Update on Facilitation of Public and Sponsor Access to the Sentinel System's Distributed Data Network to Conduct Safety Surveillance

The Food and Drug Administration Amendments Act of 2007 (FDAAA) required the Food and Drug Administration (FDA) to establish an active postmarket risk identification and analysis system. In response, the FDA established the Sentinel Initiative. A core program of the Sentinel Initiative is the Sentinel System, a national medical product safety surveillance system that includes one of the largest healthcare insurance claims multisite distributed databases dedicated to medical product safety.

In 2016, FDA officially announced the full-scale operation of the Sentinel System covering at least 100 million lives and the formal integration of the Sentinel System into the regulatory decision-making process. In 2019, FDA created the Medical Data Enterprise to build a modern system that would contain Electronic Health Record (EHR) data covering at least 10 million lives. To support this expansion, FDA established three centers:

- The Sentinel Operations Center (SOC) provided oversight to the active postmarket risk identification and analysis system, further developed the infrastructure, and maintained the distributed data network.
- The Innovation Center (IC) focused on meeting the Real-World Evidence (RWE) Medical Data Enterprise requirement by establishing a query-ready distributed data network containing EHR data covering at least 10 million lives, and applying innovative analytic methods (e.g., causal inference, feature engineering).
- The Community Building and Outreach Center (CBOC) engaged with non-FDA participants, from the clinical research enterprise to health advocacy groups, to support Sentinel's objectives.

On September 30, 2022, the President signed into law the FDA User Fee Reauthorization Act of 2022. This new law included the reauthorization of the Prescription Drug User Fee Act (PDUFA) commonly referred to as PDUFA VII (FY 2023 through 2027). As part of FDA's negotiated agreement with industry during each reauthorization, the Agency agrees to certain performance and procedural goals and other commitments that apply to aspects of the human drug review program.

One PDUVA VII commitment is for FDA to provide an update on facilitation of public and sponsor access to Sentinel's distributed data network to conduct safety surveillance. The FDA Sentinel Team has implemented multiple avenues towards exploring fuller public and sponsor access to Sentinel System data to conduct safety analyses. The intent of this report is to increase clarity and transparency around accessing the Sentinel System. Below, we include backgrounds and options to access.

Background:
The Sentinel System is supported through data housed at health care organizations, known as Data Partners. Each Data Partner keeps their own data (medical billing information and electronic health records) and controls who can access that data. The Data Partners collectively comprise the Sentinel System's distributed data network.

Each Data Partner transforms their data locally into the Sentinel Common Data Model format. The SOC develops a common program sent to the Data Partner to be run against their local data formatted to the Sentinel Common Data Model. After the Data Partner runs the analyses against their data, the Data Partner sends the deidentified results back to the SOC. FDA works with the SOC to conduct epidemiologic studies through designing the study as reflected in the programs that are distributed to the Data Partners and reviewing and interpreting the aggregated de-identified data results.

Through the Sentinel System's distributed approach, the Sentinel System maintains patient privacy and data security with the data held behind each Data Partner's firewall. FDA does not have direct access to Data Partner data and does not keep the data in-house at FDA. Although FDA cannot provide public or sponsor access to data housed behind Data Partner firewalls, FDA has explored options with the Sentinel System to address this commitment:

Options:

Options to facilitate public and sponsor access to the Sentinel System's capabilities
The Reagan-Udall Foundation for the Food and Drug Administration offers a mechanism for sponsors to access a portion of the Sentinel System resources through the Distributed Network, like the approach used by FDA. That program is referred to as "Innovation in Medical Evidence and Development Surveillance (IMEDS)" IMEDS. • The IMEDS program offers periodic public training to raise awareness of such access. An example of a 2024 training is located here: Introduction to IMEDS 2024. • IMEDS is also identified on the FDA's website under: FDA's scientific-public-private-partnerships-and-consortia. • IMEDS is also featured on the SentinelInitiative.org website here: Engage with Sentinel -- Data Inquiries.
The Sentinel System has conducted outreach through the CBOC. To help facilitate outreach and communication to the public, the Center conducted a webinar targeted to patient advocates. The webinar was created to help patient advocates navigate Sentinel System work and deliverables located on the SentinelInitiative.org website. • That publicly posted video is located here: overview-sentinel-website-health-advocates. To help facilitate outreach and communication to the public, CBOC also compiled 14 quarterly newsletters that shared Sentinel related topics, trainings, workshops, and points of interest with academia, industry, and the general public. The Sentinel newsletter included a section on how to engage with Sentinel. • As an example, the metrics for the July 2024 Sentinel newsletter indicate that the newsletter was opened by 1,278 people in industry and private entities, 428 people in academia, and 217 people in US government (outside of FDA) and by 32 international recipients. Additionally, CBOC conducted a project to encourage fuller collaboration with the Sentinel System with the objective of having the Sentinel System serve as a sustainable national resource to monitor the safety of marketed medical products and expand real-world data sources used to evaluate medical product performance. As part of that effort: • CBOC identified partnerships that would add value or gain value from interacting with Sentinel, identified opportunities, and explored options whereby the public and sponsors could more fully

benefit from the Sentinel's distributed data network.

The CBOC has completed its deliverables and is no longer active.

- The IC conducted a project to increase the pathways for external investigators to engage with the Sentinel System for methods development. To achieve this goal of broad scientific community engagement, the IC:
    - Developed and tested new research methods and analytics tools for use across the Sentinel System or systems that share its features
    - Facilitated feasibility analyses with direct data access in a secure environment that mimics the main Sentinel data infrastructure.

Those pilot projects were successful.

The Sentinel Initiative Website (https://www.sentinelinitiative.org/) includes links to Sentinel System programming on a publicly available Git Hub. This is programming developed by the Sentinel System to help the public/sponsors to align their data to the Sentinel Common Data Model and to run the programming developed and implemented by the Sentinel System. This programming is free and available to all to support work with their own data. This programming allows the public or sponsors to run the same programming against their own data if their data is formatted to the Sentinel Common Data Model.

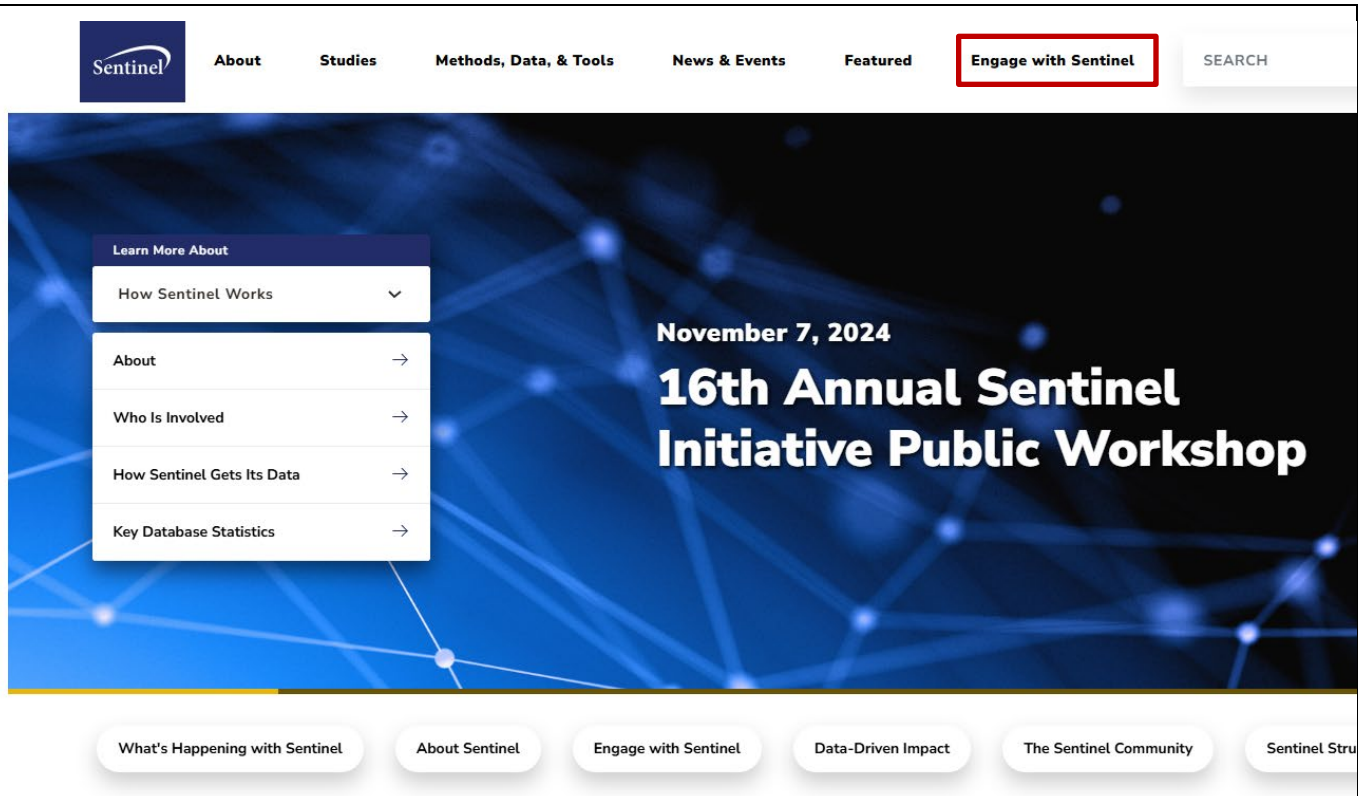
- Those links can be found here: software-packages-toolkits and methods-data-tools

The Sentinel System posts Modular Program (MP) reports which include study specifications and results on the Sentinel Initiative Website.

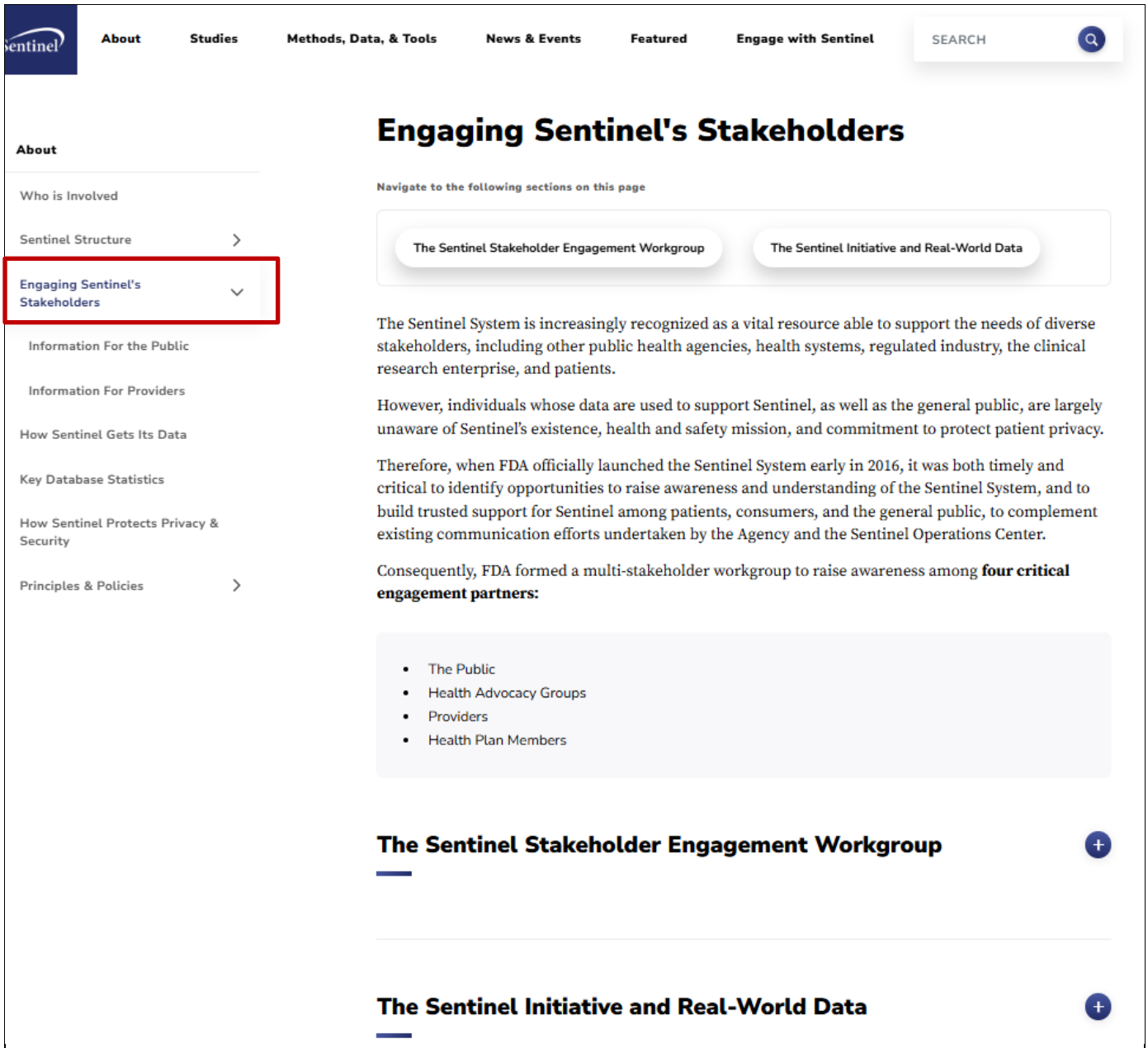
- An example is here: Modular Program Report utilization of diabetes mellitus drugs and anti-obesity medications January 1, 2008 through May 31, 2024.

The Sentinel Initiative Website includes links and contact channels for the public (including sponsors) to reach out to the SOC with questions or requests for collaboration. These requests are also shared with FDA. Those links on the website are located as a tab on the main landing page and elsewhere as follows (red box superimposed on screenshot below for ease of identification):

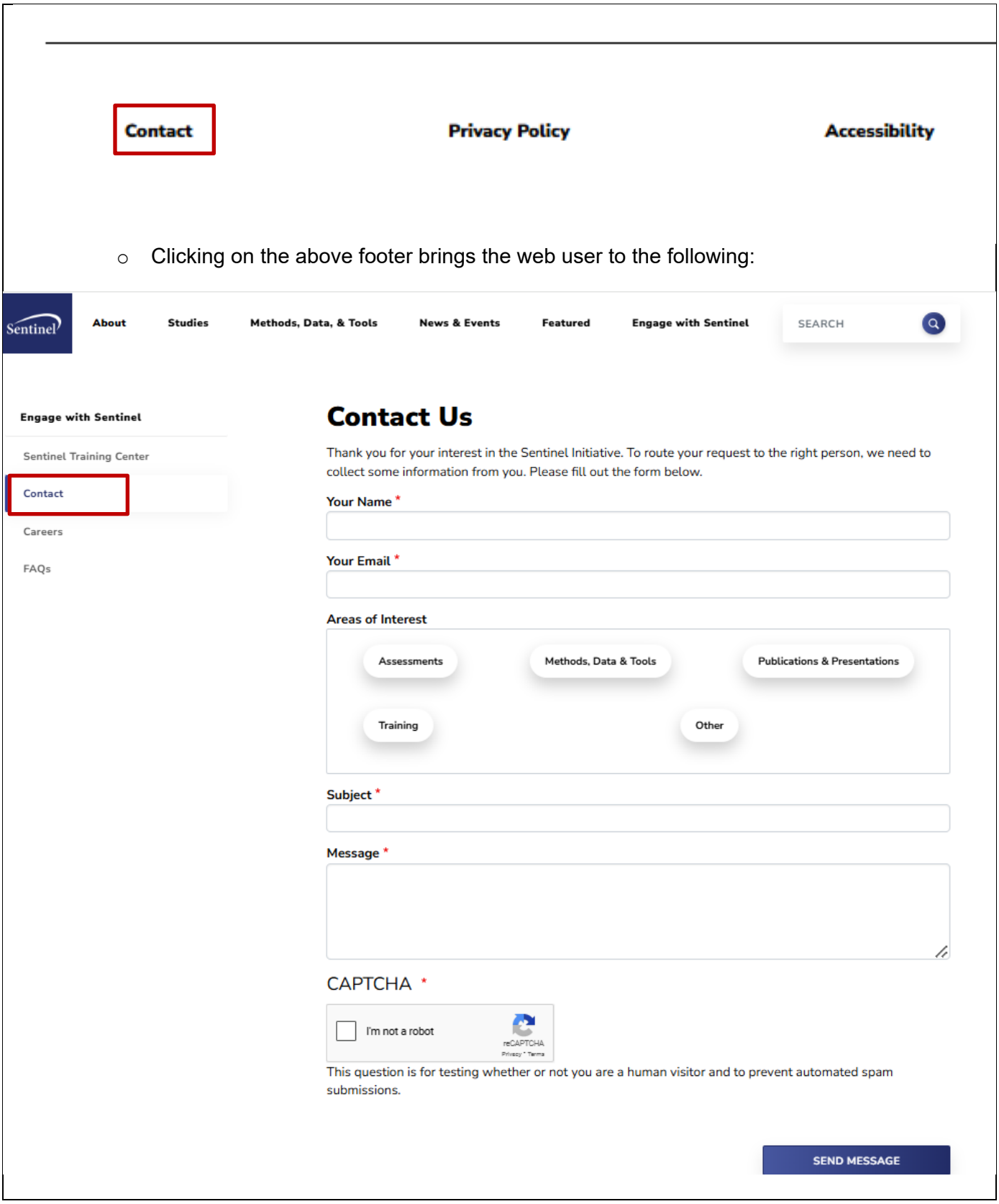
- https://www.sentinelinitiative.org/



- [engaging-sentinels-stakeholders]



- The Sentinel Initiative website also has “contact” as a standard footer.



- Clicking on the above footer brings the web user to the following:

This report and imbedded links provide an update on FDA's facilitation of public and sponsor access to Sentinel's distributed data network to conduct safety surveillance (see PDUFA VII Commitment (M.2.a iii): "By the end of FY 2025, FDA will publish on its website an update on facilitation of public and sponsor access to Sentinel's distributed data network to conduct safety surveillance.")