



The U.S. Food and Drug Administration's Sentinel System: A Post-Market Active Drug Safety Surveillance System

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Some co-authors on this abstract are employed at organizations which conduct work for government and private organizations, including pharmaceutical companies.



- The U.S. Food and Drug Administration (FDA) ensures the safety, efficacy, and security of regulated medical products.
- An efficient national drug safety surveillance system is needed to support this mission.

The Sentinel System

FDA

Sentinel

About

Studies

Methods, Data, & Tools

News & Events

Featured

Engage with Sentinel

SEARCH



Learn More About

How Sentinel Works



About



Who Is Involved



How Sentinel Gets Its Data



Key Database Statistics



FDA's Sentinel System:

**Using real-world data to
study medical product safety
and generate real-world
evidence**

What's Happening with Sentinel

About Sentinel

Engage with Sentinel

Data-Driven Impact

The Sentinel Community

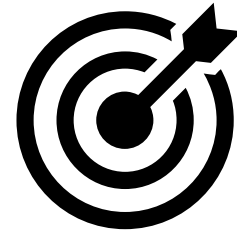
Sentinel Structure



One of FDA's post-market medical product safety surveillance systems for assessing the use and safety of regulated medical products.

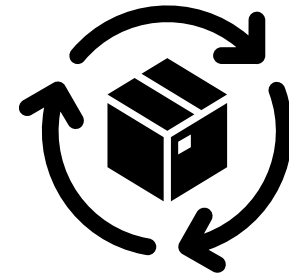
Objective

To describe the Sentinel System, its goals, implementation timeline of milestones, key components, and achievements since inception.



Methodology

We describe the FDA
Sentinel System and report
on major achievements





RESULTS

The Sentinel System

- FDA's medical product active safety surveillance system

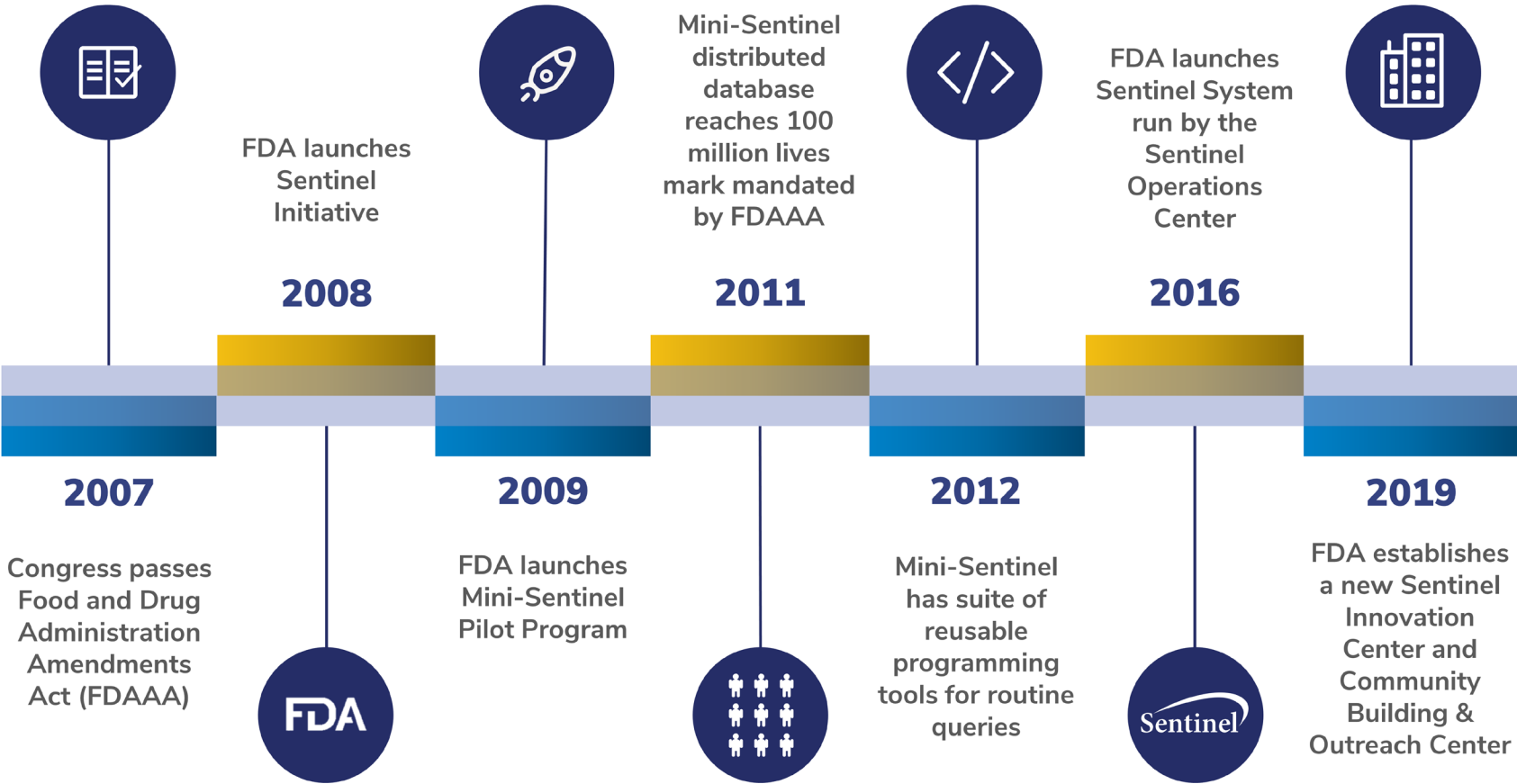
Created in response to a U.S. Congressional mandate

To assess the use and safety of regulated medical products

To develop data, informatics, and methodologic capabilities to support these activities

The Sentinel System Timeline

History of the Sentinel Initiative



Key components

Electronic healthcare data

Common data model

Distributed network of Data Partners

Pre-defined, parameterized, reusable routine querying tools

Sophisticated quality assurance process

Key components

Electronic healthcare data

Common data model

Distributed network of Data Partners

Pre-defined, parameterized, reusable routine querying tools

Sophisticated quality assurance process

Electronic Healthcare Data

- Sentinel relies on data generated from patient interactions with the U.S. healthcare system through health insurers and providers
- Principal source of data used in Sentinel is healthcare administrative claims data
- Additional types of healthcare data that complement the claims data in Sentinel include:
 - Electronic Health Records (EHRs), immunization registries, disease registries, birth and death registries

Key components

Electronic healthcare data

Common Data Model

Distributed network of Data Partners

Pre-defined, parameterized, reusable routine querying tools

Sophisticated quality assurance process



Sentinel Common Data Model

Sentinel Common Data Model

Administrative Data							Mother-Infant Linkage Data	Auxiliary Data		Feature Engineering Data
Enrollment	Demographic	Dispensing	Encounter	Diagnosis	Procedure	Prescribing	Mother-Infant Linkage	Facility	Provider	Feature Engineering
Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Mother ID	Facility ID	Provider ID	Patient ID
Enrollment Start & End Dates	Birth Date	Provider ID	Encounter ID & Type	Encounter ID & Type	Encounter ID & Type	Encounter ID	Mother Birth Date	Facility Location	Provider Specialty & Specialty Code Type	Encounter ID
Medical Coverage	Sex	Dispensing Date	Service Date(s)	Provider ID	Provider ID	Provider ID	Encounter ID & Type			Feature ID
Drug Coverage	Postal Code	Rx	Facility ID	Service Date(s)	Service Date(s)	Order Date	Mother Admission & Discharge Date			Feature
Medical Record Availability	Race	Rx Code Type	Etc.	Diagnosis Code & Type	Procedure Code & Type	Rx	Child ID			FE Code Type
	Etc.	Days Supply		Principal Discharge Diagnosis	Etc.	Days Supply	Childbirth Date			Etc.
		Amount Dispensed				Rx Route of Delivery	Mother-Infant Match Method			
						Etc.	Etc.			

Registry Data			Inpatient Data		Clinical Data		Patient-Reported Measures (PRM) Data	
Death	Cause of Death	State Vaccine*	Inpatient Pharmacy	Inpatient Transfusion	Lab Result	Vital Signs	PRM Survey	PRM Survey Response
Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Measure ID	Patient ID
Death Date	Cause of Death	Vaccination Date	Encounter ID	Encounter ID	Result & Specimen Collection Dates	Measurement Date & Time	Survey ID	Encounter ID
Date Imputed Flag	Source	Admission Date	Rx Administration Date & Time	Transfusion Administration ID	Test Type, Immediacy & Location	Height & Weight	Question ID	Measure ID
Source	Confidence	Vaccine Code & Type	National Drug Code (NDC)	Administration Start & End Date & Time	Logical Observation Identifiers Names and Codes (LOINC®)	Diastolic & Systolic BP	Etc.	Survey ID
Confidence	Etc.	Provider	Rx ID	Transfusion Product Code	Etc.	Tobacco Use & Type		Question ID
Etc.		Etc.	Route	Blood Type		Etc.		Response Text
			Dose	Etc.				Etc.
			Etc.					

*The State Vaccine table has not been in use since SCDM v6.0.

Key components

Electronic healthcare data

Common data model

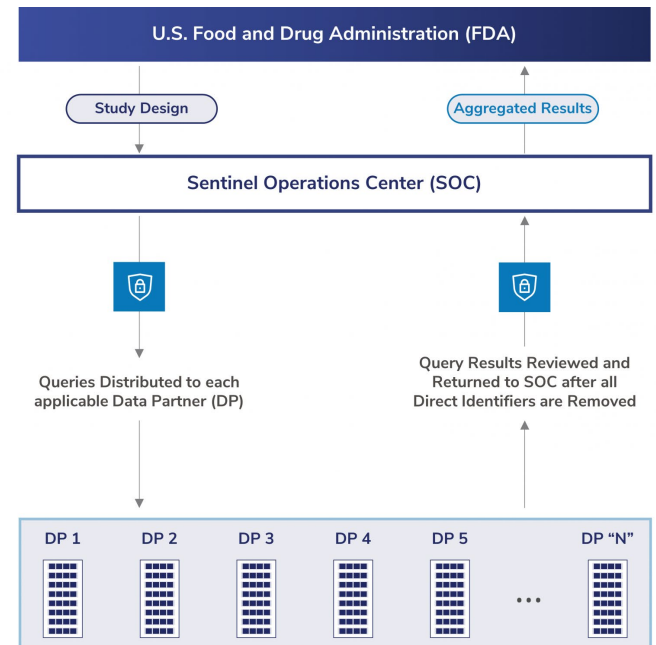
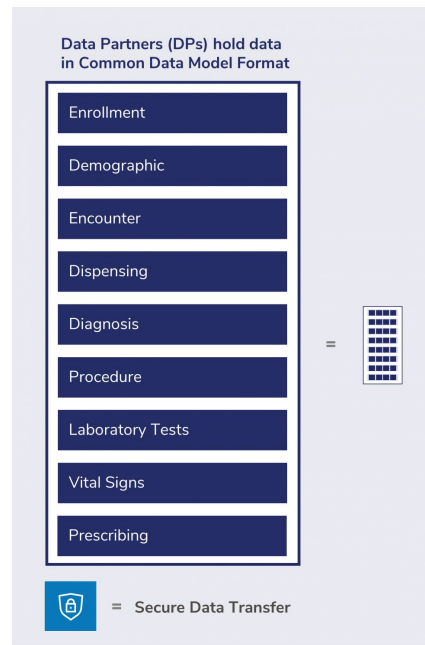
Distributed network of Data Partners

Pre-defined, parameterized, reusable routine querying tools

Sophisticated quality assurance process

Sentinel's Distributed Database

- Data Partners maintain physical and operational control over their data
- Data Partners execute standardized queries against their own data and return aggregated results to the Sentinel Operations Center
- Preserves patient privacy and institutional proprietary interests



Key components

Electronic healthcare data

Common data model

Distributed network of Data Partners

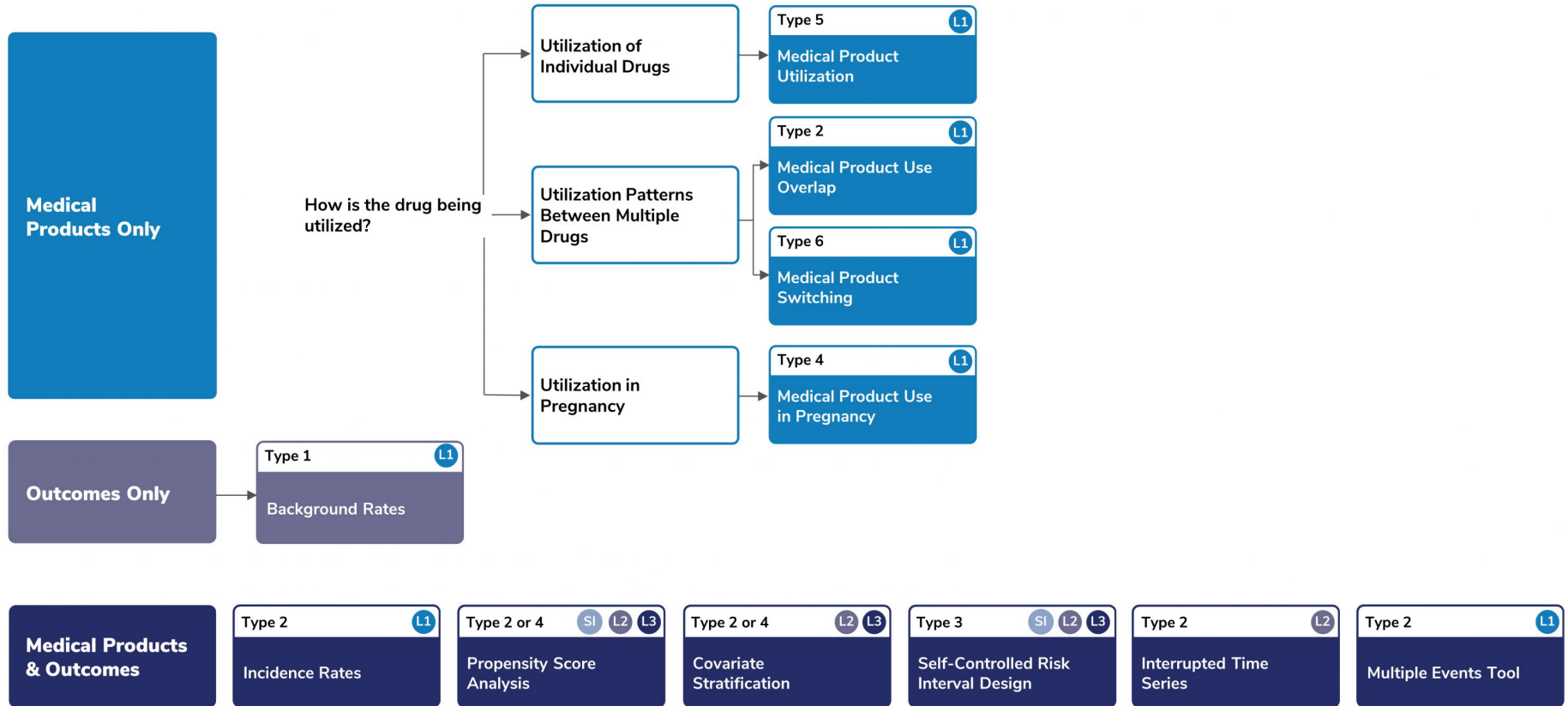
Pre-defined, parameterized, reusable routine querying tools

Sophisticated quality assurance process

Routine Querying Tools

What are you investigating?

SI Signal Identification
 L1 Level 1 Analysis
 L2 Level 2 Analysis
 L3 Level 3 Analysis



<https://www.sentinelinitiative.org/methods-data-tools/routine-querying-tools>

Key components

Electronic healthcare data

Common data model

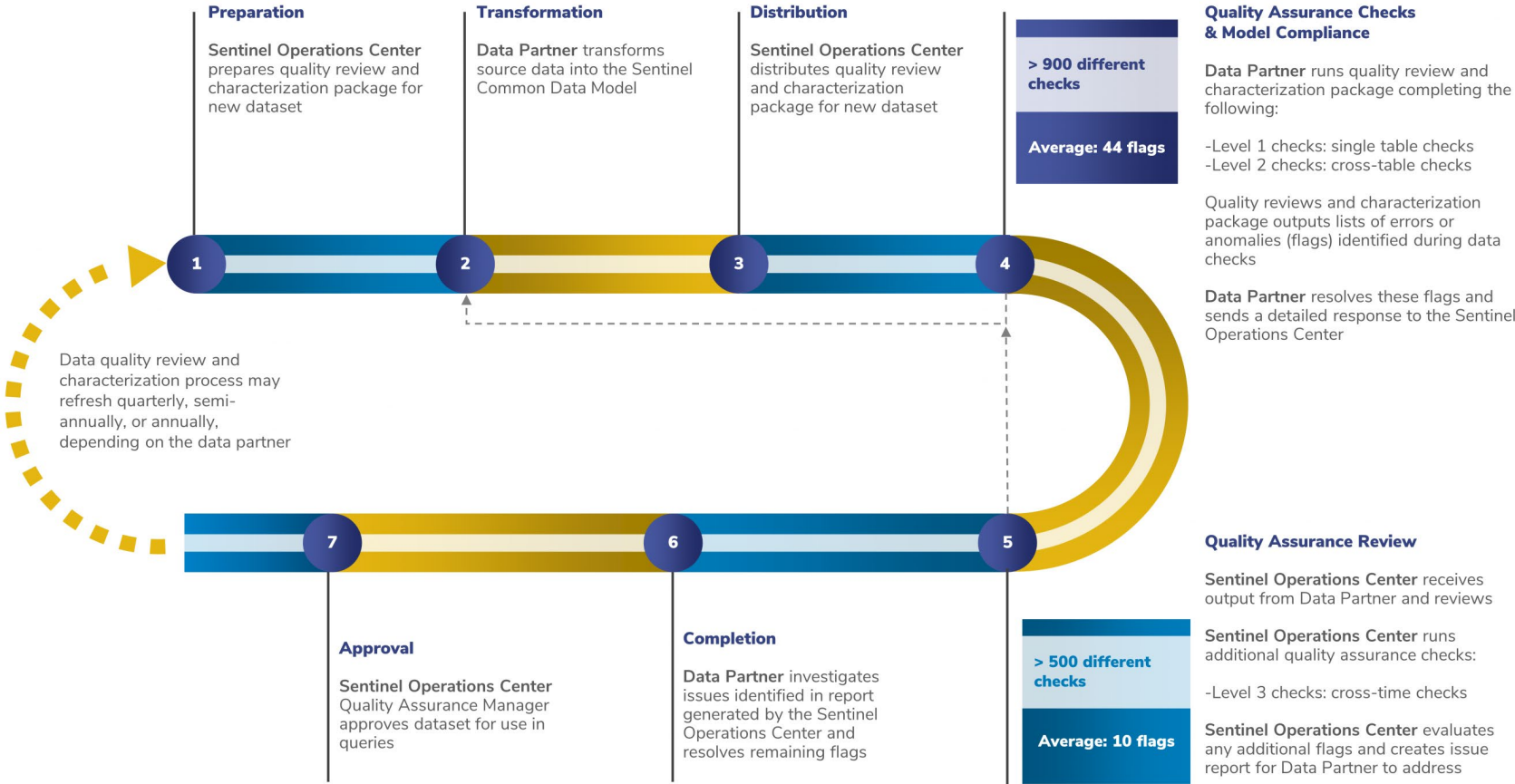
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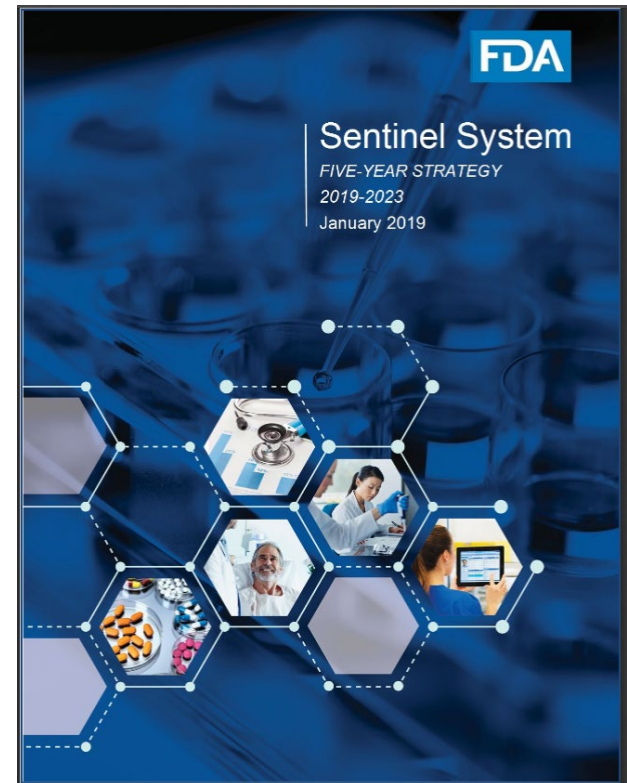
Data Quality Assurance Process

Sentinel Data Quality Review and Characterization Process



Sentinel's Strategic Plan 2019-2023

- Maintain and enhance the Sentinel System's foundation, preserving FDA's long-term investment in Sentinel's analysis tools and data infrastructure
- Diversify data sources, especially EHRs and claims linked to EHR
- Selectively incorporate advanced analytics
- Broaden touch points for participating in Sentinel's development
- Establish a Sentinel scientific community and disseminate knowledge to improve public health



<https://www.fda.gov/media/120333/download>

Sentinel's Three Centers

- In 2019, FDA established three distinct Sentinel centers
 - Sentinel Operations Center (SOC)
 - Innovation Center (IC)
 - Community Building and Outreach Center (CBOC)



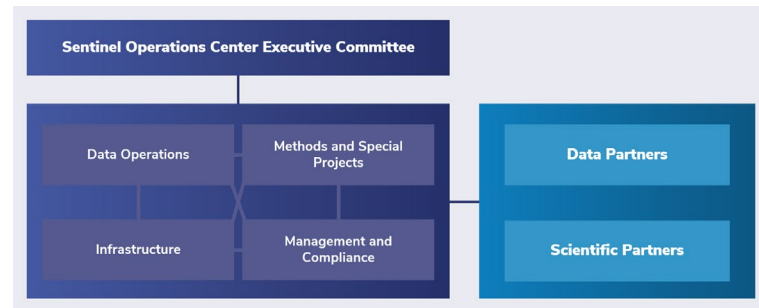
Sentinel Operations Center (SOC)

Lead: Harvard Pilgrim Health Care Institute

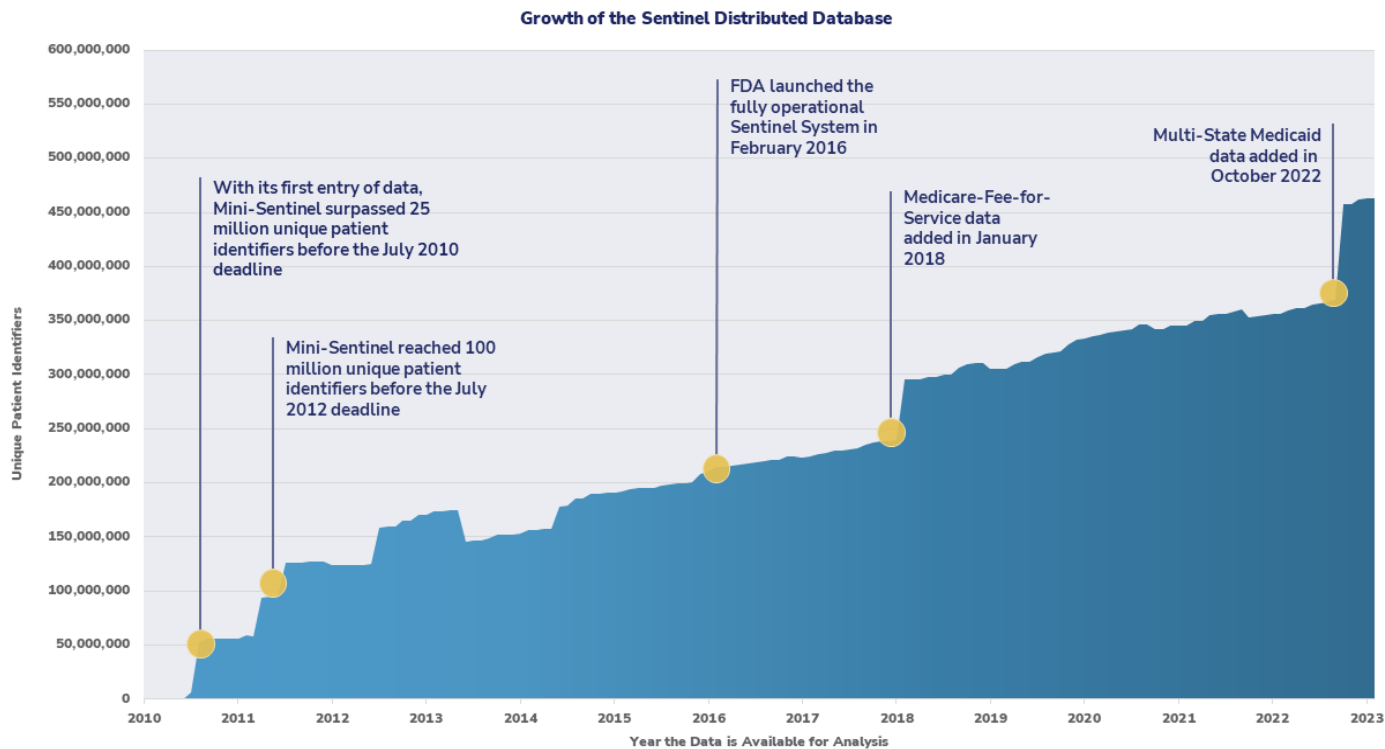
- Includes >40 collaborating entities, Data Partners, scientific/methods expertise

Roles

- **ARIA system**
 - Maintain data partner network, Common Data Model, analysis tools
 - Conduct analyses to evaluate the safety and effectiveness of medical products
 - Post analytic packages, results, Regulatory Outcomes
- **Core infrastructure development**
 - Integrate new data sources into the query-ready distributed database
 - Create new analytic tools capable of operating in a distributed environment



- The SOC maintains the SDD with 13 data partners contributing electronic health data from all U.S. geographic regions to the SDD.
- By 2023, the SDD had accrued 463.3 million unique patient identifiers.



Note: If patients move between health plans, they may have more than one patient identifier



Innovation Center (IC)

Lead: Harvard Pilgrim Health Care Institute

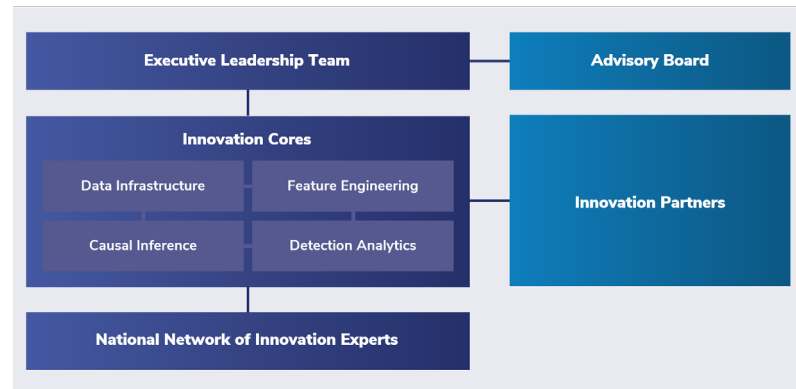
- Includes >50 collaborating entities

Innovation Cores:

1. Data Infrastructure
2. Feature Engineering
3. Causal Inference
4. Detection Analytics

Roles:

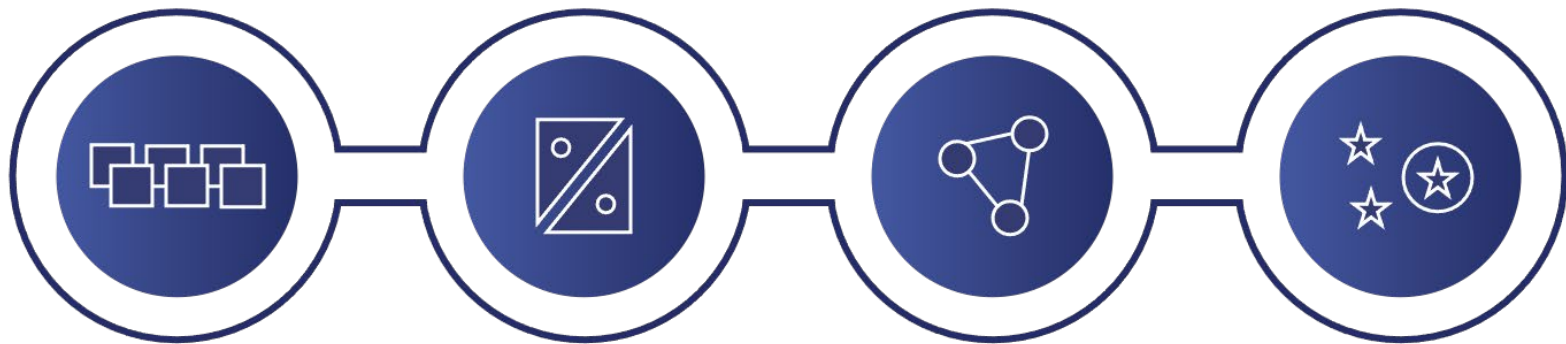
- Engage with academia and technology industry to develop innovative methods to further advance Sentinel, with a focus on early phases of methods development
- Develop methods to use EHR data, signal detection, causal inference approaches, and advanced analytics
- Develop a linked claims-EHR data network
- Host an Innovation Day public meeting



Innovation Center (IC)

- The IC has over 20 cutting-edge projects completed or in progress within these four key priority areas

Innovation Center Cores



Data Infrastructure

- Data partners
- Data elements
- Governance
- Harmonization
- Data Quality Assurance

Feature Engineering

- Natural language processing
- Automated feature extraction
- Computable phenotyping

Causal Inference

- Target trial design
- Advanced, semi-automated analytics
- Subset calibration
- Distributed methods

Detection Analytics

- Methodological framework
- Statistical methods
- Cancer outcomes
- Pregnancy and birth outcomes

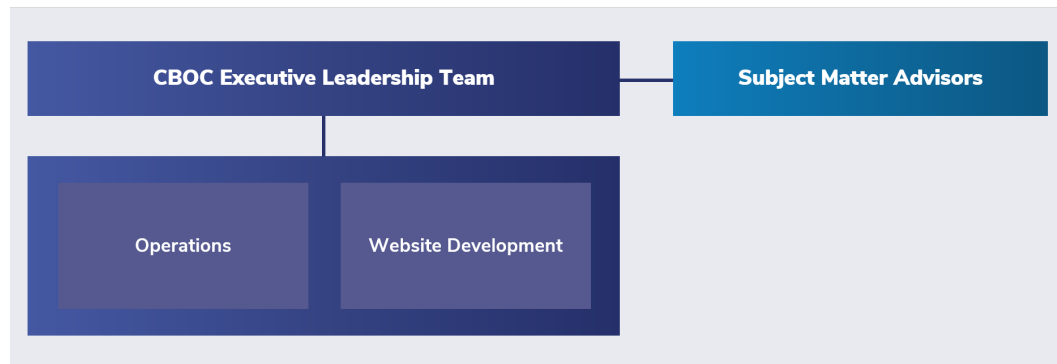
- Two Use Case projects are being implemented to demonstrate how the EHR-claims network will enhance Sentinel's data capabilities

Community Building and Outreach Center (CBOC)

Lead: Deloitte Consulting

Roles

- Transform Sentinel into a vigorous scientific community
- Maintain the Sentinel website and develop novel public portals to enhance usability, search, information management, and community engagement around Sentinel projects, tools, and results
- Increase adoption and use of the Sentinel CDM and tools through external training, direct support, and stakeholder engagement



Community Building and Outreach Center (CBOC)

- Formed a multi-stakeholder workgroup comprising
 - U.S. health agencies
 - Patient advocacy organizations
 - Informatics community
 - Industry
 - International regulatory agencies
 - Academia
 - Additional groups
- Hosted two webinars with a total of 139 attendees
- Attained a wide reach via the Sentinel website and newsletters.

Sentinel System Overall

Approximately 112.9 million members are currently accruing new data in Sentinel

Key Database Statistics >

Safety concerns evaluated from 2016-2023 = 170

Since 2016, more than 65 Sentinel drug studies have contributed to FDA regulatory actions or discussion

Drug Studies >

Since the founding of the Sentinel Initiative in 2009, 234 scientific papers have been published

Scientific Publications >

- 15 Annual Sentinel Initiative Public Workshops (through a cooperative agreement with the Duke-Margolis Center for Health Policy) - with a wide reach of 1000+ participants.
- Sentinel Views, a web-based data visualization application, developed in 2022 to increase access to study results from the Sentinel System

Recent Sentinel Enhancements

- Expanded access to novel data sources
 - EHRs, patient health trackers, disease registries linked with patient reported outcomes and healthcare utilization
 - Via the SOC's Data Partner network and the IC's innovation partners
- Enhanced analytic tools
 - Example topic areas: natural language processing, data model interoperability, machine learning, artificial intelligence, distributed data methods, advanced epidemiologic and biostatistical methods
- Strengthened network of scientific collaborators

Conclusion

- The U.S. FDA's Sentinel System was set up for post-market active monitoring of medical products based on a U.S. congressional mandate
- The Sentinel System has a wide coverage of the U.S. population
- The Sentinel System operates via three centers applying sound scientific expertise and innovative methods to real-world data to advance FDA's mission.



- The Sentinel System is supported by the U.S. Food and Drug Administration (FDA) contract 75F40119D10037.



OPERATIONS CENTER COLLABORATING ORGANIZATIONS

DEPARTMENT OF
POPULATION
MEDICINE



Harvard Pilgrim
Health Care Institute



Aetna, part of the CVS Health Family of companies.





Innovation Center Collaborating Organizations: Data & Scientific Partners

A collage of logos for various collaborating organizations, including:

- Aetion**
- aws**
- AMIA** (INFORMATICS PROFESSIONALS. LEADING THE WAY.)
- Kaiser Permanente** (Colorado Institute for Health Research)
- ORACLE**
- CMS** (CENTERS FOR MEDICARE & MEDICAID SERVICES)
- THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL**
- MICHIGAN MEDICINE** (THE UNIVERSITY OF MICHIGAN)
- Optum**
- COLUMBIA UNIVERSITY**
- Microsoft Research**
- VANDERBILT UNIVERSITY MEDICAL CENTER** (Department of Biomedical Informatics)
- Stanford University**
- INSTITUTE FOR HEALTH INFORMATICS** (UNIVERSITY OF MINNESOTA, Driven to Discover®)
- University of Pittsburgh**
- THE UNIVERSITY OF TENNESSEE KNOXVILLE**
- CORVITAS** (Excellence in Evidence)
- Duke** (Robert J. Margolis, MD, Center for Health Policy)
- MyHealth ACCESS NETWORK**
- UNIVERSITY of FLORIDA** (College of Pharmacy)
- UIC** (PHARMACY CHICAGO • ROCKFORD)
- Perelman School of Medicine** (UNIVERSITY OF PENNSYLVANIA)
- DEPARTMENT of BIostatistics EPIDEMIOLOGY & INFORMATICS**
- CCEB**
- Epic**
- flatiron**
- OHDSI** (OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS)
- Northeastern University**
- Optum Labs**
- John Snow LABS**
- TriNetX**
- STAR** (Stakeholders, Technology, and Research CRN)
- PennState**
- Berkeley** (UNIVERSITY OF CALIFORNIA)
- UNIVERSITY of WASHINGTON**
- HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH**
- UAB**
- COERE** (Center for Outcomes & Effectiveness Research & Education)
- National Jewish Health** (Breathing Science is Life.®)
- RUTGERS HEALTH** (Institute for Health, Health Care Policy and Aging Research)
- IOWA**
- College of Public Health**
- THE UNIVERSITY OF UTAH**
- TLC REVOLUTION LLC**
- Department of Population Health Sciences** (Duke University School of Medicine)
- BWH** (Division of Pharmacoepidemiology & Pharmacoeconomics, Brigham & Women's Hospital, Harvard Medical School)
- Kaiser Permanente** (Kaiser Permanente Washington Health Research Institute)

