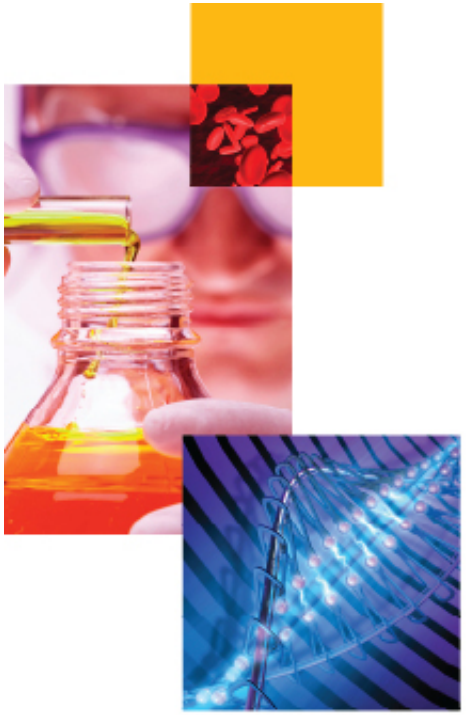

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP

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Observational Databases & Observational Medical Outcomes Partnership

Patrick Ryan, GlaxoSmithKline
on behalf of
Paul Stang, PhD, Johnson & Johnson R&D
and
The Observational Medical Outcomes Partnership (OMOP)

If You Make It Through The Hour, You May Hear About….

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- Observational data and its emerging place in the universe
- OMOP governance and research plan
- How OMOP will inform Sentinel Initiative
- Some of the key interesting bits for quantitative folks
  - Why should you care
  - Why should you get involved

FDAAA's Impact on Pharmacovigilance

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SEC. 905. ACTIVE POSTMARKET RISK IDENTIFICATION AND ANALYSIS.

(a) IN GENERAL.—Subsection (k) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) is amended by adding at the end the following:

"(3) ACTIVE POSTMARKET RISK IDENTIFICATION.—

"(A) DEFINITION.—In this paragraph, the term 'data' refers to information with respect to a drug approved under this section or under section 351 of the Public Health Service Act, including claims data, patient survey data, standardized analytic files that allow for the pooling and analysis of data from disparate data environments, and any other data deemed appropriate by the Secretary.

"(B) DEVELOPMENT OF POSTMARKET RISK IDENTIFICATION AND ANALYSIS METHODS.—The Secretary shall, not later than 2 years after the date of the enactment of the Food and Drug Administration Amendments Act of 2007, in collaboration with public, academic, and private entities—

"(i) develop methods to obtain access to disparate data sources including the data sources specified in subparagraph (C);

"(ii) develop validated methods for the establishment of a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with the goals of including, in aggregate—

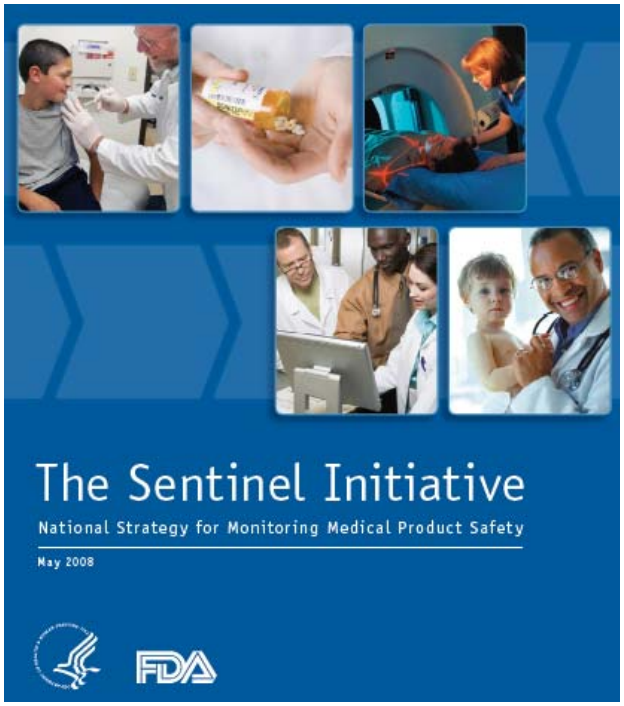
"(I) at least 25,000,000 patients by July 1, 2010; and

"(II) at least 100,000,000 patients by July 1, 2012; and

"(iii) convene a committee of experts, including individuals who are recognized in the field of protecting data privacy and security, to make recommendations to the Secretary on the development of tools and methods for the ethical and scientific uses for, and communication of, postmarketing data specified under subparagraph (C), including recommendations on the development of effective research methods for the study of drug safety questions.

"(C) ESTABLISHMENT OF THE POSTMARKET RISK IDENTIFICATION AND ANALYSIS SYSTEM.—

- SEC 905 establishes SENTINEL network of distributed observational databases (administrative claims and electronic health records) to monitor the effects of medicines post-approval



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Observational Medical Outcomes Partnership

Midwest Biopharmaceutical Statistics Workshop

May 2009

Observational Medical Outcomes Partnership (OMOP)

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A public-private partnership to serve the public health by testing whether multi-source observational data can improve our ability to assess drug safety and benefits. The design was developed through a Public-Private Partnership among industry, FDA and FNIH.

- **OMOP Objectives**
  - To determine the feasibility of assembling the required data into an infrastructure that enables active, systematic monitoring of observational data
  - To determine value of using observational data to identify and evaluate the safety and benefits of prescription drugs, as a supplement to currently available tools
  - To test required governance structures
- **OMOP Phases**
  - Phase I: Feasibility of Data and Infrastructure
  - Phase II: Feasibility of Analyses
  - Phase III: Performance Measurements
  - Phase IV: Utility of Analyses and Process & Summarize Research Results

OMOP and Sentinel Initiative

- OMOP is an approved, agreed upon and defined two-year **methodological research** initiative

- OMOP's primary goal is to provide objective evidence to inform practice about using observational data for identifying and evaluating the effects of medicines
  - Data and Infrastructure
  - Methods and Interpretation
  - Governance

- OMOP research results, tools and lessons learned will be publicly available throughout the project to inform the broader research community

Research frameworks of observational pharmacovigilance research

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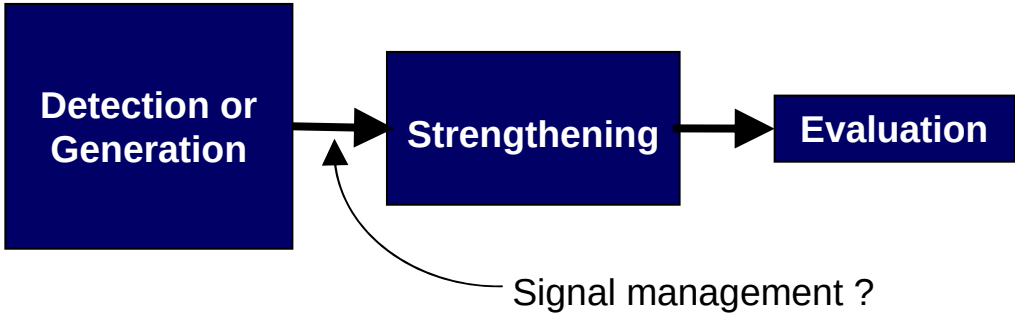
2 x 2

Process

Conditions	Identification	Evaluation
Health Outcomes of Interest (HOI)	I	II
Non-specified conditions	III	IV

Linear



- Non-specified (III)

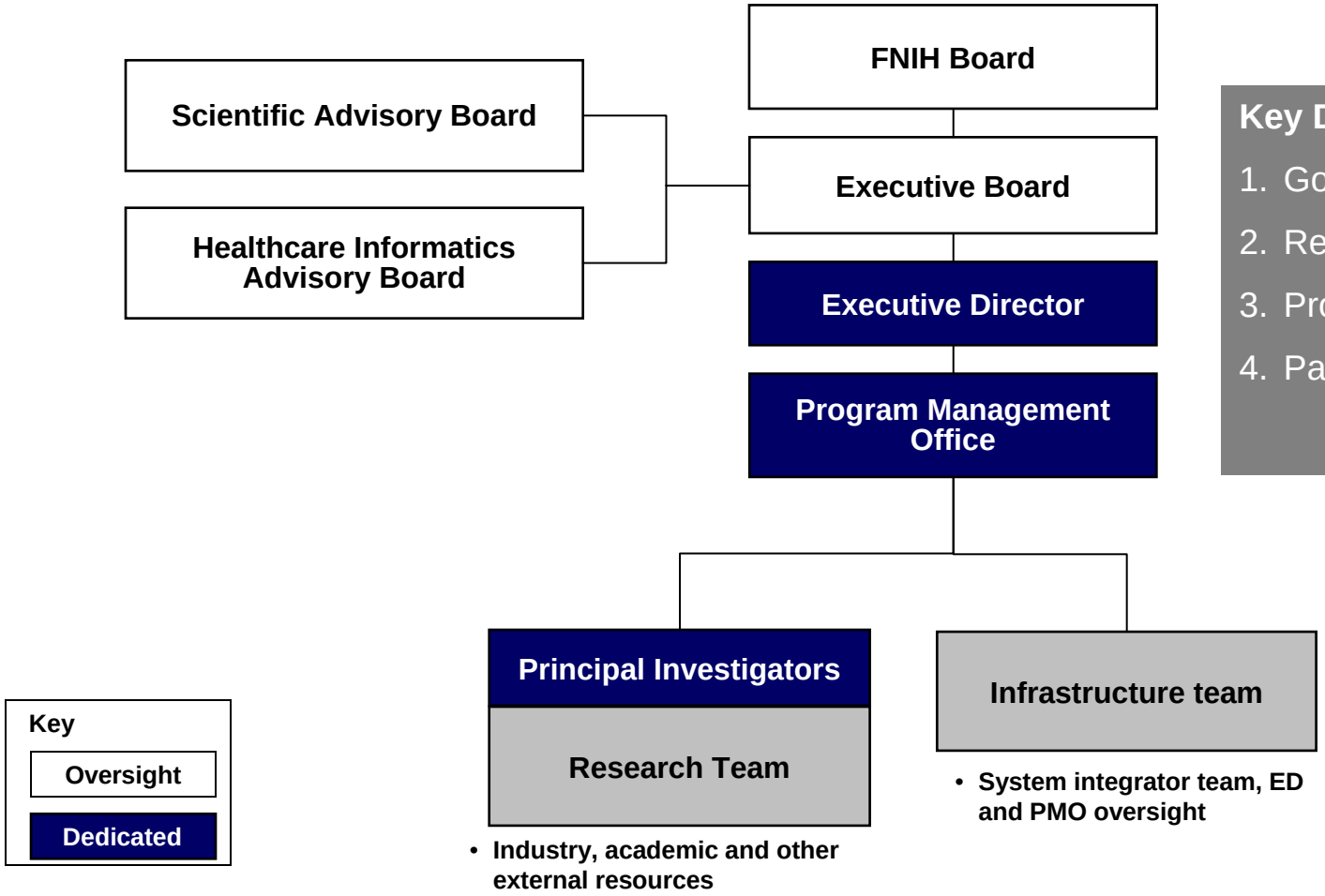
- Pre-specified HOI (I)
- Non-specified (III) subset

- Pre-specified subset (II)
- Non-specified (IV) subset

Partnership Structure

Governance Provided by an Executive Board

Scientific and Informatics advisory boards to inform decisions



- Industry, academic and other external resources
- System integrator team, ED and PMO oversight

Key Design Elements:

1. Governance and Oversight
2. Research Leadership
3. Program Management
4. Partners & Collaborators

Executive Board

A multi-stakeholder group, the OMOP Executive Board oversees the operation of the Partnership.

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP
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Janet Woodcock, MD
Director, Center for Drug Evaluation and Research, Food and Drug Administration
Chair, Observational Medical Outcomes Partnership Executive Board

Rebecca Burkholder
Vice President of Health Policy, The National Consumers League

Sherine Gabriel, MD, MSc
Professor of Medicine and Epidemiology, The Mayo Clinic

Cynthia Gilman, JD
Special Assistant to the President for Advancement of Cancer Research and Collaborative Partnerships, Henry Jackson Foundation

Jesse L. Goodman, MD, MPH
Director, Center for Biologics Evaluation and Research, Food and Drug Administration

Ronald L. Krall, MD
Former Senior Vice President and Chief Medical Officer, GlaxoSmithKline

Richard Platt, MD, MSc
Professor and Chair of the Department of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim Health Care

Stephen Spielberg, MD, PhD
Marion Merrell Dow Chair in Pediatric Pharmocogenomics, Children's Mercy Hospital and Dean Emeritus, Dartmouth Medical School

Brian Strom, MD, MPH
George S. Pepper Professor of Public Health and Preventive Medicine; Professor of Biostatistics and Epidemiology, Medicine, and Pharmacology; Chair, Department of Biostatistics and Epidemiology; Director, Center for Clinical Epidemiology and Biostatistics; Vice Dean for Institutional Affairs, University of Pennsylvania School of Medicine
Senior Advisor to the Provost for Global Health Initiatives, University of Pennsylvania

David Wheadon, MD
Senior Vice President, Pharmaceutical Research and Manufacturers of America (PhRMA)

Research Investigators

The Principal Investigators (PIs) are the lead scientists for the OMOP project and guide and participate in the research across all four project phases

Marc Overhage, MD, PhD

Director, Medical Informatics and Research Scientist, Regenstrief Institute, Inc.

Regenstrief Professor of Medical Informatics, Indiana University School of Medicine,CEO

President of the Indiana Health Information Exchange

Paul Stang, PhD

Senior Director, Pharmacoepidemiology, Johnson & Johnson Pharmaceutical Research and Development

Abraham G. Hartzema PharmD, MSPH, PhD, FISPE

Office of Critical Path Programs, Office of the Commissioner, US Food and Drug Administration

Patrick Ryan

Manager Drug Development Sciences, GlaxoSmithKline Research and Development

OMOP Co-Investigator

Foundation for the NIH Staff

The FNIH staff are responsible for managing the day-to-day operations of the Partnership under the direction and guidance of the Partnership's Executive Board and the FNIH Board.

Thomas Scarnecchia, MS
Executive Director, Observational Medical Outcomes Partnership

Emily Welebob, RN, MS
Senior Program Manager, Research

Christian Reich, MD, PhD
Senior Program Manager, Technology

Kay Jenkins
Executive Assistant

OMOP Advisory Boards

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP
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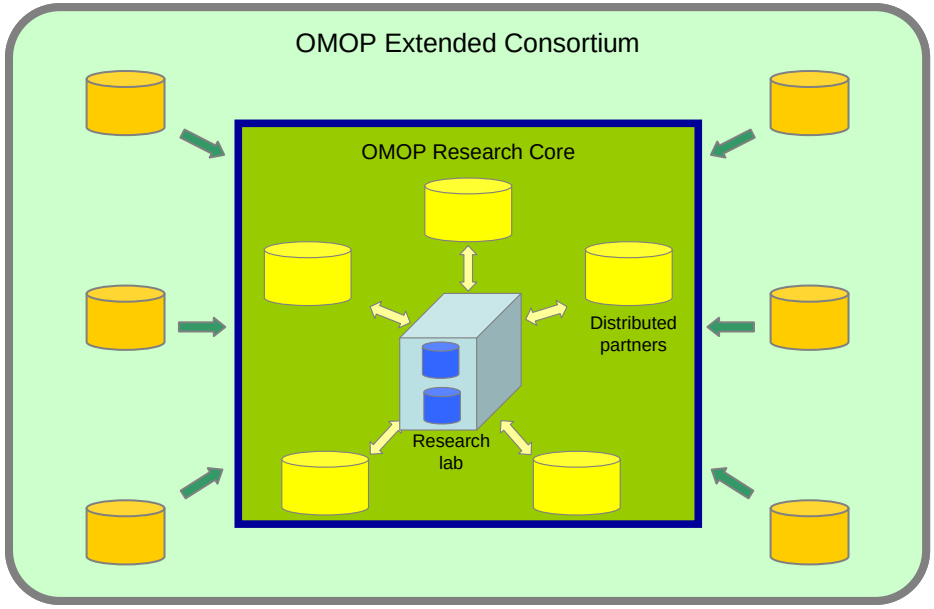
A Scientific Advisory Board (SAB) will provide independent review of and expert input into the scientific aspects of OMOP's activities.

- Andrew Bate, WHO Monitoring Center; Uppsala, Sweden
- Jesse Berlin, Johnson & Johnson
- Robert Davis, Kaiser Permanente
- Steve Findlay, Consumer Union
- Sean Hennessy, University of Pennsylvania
- Mike Katz, FDA patient representative
- Allen Mitchell, Boston University
- David Page, University of Wisconsin
- Ken Rothman, RTI Health Solutions
- Judy Staffa, FDA
- Alec Walker, WHISCON

A Health Informatics Advisory Board (HIAB) will provide independent review and expert input into the OMOP's technology governance and project requirements related to privacy and security, terminology and coding, data and data models.

- Col. Kevin Abbott
- Jeff Brown, Harvard Medical School
- Stan Huff, Intermountain Healthcare
- Diane MacKinnon, IBM (retired)
- Ken Mandl, Harvard University
- Clem McDonald, National Library of Medicine
- David Memel, Aetna
- Rob Thwaites, United BioSource Corporation

OMOP Research Community



- **OMOP Research Lab** will be used to manage analysis process across all data sources within the Research Core.

- **OMOP Research Core** is responsible for designing, developing and managing the execution of the approved research proposals.
- **Distributed Research Partners** will:
  - Implement the Common Data Model
  - Collaborate on the design of all studies
  - Execute protocols within their data environment
  - Report back summary analyses into OMOP research lab
  - Support interpretation and publication of results
- OMOP will encourage the participation of the broader scientific community as members of the **Extended Consortium.**

OMOP Timeline

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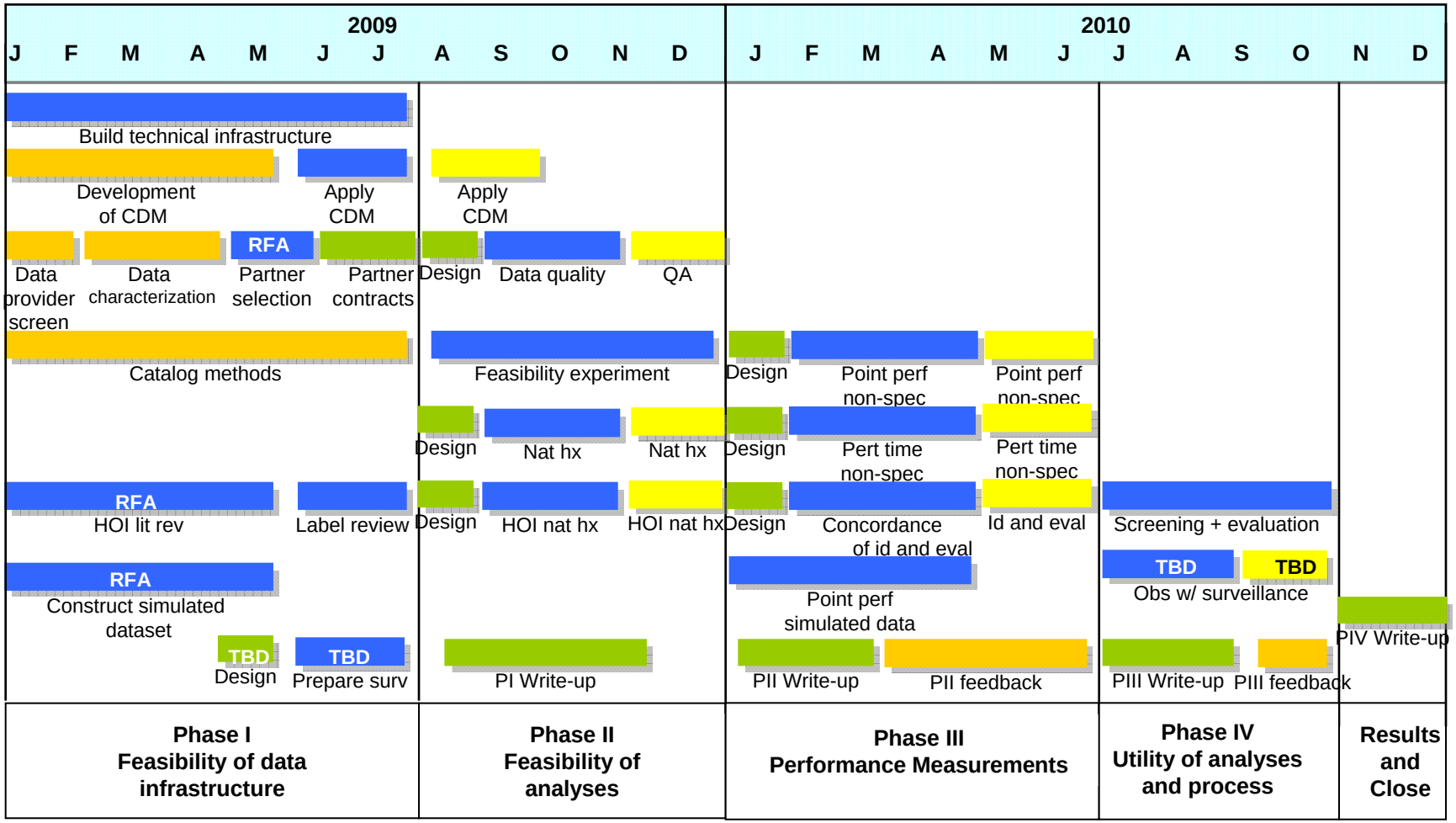

Central Research Core

Distributed Research Core only

Central and Distributed Research Core

Extended Consortium

Accomplishments

Phase 1 Research Projects

- **Common Data Model (CDM)**
  - "Points to Consider in Developing a Common Semantic Data Model and Terminology Dictionary for Observational Analyses" white paper published on website
- **Health Outcomes of Interest**
  - RFA for Health Outcomes of Interest Definitions – 2 contracts awarded
- **Simulated Data Set**
  - RFA for Simulated Data Set – 1 contract awarded
  - "Specifications for the Simulation of Observational Data to Facilitate Active Surveillance Methodological Research" drafted
- **Analysis Methods**
  - "Review of Observational Analysis Methods" white paper published on website
  - Call for participation for methods implementation and development issued
- **Data Assessments and Research Partners**
  - Completed Data Screen: 39/70 (56% response rate)
  - Completed Data Profile: 20 profiles submitted
  - RFA for Distributed Partners issued

Simulated Dataset

- OMOP will test a modest number of real observational data sources
- Observational data is poorly characterized
- Methodological research typically requires some benchmark to measure performance:
  - One research question: How well does a method correctly **identify** 'true associations' and discriminate between 'false associations'?
  - 'Truth' is often difficult to obtain in real-world observational data, as 'known' associations may not be observed in practice due to sample size, adequacy of data capture, confounding, etc.
  - Simulated data can supplement methods evaluation by providing a source with well-defined characteristics of 'true' and 'false' associations
- Simulated datasets, comprised of hypothetical persons with fictitious drug exposure and condition incidence, can be created with known characteristics that represent the types of scenarios expected in real observational sources

Possible Methods to Consideration for Exploratory Analyses

- **Epidemiologic study designs**: cohort, case-control, case-cohort, self-controlled case series, case-crossover
- **Group Sequential methods**: SPRT, maxSPRT
- **Disproportionality analysis approaches**: PRR, ROR, MGPS, empirical Bayes
- **Other data mining and surveillance:** CUSUM, Bayesian updating statistic, MUTARC, HealthMiner, PROFILE, HYPERCUBE

Particular Thorny Analysis Issues

- Managing false positives
- Multiplicity
- Thresholds for action for each method
- Replication of findings across datasets
- Interval for ‘testing’
- What is the border between surveillance and signal amplification?
- What is the ‘natural history’ of a signal?
- Conversion to a common data model- does it impact performance characteristics of methods?

How Can You Contribute?

- Register on the OMOP website and take advantage of content
  - http://omop.fnih.org
- We are harvesting
  - Brains
  - Ideas
  - Time
- Distributed Research Partners
  - Run the protocols in your own data and report it back to us
  - Participate in public forum

How to Find OMOP

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP
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http://omop.fnih.org