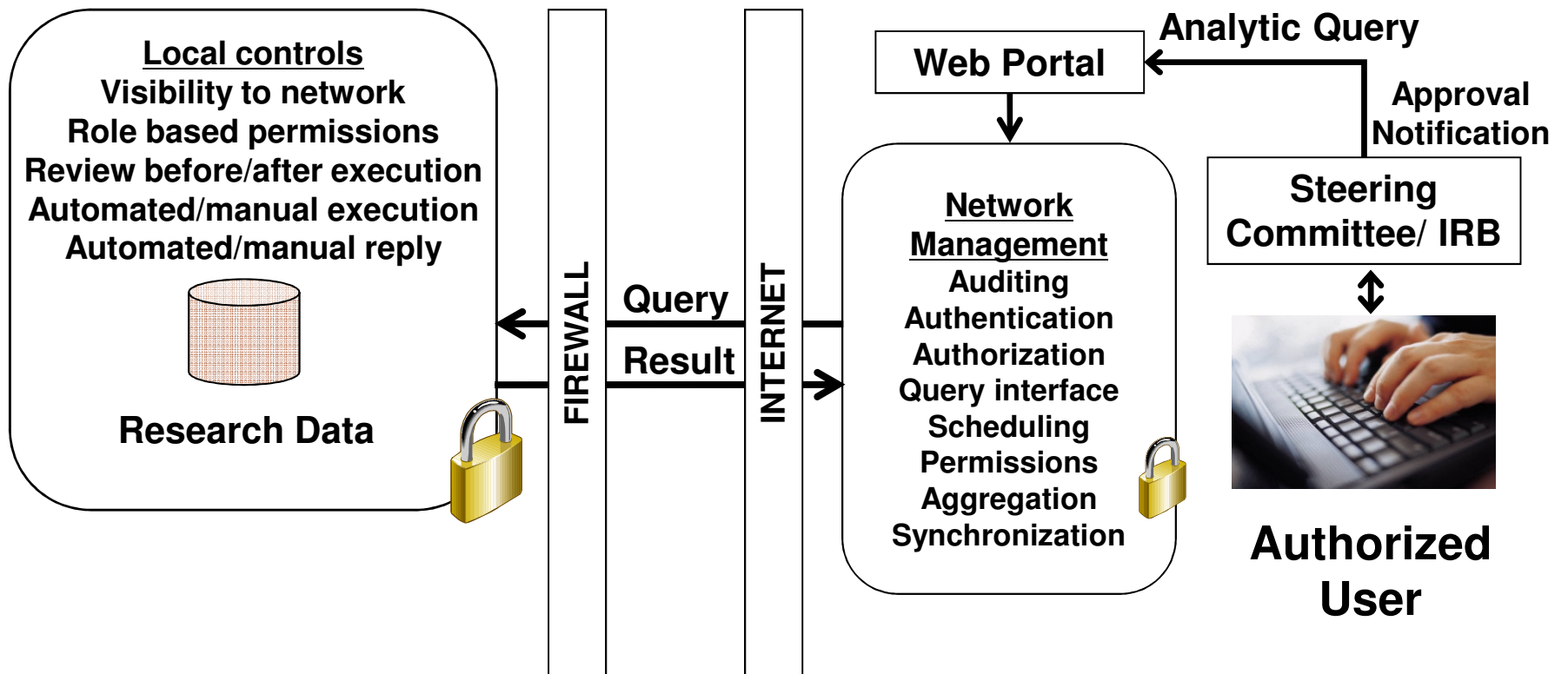


Analysis from a distance

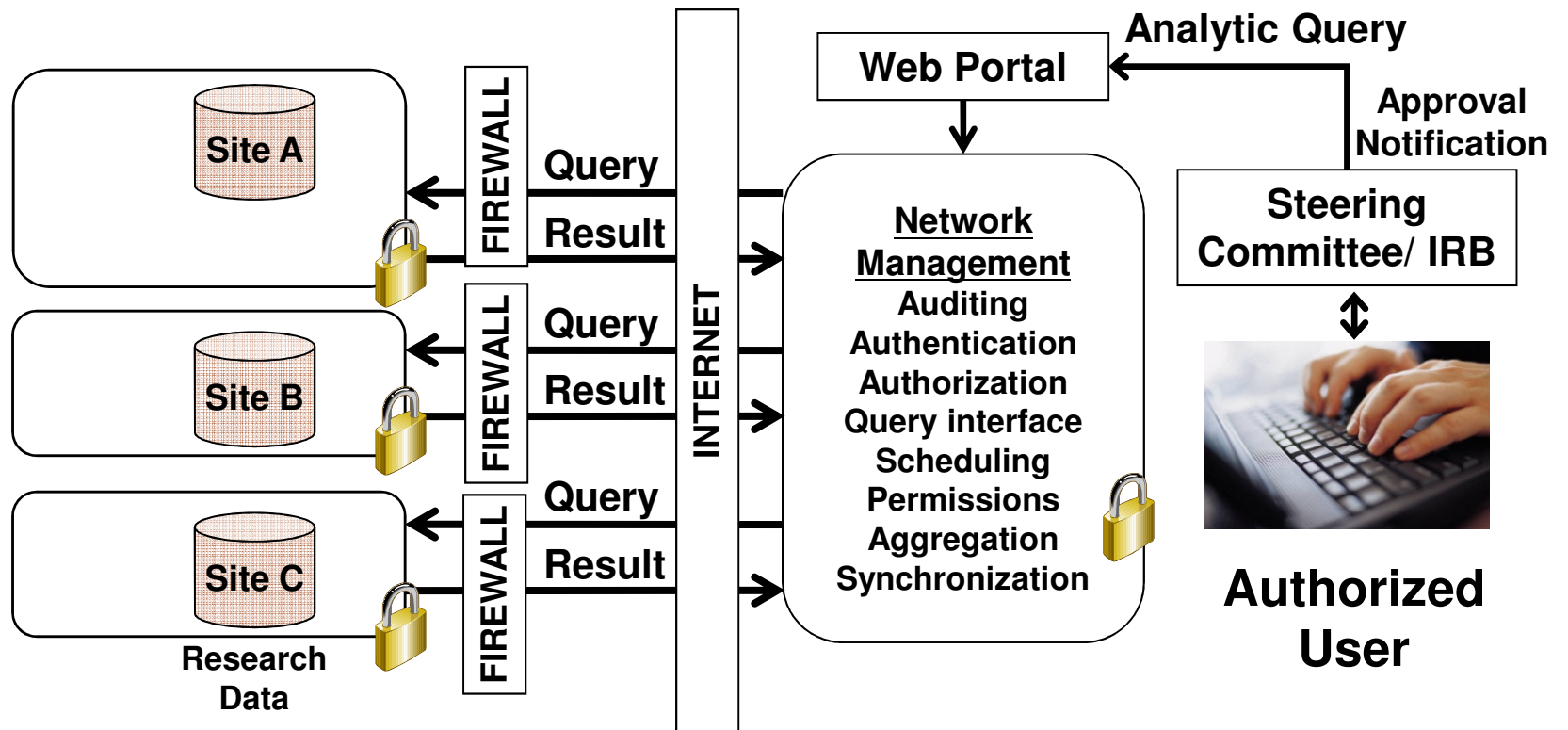


Analysis from a distance: protected

Add oversight, security and local control

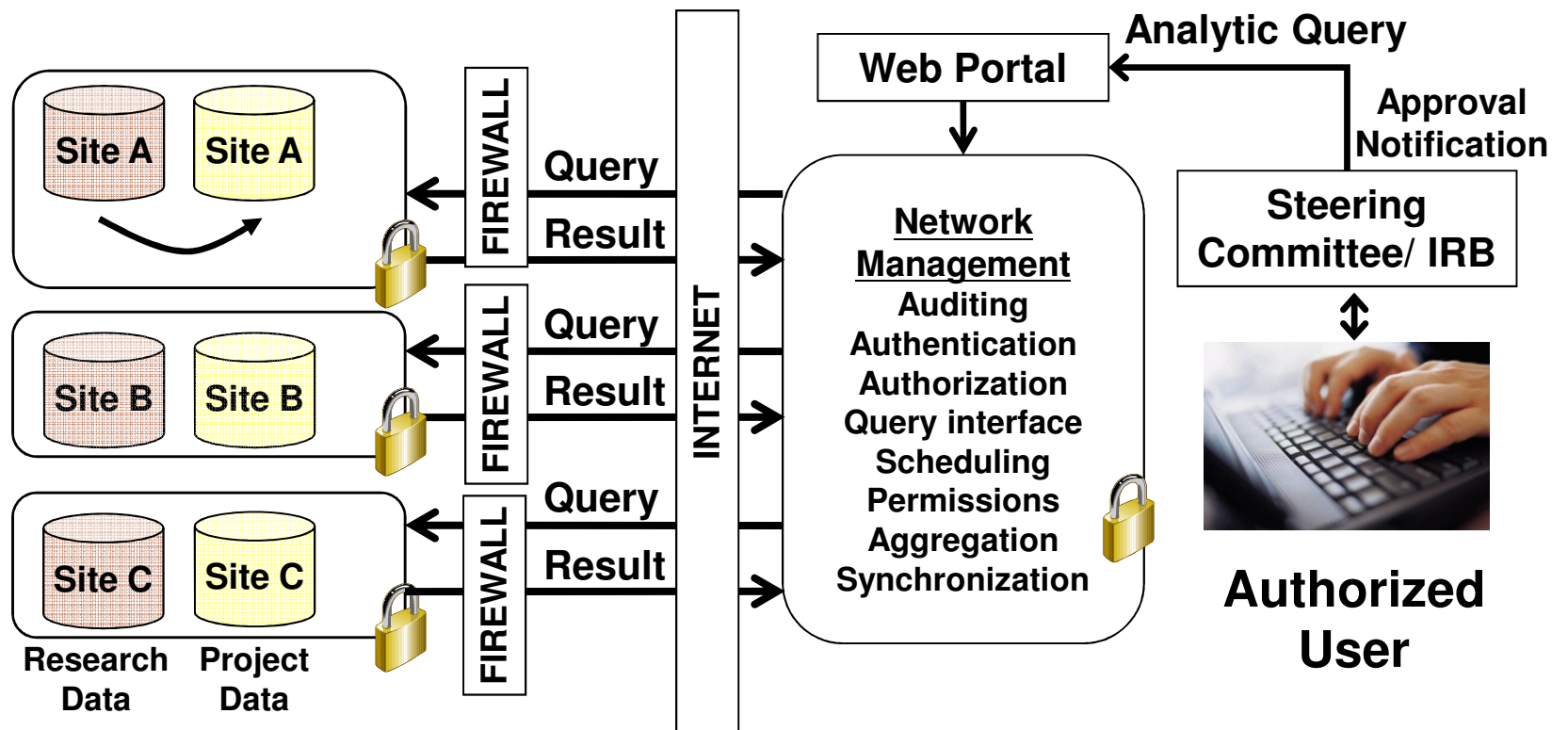


Analysis from a distance: multiple sites



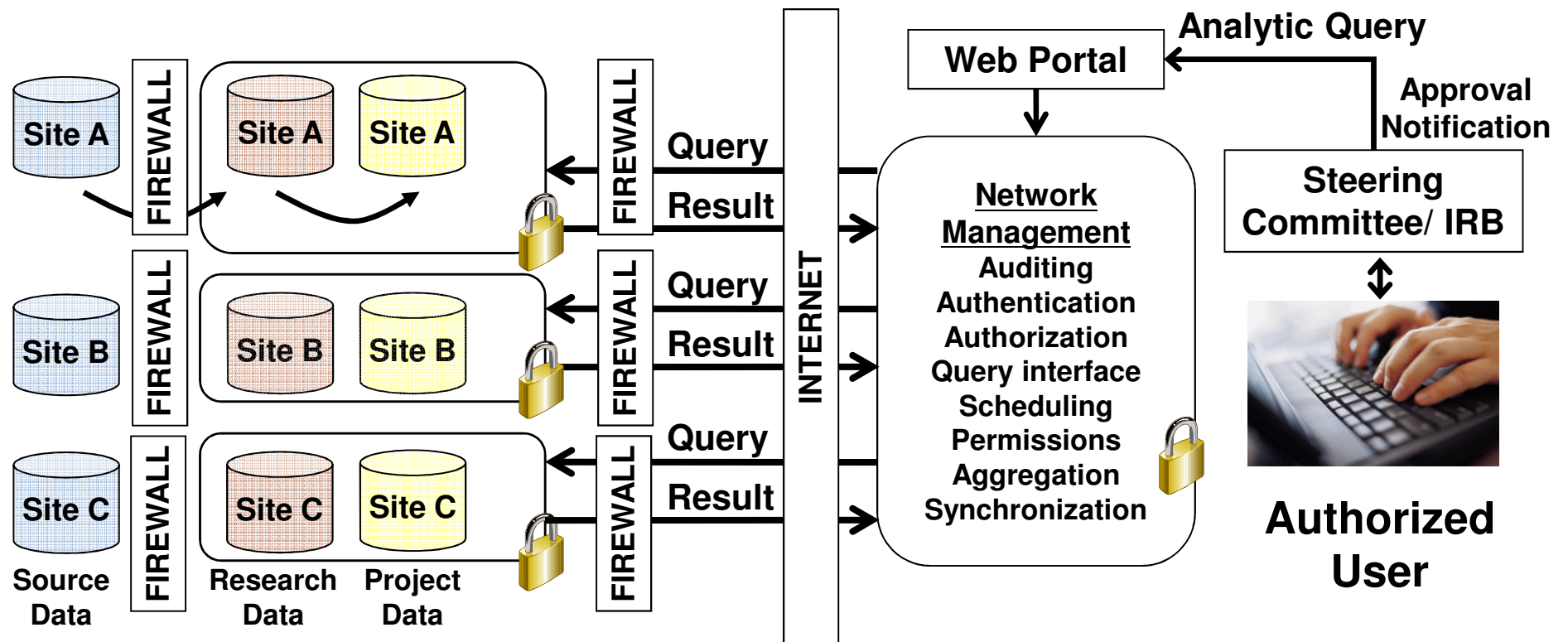
Analysis from a distance: multiple sites

Queries can be restricted to project data derived from a larger research data set

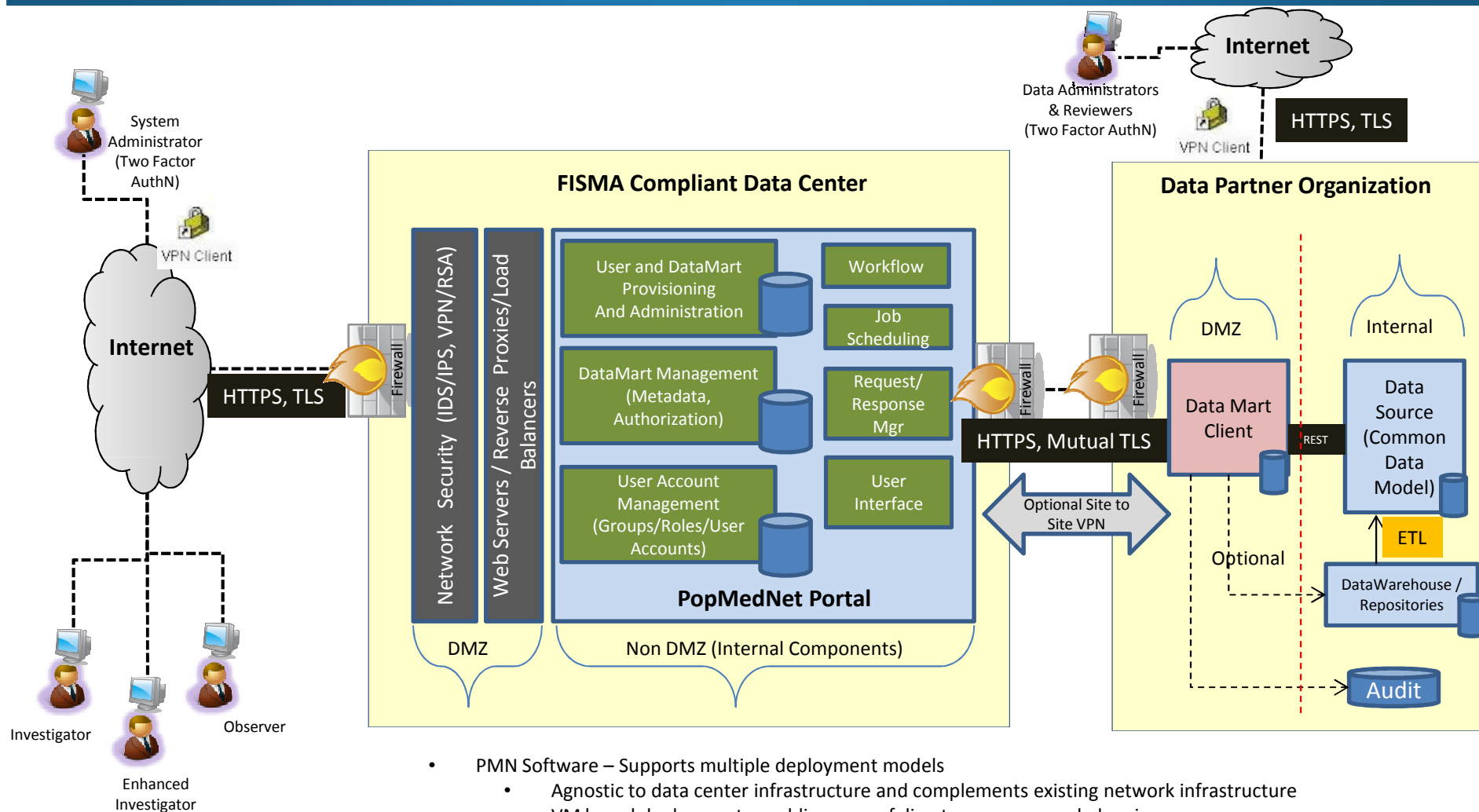


Analysis from a distance: multiple sites

Research data set is derived from routinely collected electronic health data



PopMedNet Architecture – Deployment Overview



- PMN Software – Supports multiple deployment models
 - Agnostic to data center infrastructure and complements existing network infrastructure
 - VM based deployments enabling ease of disaster recovery and planning
 - Seamless overlay of VPN Connections (Remote Access, Site to Site, Two Factor User Authentication)
 - Supports consolidation of remote sites into the data center for central management (Data Partner Components can be hosted in a central data center similar to the PMN Portal)
 - Secure End to End connection (Encrypted Transport using X.509 certificates)
 - Supports industry standard RBAC configuration for users
 - Supports Data Source provisioning based on RBAC and additional data source specific metadata
 - Data Partners execute queries using PULL model instead of PUSH model

FDA Mini-Sentinel Partner Organizations

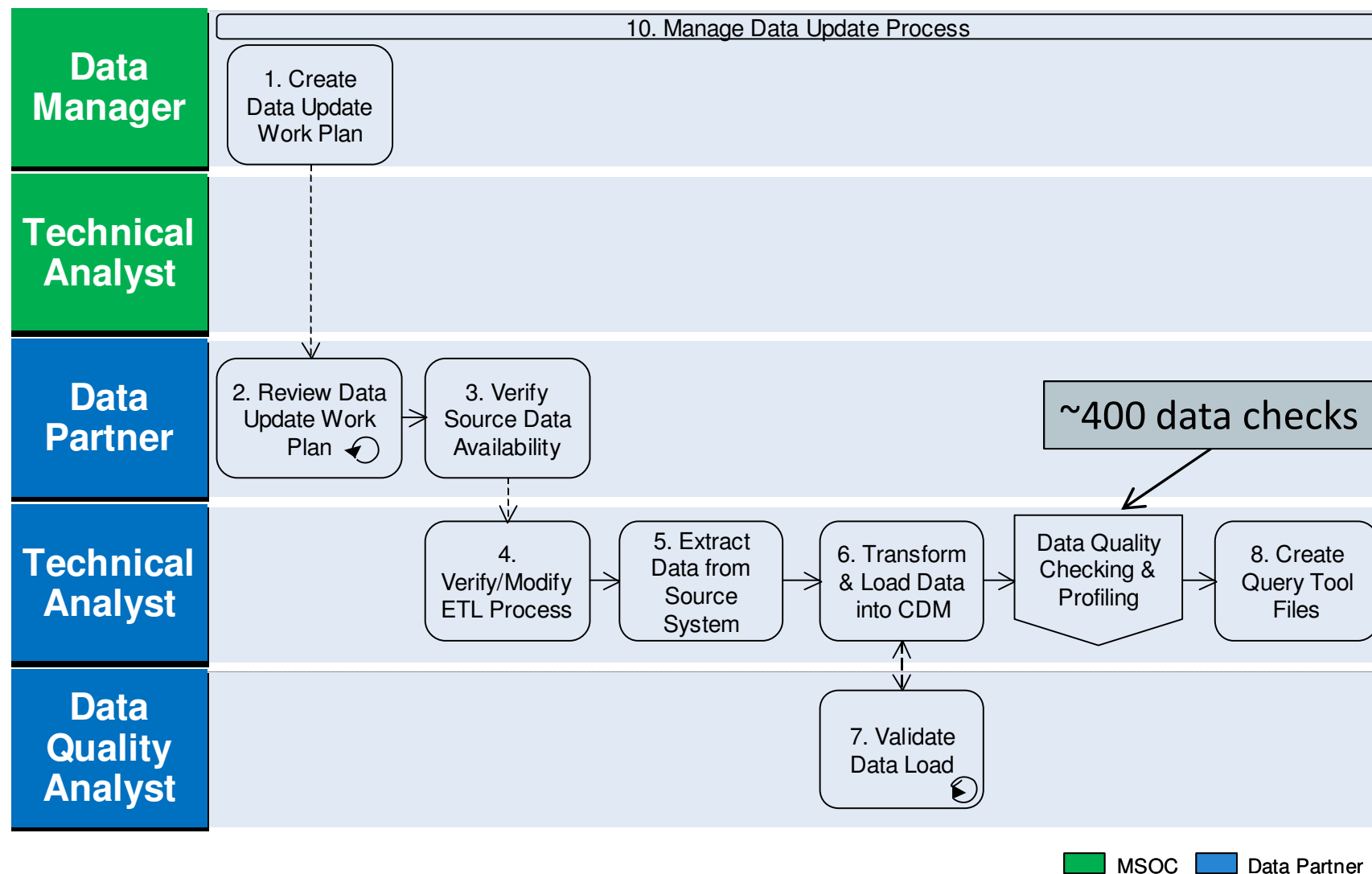


Mini-Sentinel Distributed Database

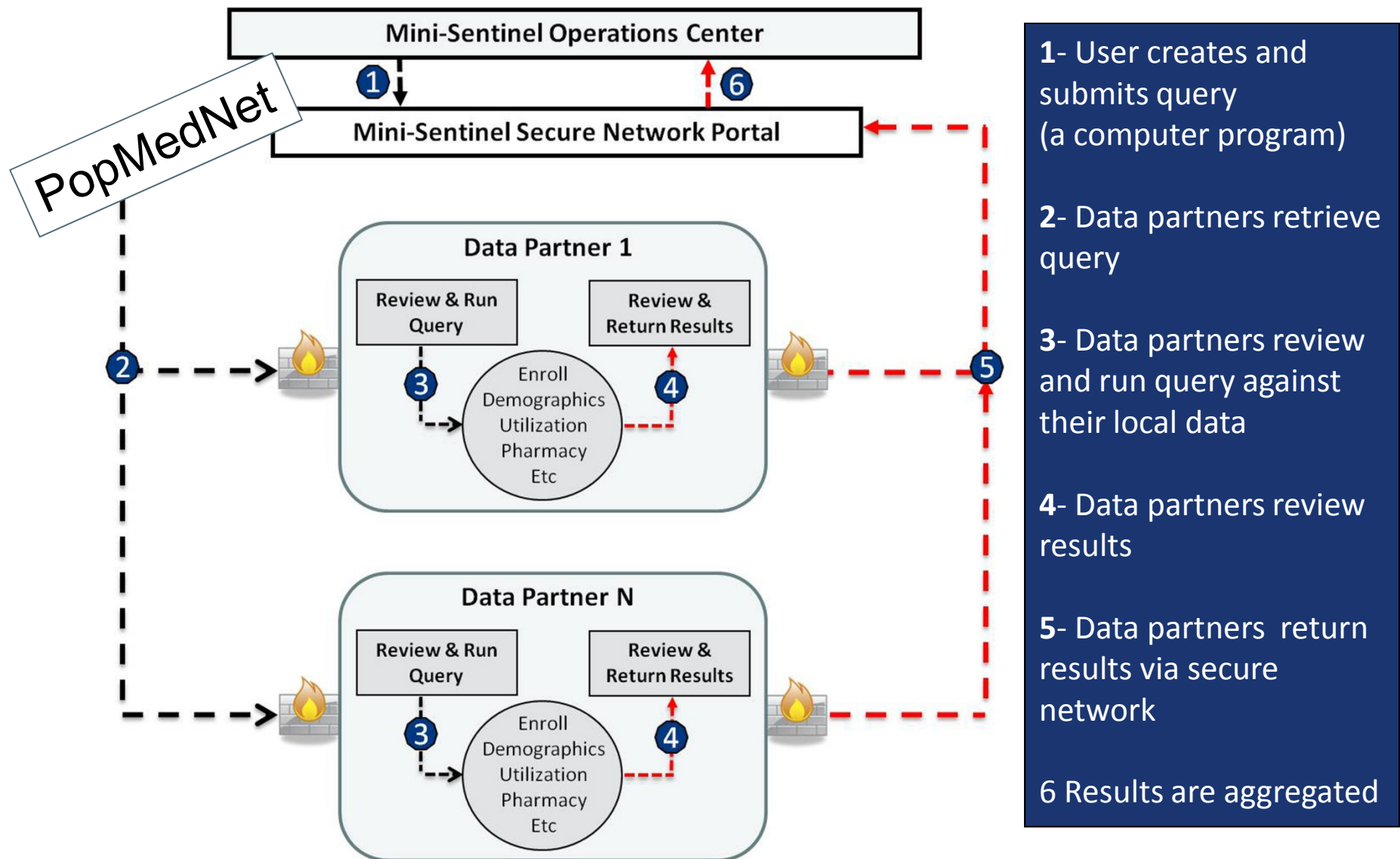
- ❑ Populations with well-defined person-time for which most medically-attended events are known
- ❑ 126 million individuals*
 - 345 million person-years of observation time
- ❑ 3 billion dispensings
- ❑ 2.4 billion unique encounters
 - 40 million acute inpatient stays
- ❑ 13 million people with ≥ 1 laboratory test result

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

Mini-Sentinel Data Refreshes



Mini-Sentinel Distributed Analysis



Angioedema events and drugs that target the renin-angiotensin-aldosterone system

A Mini-Sentinel protocol-based assessment

Mini-Sentinel angioedema workgroup

Name	Affiliation	Role
Marsha Reichman	OSE/CDER/FDA	Co-Lead
Monika Houstoun	OSE/CDER/FDA	Co-Lead
Sean Hennessy	University of Pennsylvania	Co-Lead
Darren Toh	Harvard Pilgrim Health Care Institute	Co-Lead
Mark Levenson	OTS/CDER/FDA	Member
Xiao Ding	OTS/CDER/FDA	Member
Azadeh Shoaibi	OMP/CDERFDA	Member
Carolyn McCloskey	OSE/CDER/FDA	Member
Gwen Zornberg	OSE/CDER/FDA	Member
Eileen Wu	OSE/CDER/FDA	Member
Mary Ross Southworth	OND/CDER/FDA	Member
Lingling Li	Harvard Pilgrim Health Care Institute	Member
Adrian Hernandez	Duke University School of Medicine	Member

Question

- ☐ Are ACEIs, ARBs or aliskiren associated with similar risks of angioedema when compared with a common referent group, β -blockers?

Cohort

- ❑ Individuals aged ≥ 18 years with a first Rx of an oral ACEIs, ARBs, aliskiren, or β -blockers in 2001-2010
- ❑ Index date: Dispensing date of first Rx of a drug of interest
- ❑ Additional eligibility criteria
 - ≥ 183 days continuous enrollment with pharmacy & medical benefits prior to the index date
 - No Rx of any study drugs in 183 days prior to the index date
 - No diagnosis of angioedema in 183 days prior to the index date
 - No initiation of more than one drug of interest on the index date

Outcome

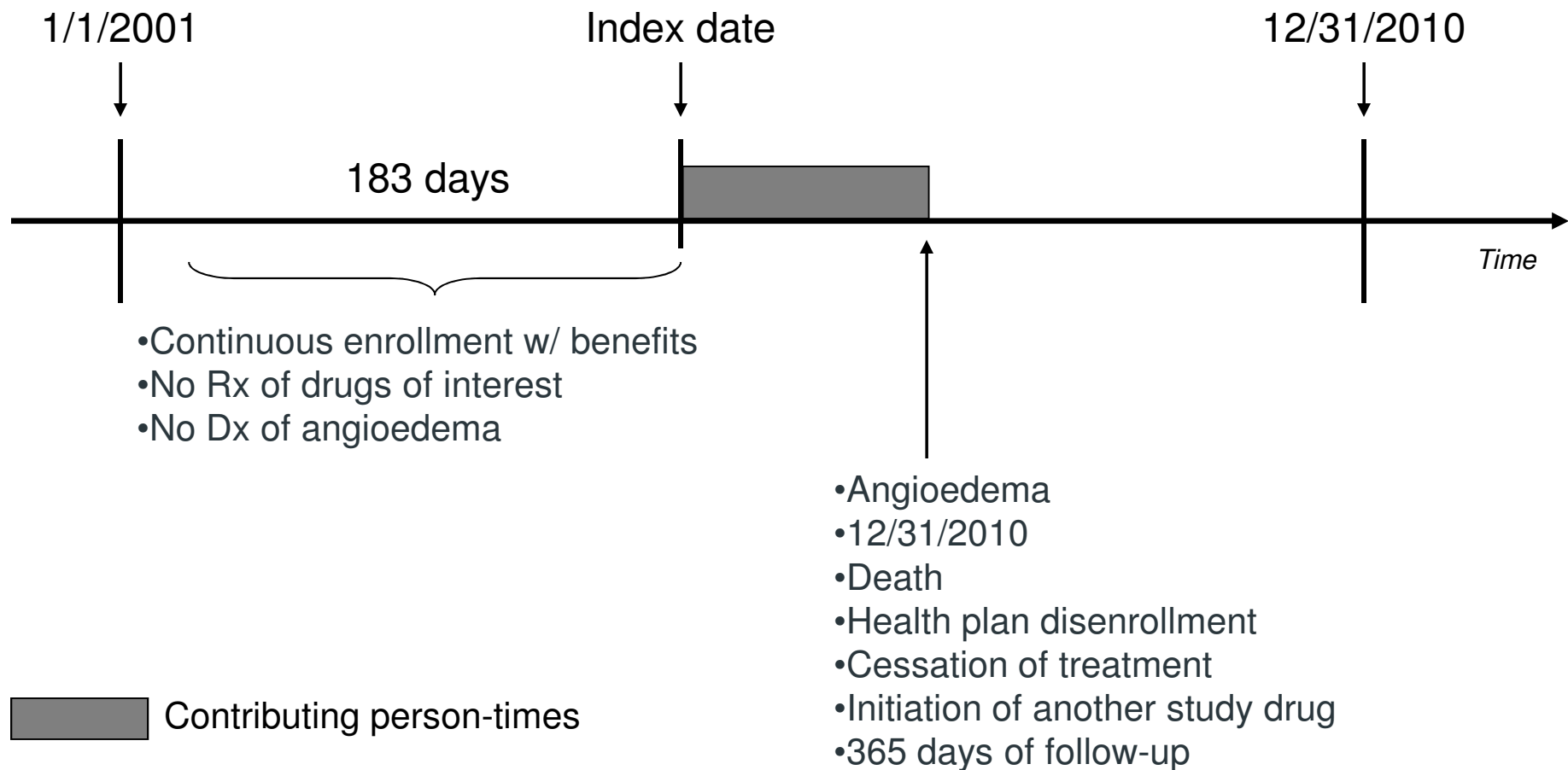
❑ **Primary outcome – Angioedema**

- ICD-9-CM code 995.1 in any position during an outpatient, inpatient, or emergency department visit (PPV 90% to 95%) (Brown et al 1996 & Miller et al 2008)

❑ **Secondary outcome – Serious angioedema**

- Angioedema w/ airway obstruction requiring inpatient care
- Inpatient ICD-9-CM code 995.1 *plus* a code indicating ICU admission, intubation, tracheostomy, or laryngoscopy occurring within two days of the date of hospital admission

Follow-up



Potential confounders

Confounder*	Categorization
Age as of the index date	18-45, 45-54, 55-64, ≥65 yrs
Sex	Male/Female
Diagnosis of	
Allergic reactions	Yes/No
Diabetes	Yes/No
Heart failure	Yes/No
Ischemic heart disease	Yes/No
Prescription NSAID use	Yes/No

*Identified during the 183-day baseline period prior to the index date

Statistical analysis

□ Descriptive analysis

- Baseline characteristics
- Unadjusted incidence and incidence rate

□ Statistical analysis

- Pair-wise comparison with β -blockers as referent group
- Site-adjusted and Propensity Score-adjusted HRs and 95% CIs
- Propensity Scores calculated at each site; common model
- Mini-Sentinel-wide estimates
 - Case-centered logistic regression* (primary)
 - Inverse variance-weighted meta-analysis

*Fireman et al, *Am J Epidemiol* 2009;170:650-656

Secondary & sensitivity analysis

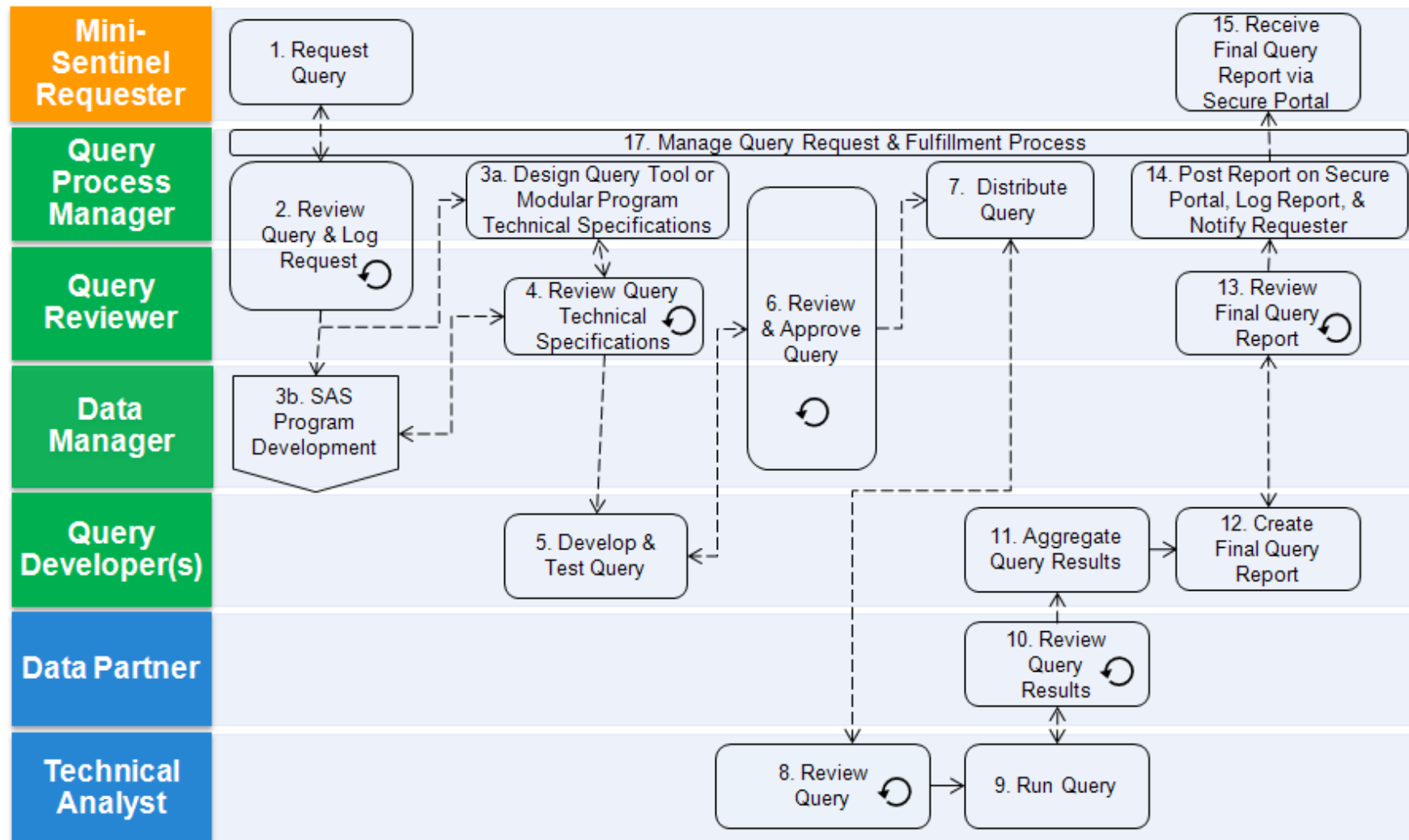
☐ Stratified analysis

- Age group
- Sex
- Follow-up period

☐ Sensitivity analysis

- 365-day look-back period
- Restricted to inpatient and ED diagnosis of angioedema
- Restricted to data after aliskiren approval

Mini-Sentinel Query Fulfillment SOP



MSOC Data Partner MS Collaborator

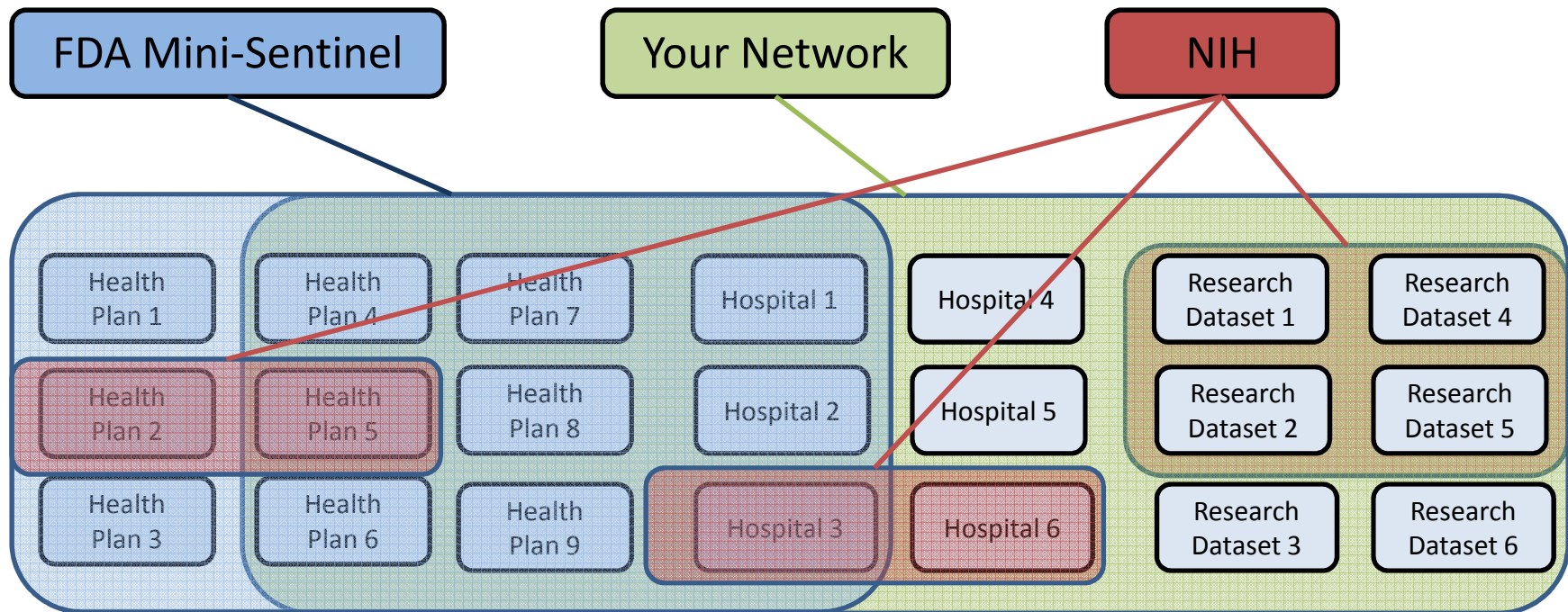
Data sharing

- ☐ None!
- ☐ No person level data was exchanged

Information sharing

- ☐ Complete!
- ☐ Every analysis of interest was performed

Multiple Networks Sharing Infrastructure



- Each organization can choose to participate in multiple networks
- Each network controls its governance and coordination
- Networks share infrastructure, data curation, analytics, lessons, security, software development

NIH Distributed Research Network

of the Health Care Systems Research Collaboratory

