



Sentinel Distributed Database: Use of Real-World Data for Surveillance of Medications in Pregnancy

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Disclaimer



The views expressed are my own and are not necessarily those of the U.S. Food and Drug Administration

I have no conflicts of interest to disclose

Overview



- Background and database statistics
- Pregnancy activities
- Sentinel's PDUFA VII pregnancy commitments

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- FDA's medical product active safety surveillance system
 - To assess the use and safety of regulated medical products and to inform FDA's understanding of how real-world data can generate real-world evidence for medical product effectiveness
 - To develop data, informatics, and methodologic capabilities to support these activities
 - Created in response to a U.S. Congressional mandate
- 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

Administrative Data						
Enrollment	Demographic	Dispensing	Encounter	Diagnosis	Procedure	Prescribing
Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID
Enrollment Start & End Dates	Birth Date	Provider ID	Encounter ID & Type	Encounter ID & Type	Encounter ID & Type	Encounter ID
Medical Coverage	Sex	Dispensing Date	Service Date(s)	Provider ID	Provider ID	Prescribing ID
Drug Coverage	Postal Code	Rx	Facility ID	Service Date(s)	Service Date(s)	Provider ID
Medical Record Availability	Race	Rx Code Type	Etc.	Diagnosis Code & Type	Procedure Code & Type	Order Date
	Etc.	Days Supply		Principal Discharge Diagnosis	Etc.	Rx Source
		Amount Dispensed				Rx Route of Delivery
						Etc.

Clinical Data	
Lab Result	Vital Signs
Patient ID	Patient ID
Result & Specimen Collection Dates	Measurement Date & Time
Test Type, Immediacy & Location	Height & Weight
Logical Observation Identifiers Names and Codes (LOINC®)	Diastolic & Systolic BP
Etc.	Tobacco Use & Type
	Etc.

Registry Data		
Death	Cause of Death	State Vaccine
Patient ID	Patient ID	Patient ID
Death Date	Cause of Death	Vaccination Date
Death Imputed Date	Source	Admission Date
Source	Confidence	Vaccine Code & Type
Confidence	Etc.	Provider
Etc.		Etc.

Inpatient Data	
Inpatient Pharmacy	Inpatient Transfusion
Patient ID	Patient ID
Encounter ID	Encounter ID
Rx Administration Date & Time	Transfusion Administration ID
National Drug Code (NDC)	Administration Start & End Date & Time
Rx ID	Transfusion Product Code
Route	Blood Type
Dose	Etc.
Etc.	

Mother-Infant Linkage Data
Mother-Infant Linkage
Mother ID
Mother Birth Date
Encounter ID & Type
Mother Admission & Discharge Date
Child ID
Child Birth Date
Mother-Infant Match Method
Etc.

Auxiliary Data	
Facility	Provider
Facility ID	Provider ID
Facility Location	Provider Specialty & Specialty Code Type

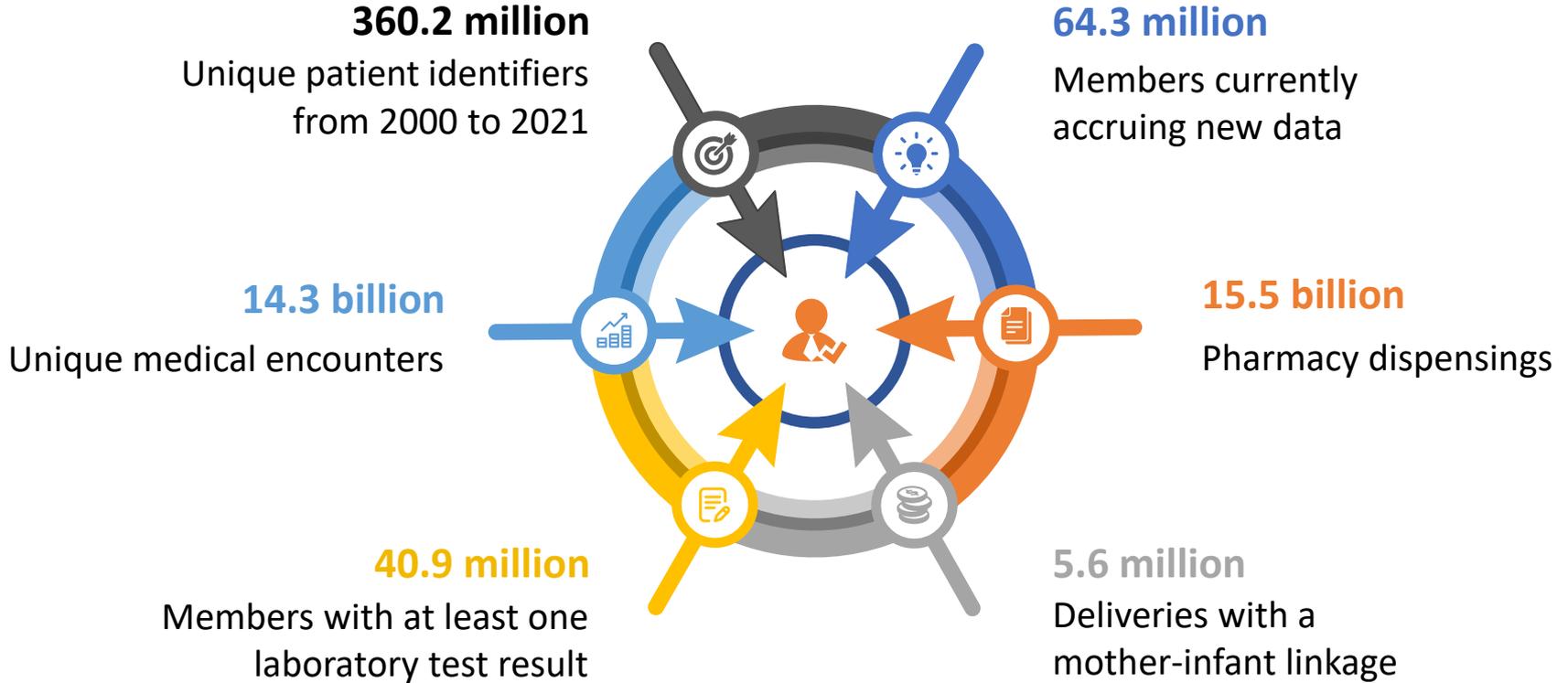


Sentinel's Data Partners

1. Aetna, a CVS Health company
2. Duke University School of Medicine: Department of Population Health Sciences (Medicare Fee-for-Service data)
3. HealthCore/Anthem
4. HealthPartners Institute
5. Humana, Inc.
6. Kaiser Permanente Colorado Institute for Health Research
7. Kaiser Permanente Hawai'i, Center for Integrated Health Care Research
8. Kaiser Foundation Health Plan of the Mid-Atlantic States, Inc.
9. Kaiser Permanente Northwest Center for Health Research
10. Kaiser Permanente Washington Health Research Institute
11. Marshfield Clinic Research Institute
12. Optum (OptumInsight Life Sciences Inc. and Optum Labs®)
13. Vanderbilt University Medical Center, Department of Health Policy (Tennessee Medicaid data)

* As of April 2022

Key Database Statistics



Overview



- Background and database statistics
- **Pregnancy activities**
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Mother-Infant Linkage

- Established in 2018 and routinely refreshed (four data partners)
- 79.1% linkage rate
- Mostly deterministic linkage approach
- Used to identify:
 - Deliveries that resulted in a live birth
 - Mother-infant pairs
 - Certain infant characteristics
- Pregnancies can be selected from linked mother-infant pairs
- All deliveries or only linked deliveries

Pregnancy-related Sentinel Analyses



Descriptive Analyses

Medical product use among pregnancies with live-birth deliveries

Inferential Analyses

Association between exposure to a certain medical product in pregnancy and a prespecified outcome of interest among infants

Signal Identification

Identification of potential adverse events related to the use of medical products in pregnancy without prespecifying an outcome of interest



Pregnancy Activities in Sentinel



The screenshot shows the Sentinel website's 'Featured' section. The 'Pregnancy' category is selected in the left sidebar. The main content area features a heading 'Pregnancy' followed by a paragraph describing the focus on medical product utilization, safety, and effectiveness during pregnancy. Below this is a 'Card View' link and a search bar. A table displays search results for pregnancy-related activities, sorted by date. The table has columns for 'Title' and 'Date'.

Title	Date
CNODES Webinar: Surveillance of Adverse Infant Outcomes Following Maternal Medication Use During Pregnancy Using Tree-Based Scan Statistics	03/09/2022
Use of Multiple Sclerosis Drugs Among Pregnant Women with Live-Birth Deliveries: A Descriptive Analysis	10/20/2021
Making Medicaid Data More Accessible Through Common Data Models and FHIR APIs	09/24/2021
Use of a Mobile App to Capture Supplemental Health Information During Pregnancy: Implications for Clinical Research	08/23/2021

Pregnancy Activities in Sentinel

Sentinel Public Training on Maternal Health and Pregnancy

Show

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Date: Monday, November 2, 2020

Time: 9:00am - 12:00pm EST

Event Type: Training

Description:

The 2020 Sentinel Public Training consisted of presentations on the Sentinel System's distributed database and broad analytic capabilities. We discussed pregnancy-related analyses including how Sentinel links and uses mother and infant data, cohort identification approaches for assessing medical product use during pregnancy, and a case study that employs a new inferential analysis tool. The training was conducted by Sentinel epidemiologist investigators.

If you have any questions or concerns, please email info@sentinelssystem.org.

Event Materials:

Training Presentation

- [Overview of Sentinel Tool Capabilities, Mother-Infant Linkage and Pregnancy Analyses](#)

Webcast

- View a recording of the presentation [here](#).

News & Events

Recent Sentinel Activity

Meetings, Workshops, & Trainings

Publications & Presentations

FDA Safety Communications & Labeling Changes

FDA Advisory Committee Meetings



American Journal of Obstetrics & Gynecology

MFM

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Original Research

Prescription medication use and baseline health status of women with live-birth deliveries in a national data network

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<https://doi.org/10.1016/j.ajogmf.2021.100512>

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BACKGROUND

The US Food and Drug Administration increasingly uses administrative databases to conduct surveillance of medications used during pregnancy. To assess adverse fetal effects, administrative records must be linked between the mother and infant. The Sentinel Initiative's Mother-Infant Linkage Table provides a large cohort of linked deliveries from national, regional, and public insurance claims in the United States for the US Food and Drug Administration to conduct surveillance.

OBJECTIVE

This study aimed to describe baseline health conditions and prescription medication use during pregnancy in cohorts of women with a live-birth delivery linked and not linked to an infant.

Overview



- Background and database statistics
- Pregnancy activities
- **Sentinel's PDUFA VII pregnancy commitments**

Sentinel's PDUFA VII Commitments



M. ENHANCEMENT AND MODERNIZATION OF THE FDA DRUG SAFETY SYSTEM

FDA will continue to use user fees to enhance the drug safety system, including adopting new scientific approaches, improving the utility of existing tools for the detection, evaluation, prevention, and mitigation of adverse events, modernizing REMS assessments, and coordinating regulatory activity in the pre-market and post-market settings. Enhancements to the drug safety system will improve public health by increasing patient protection while continuing to ensure access to needed medical products.

User fees will provide support for 1) modernization and improvement of REMS assessments and 2) optimization of the Sentinel Initiative through a) maintenance of Sentinel Initiative capabilities and continued integration into FDA drug safety activities and b) enhancement of analytic capabilities of the Sentinel Initiative to address questions of product safety and the understanding of how real-world evidence can be used for studying effectiveness.

1. Modernization and Improvement of REMS Assessments

FDA will use user fee funds to modernize and improve REMS assessments by incorporating REMS assessment planning into the design of REMS, clarifying expectations regarding methods to evaluate the effectiveness of REMS.

PDUFA VII: FY 2023-2027

2. Optimization of the Sentinel Initiative

The user fee funds initially provided in PDUFA VI to expand the Sentinel program will continue to systematically implement and integrate Sentinel and BEST (Biologics Effectiveness and Safety) Systems in FDA drug safety activities by sustaining the high quality and large quantity of data available, allowing continued application of advanced methods for determining when and how those data are utilized, and ensuring comprehensive training of review staff on the use of Sentinel and BEST. These capabilities will support the use of the Sentinel Initiative for regulatory decision making to address questions of product safety and advance our understanding of how real-world evidence can be used for studying effectiveness.

a. Maintenance of the Sentinel Initiative Capabilities and Continued Integration into FDA Drug Safety Activities

FDA will use user fee funds to maintain the quality and quantity of data available through the Sentinel Initiative (Sentinel and BEST), to maintain the processes and tools for determining when and how those data are utilized, and to support comprehensive training of review staff on the use of Sentinel.

Sentinel's PDUFA VII Commitments



M. ENHANCEMENT AND MODERNIZATION OF THE FDA DRUG SAFETY SYSTEM

1. Modernization and Improvement of REMS Assessments
2. Optimization of the Sentinel Initiative
 - a. Maintenance of the Sentinel Initiative Capabilities and Continued Integration into FDA Drug Safety Activities
 - b. Enhancement of the Analytic Capabilities of the Sentinel Initiative to Address Questions of Product Safety and Advance the Understanding of How Real-World Evidence Can Be Used for Studying Effectiveness
 - i. Pregnancy Safety
 - ii. Use of Real-World Evidence – Negative Controls

Sentinel's PDUFA VII Commitments

Pregnancy Safety



i. Pregnancy Safety

The goal of pregnancy safety post-market requirements and commitments studies is to inform labeling on the safety of use in pregnancy and to detect or evaluate safety signals in a timely manner.

- (1) FDA will develop a framework describing how data from different types of post-market pregnancy safety studies might optimally be used, incorporating knowledge of how different types of post-market studies have been used by FDA and industry and identifying gaps in knowledge needed to be filled by demonstration projects. The framework would consider factors such as, but not limited to, purpose of study, types of post-market studies, anticipated exposure in females of reproductive potential (FRP) and pregnant women, potential toxicity of the drug and proposed risk mitigation, benefits of the drug, and magnitude and type of risk to be detected. The framework would specifically address the use of pregnancy registries and electronic healthcare data sources including Sentinel, with a goal of ensuring the most efficient means of obtaining highest quality safety data available.

- By Sep 30, 2023:
 - Hold a public workshop on post-marketing safety studies in pregnant women
- By Sep 30, 2024:
 - Publish a workshop report describing the proposed framework

Sentinel's PDUFA VII Commitments

Pregnancy Safety



(2) Incorporating feedback from (1), conduct 5 demonstration projects to address gaps in knowledge about performance characteristics of different study designs. FDA will initiate the following demonstration projects which may be modified as needed, before September 30, 2024:

- (d) Assess the performance of major congenital malformations (MCM) as a composite outcome in signal detection and evaluation when there is true risk for some but not all specific malformations.
- (e) Assess the performance of an algorithm using electronic health record (EHR) and claims-linked healthcare data for a pregnancy-related outcome, or composite of outcomes (e.g., spontaneous abortion, stillbirth, congenital malformations), after use of vaccines in pregnant women. The parameters of the pregnancy-outcome algorithm will be developed to have general usability with therapeutic products.

- By Sep 30, 2027:
 - Update the proposed framework and develop a guidance or MAPP/SOPP as appropriate to implement a standardized process for determining necessity and type of pregnancy postmarketing studies including PMRs



<https://sentinelinitiative.org/>