

Using the Sentinel System to Assess Generic Drug Safety in the Post- Approval Setting

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Center for Drug Evaluation and Research

Office of Surveillance and Epidemiology

What I'll Cover

- What is Sentinel?
- How does Sentinel fit into generic drug review and monitoring?
- Who can use Sentinel?
- What's next for Sentinel?

What I'll Cover

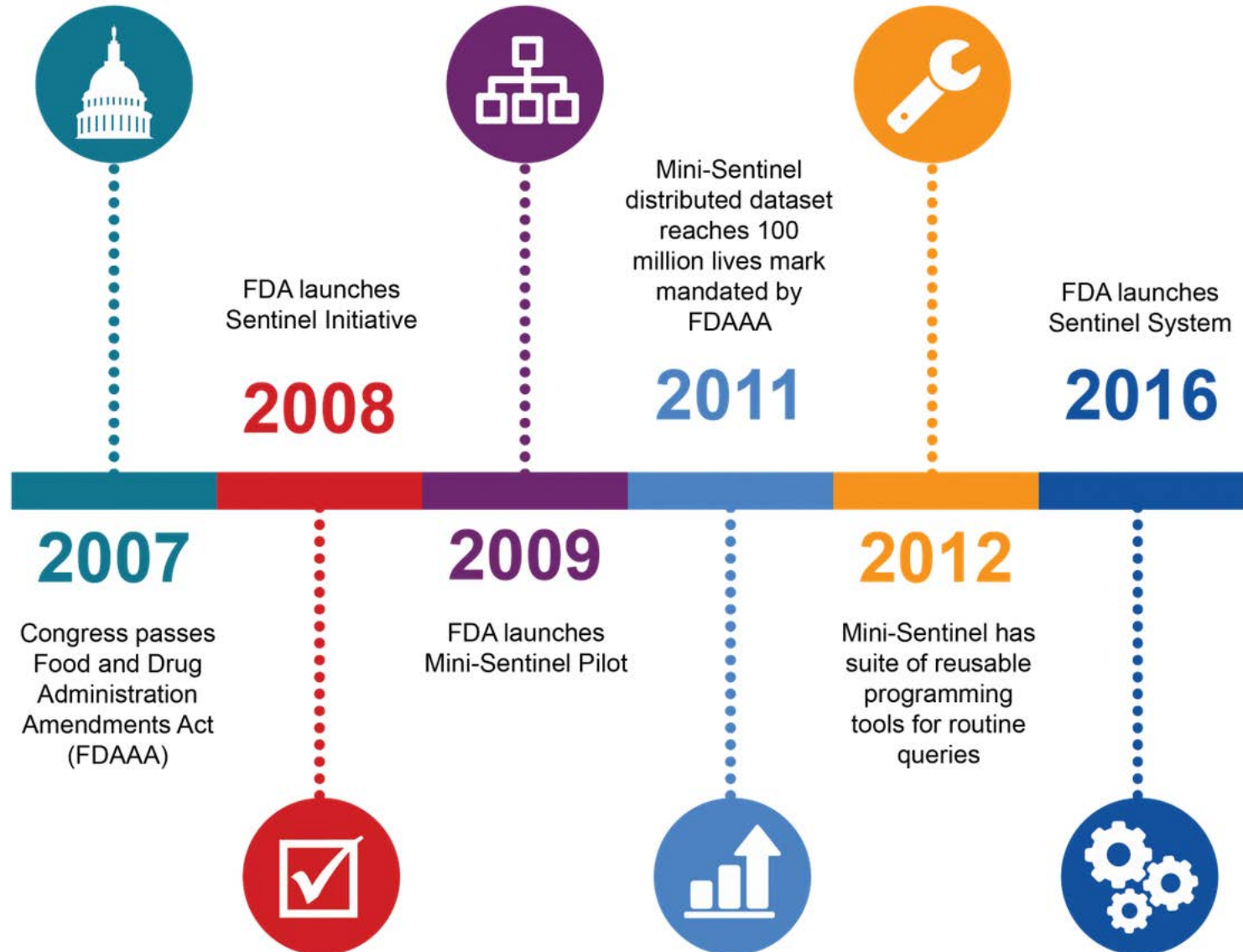
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Sentinel's Origins

- Developed in response to Section 905 of Food and Drug Administration Amendments Act (FDAAA; 2007)
 - Mandated creation of an active electronic postmarket surveillance system for regulated products

Sentinel's Timeline



Sentinel Characteristics

- Primarily claims data
- Common data model
- Distributed data network

Claims Data

Bob's Story



Claims Data

Advantages

- Capture all reimbursed healthcare usage
- Data are longitudinal and can produce incidence rates
- Use for payment contributes to data quality
- Common billing standards allow aggregation into large sample sizes

Disadvantages

- Data are not collected specifically for research
- Economic incentives affect data
- Missing OTC, low-cost generics paid out of pocket, drug samples, etc.
- Challenging to get key lifestyle factors (e.g., smoking, diet, exercise)

Sentinel System: Data Snapshot

- 223 million members* 2000-2016
 - 178 million members* with both medical and pharmacy benefits)
- 425 million person-years of observation time
- 43 million people currently accruing new data
- 5.9 billion pharmacy dispensings
- 7.2 billion unique medical encounters
- 42 million people with at least one laboratory test result

*Counts distinct patient ID values in the database

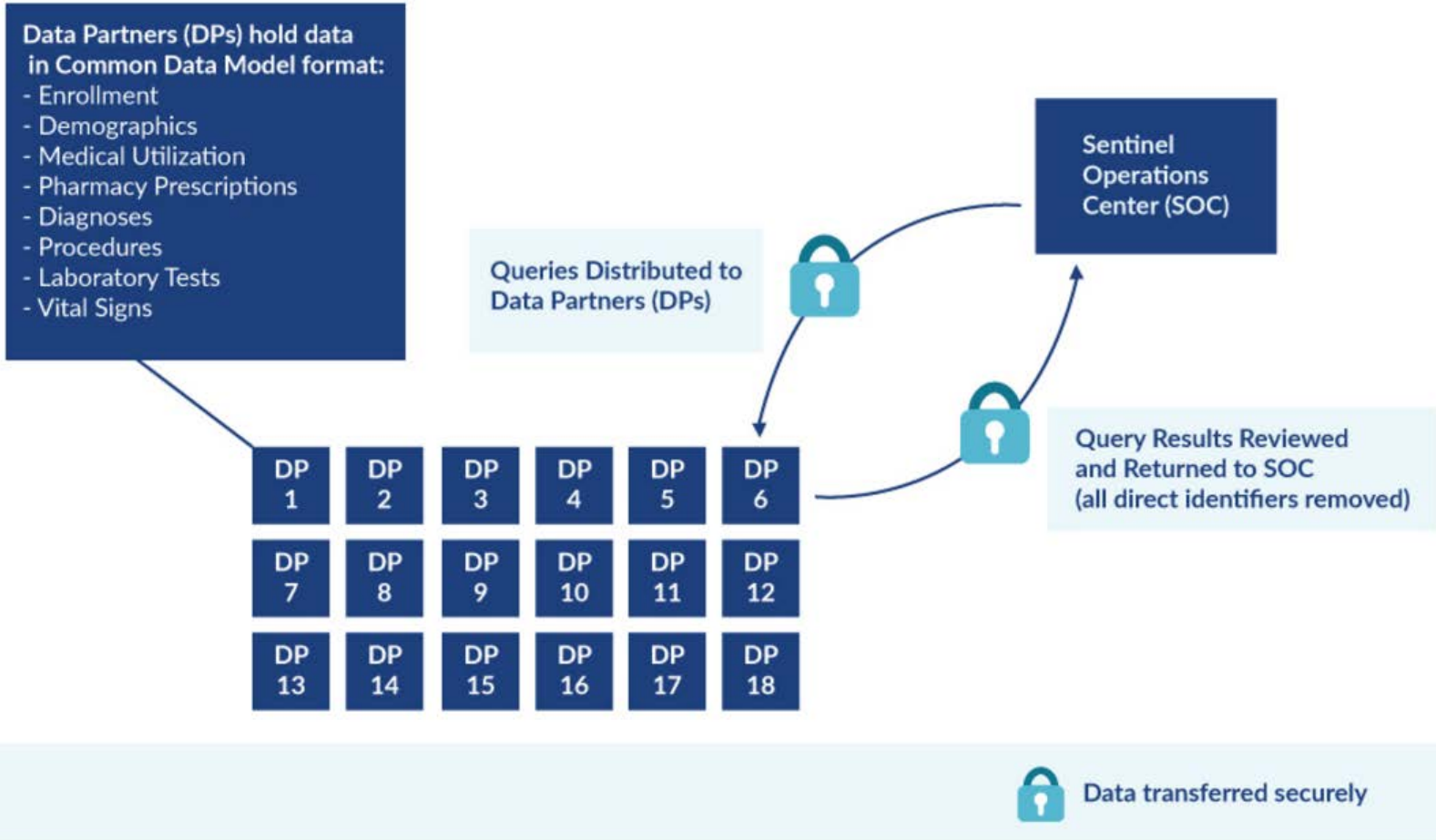
Sentinel Common Data Model



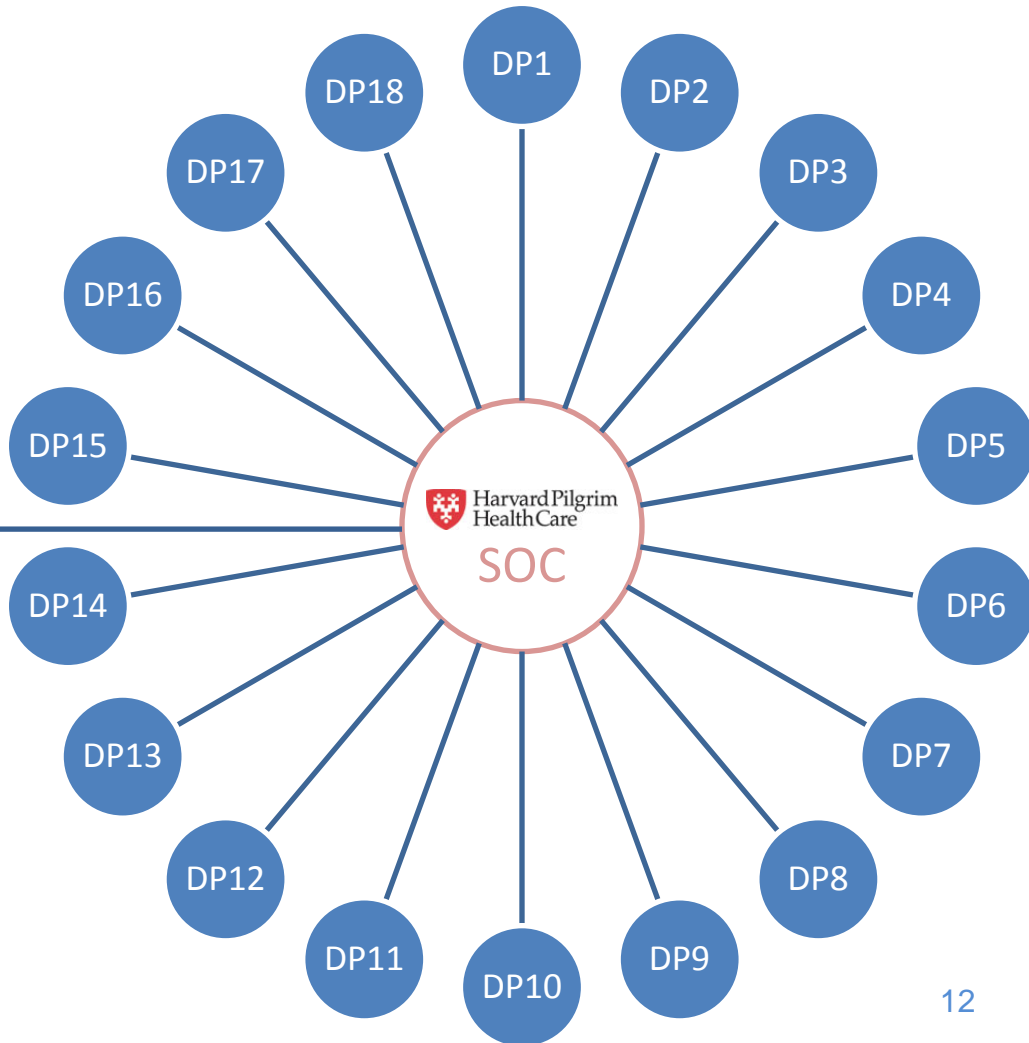
- Enrollment
- Demographics
- Medical utilization
- Pharmacy prescriptions
- Diagnoses
- Procedures
- Lab tests
- Vital signs

Data Partners transform data locally into the Common Data Model, which enables them to run standardized computer programs that run identically at each Data Partner site

Common Data Model



Distributed Database: A Hub-and-Spoke Model



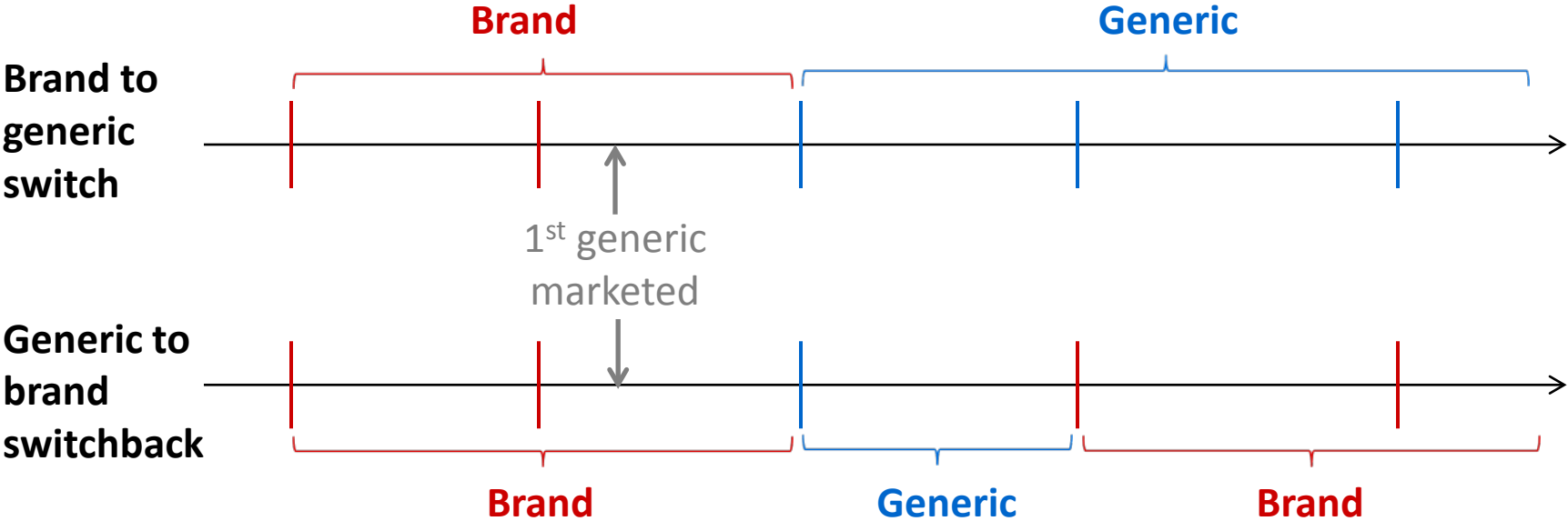
SOC – Sentinel Operations Center
DP – Data Partner

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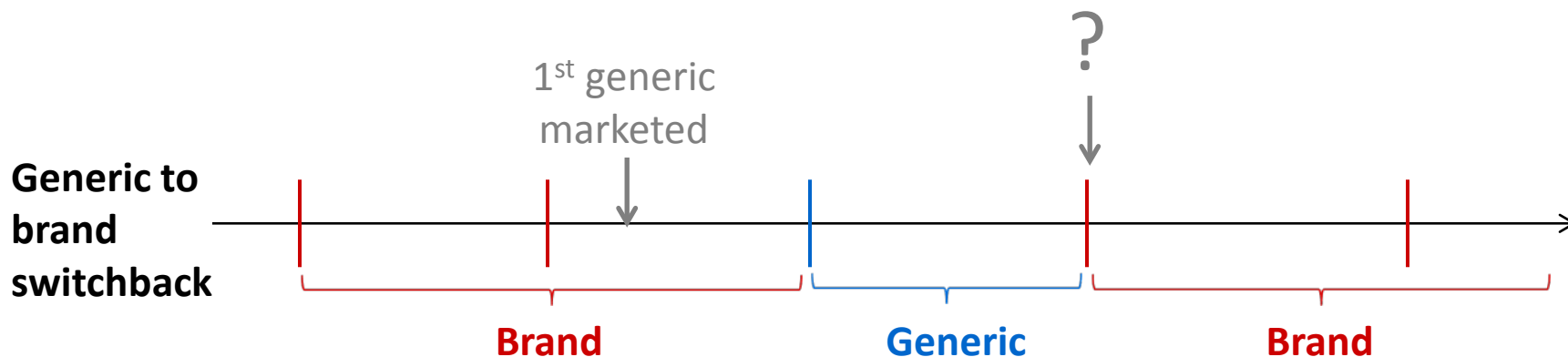
Generic Drug Surveillance

What evidence can utilization and switching patterns provide on generic substitution in the real-world?



Generic Drug Surveillance

- What is prompting the switchback?
 - Adverse events
 - Effectiveness
 - Other factors



Design and Analysis Considerations: Studying Generic Drugs



- Confounding
 - Patients switch to newly-released generic, leading to difficulty identifying an appropriate comparison group
- Selection bias
 - Patients who stay on brand when generic is available may be different in some way
- Outcome ascertainment
 - Outcome of interest may be no difference between groups
- Secular factors
 - Pharmacy inventory; provider preference

Strategies: Studying Generic Drugs



- Confounding
 - Self-controlled design; propensity score (PS) matching; historical controls
- Selection bias
 - Censoring; appropriate comparator group selection; restriction/stratification
- Outcome ascertainment
 - Power
- Secular factors
 - PS matching; restriction/stratification; instrumental variables

Sentinel Methods Development: Generic Drug Surveillance Tool

- Aims:
 - Design, develop, test and evaluate a flexible and reusable prototype analytic tool that could be used to conduct rapid population-based assessments on new generic products in the future; and
 - Use the Sentinel System to characterize utilization and switching patterns associated with the two use-cases for modified-release products
- Can handle multiple switch patterns and product groupings
- No outcomes yet, but planned for future development
- In progress – stay tuned!

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IMEDS

- Innovation in Medical Evidence Development and Surveillance from the Reagan-Udall Foundation
- Supports FDA's vision of providing the Sentinel System as a broader resource for public health and medical evidence generation
- Launched and running analyses



Who Can See What Sentinel Does?



- All analyses are ultimately posted on the Sentinel public website and are available for viewing
- Other avenues of communication:
 - Presentations at scientific conferences
 - Publications in journals
 - Public workshops and meetings



New Sentinel Webpage

www.sentinelinitiative.org



- Sentinel
- Drugs
- Vaccines, Blood & Biologics
- FDA-Catalyst
- Communications
- Report Finder

Sentinel is a National Medical Product Monitoring System

LEARN MORE



ABOUT

- Background



MEDICAL PRODUCT ASSESSMENTS

- Active Risk Identification and Analysis System

Latest Postings

SPOTLIGHT

- 33rd International Conference on Pharmacoepidemiology & Therapeutic Risk Management

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Sentinel: What's Next

- Medicare data expansion: Fall 2017
 - >50 million beneficiaries
- Yearly infrastructure and tool enhancements
 - Mother-baby linkage (launched)
 - Generic switching tool (launched)
- Continued scientific collaboration and outreach
- Develop a comprehensive training program for review staff
- Ongoing standardization of processes and communications
- Evaluate new ways to enhance access to Sentinel for stakeholders

Links

- Sentinel website: <https://www.sentinelinitiative.org/>
- Switching methods protocol: [https://www.sentinelinitiative.org/sites/default/files/Methods/Sentinel Methods Manufacturer-Level-Drug-Utilization-Switching-Patterns.pdf](https://www.sentinelinitiative.org/sites/default/files/Methods/Sentinel%20Methods%20Manufacturer-Level-Drug-Utilization-Switching-Patterns.pdf)
- PDUFA VI: <https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm446608.htm>
- IMEDS: <http://reaganudall.org/innovation-medical-evidence-development-and-surveillance>
- Sentinel interim and final assessments: <https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm464042.htm>

Thank you!

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