



Prescription Drug User Fee Act (PDUFA) Reauthorization

FDA and Industry Post-market Safety Subgroup

December 4, 2025 | 1:00 pm-2:30 pm

FDA White Oak Campus, Silver Spring, MD

MEETING PURPOSE

The purpose of this meeting was to continue discussion between FDA and Industry Post-market Safety Subgroups for PDUFA VIII negotiations and included FDA presentations on Sentinel's safety, regulatory, and Real-World Evidence methodological contributions; resource allocations from PDUFA VI and VII; and proposals for maintenance of Sentinel capabilities.

PARTICIPANTS

FDA

Amy Ramanadham	CDER
Jason Bunting	CDER
Bob Ball	CDER
Neha Gada	CDER
Craig Zinderman	CBER

Industry

Katrin Rupalla	PhRMA (Johnson & Johnson)
Mark Taisey	BIO (Amgen)
Lucy Vereshchagina	PhRMA
Derek Scholes	BIO
Ryan Kaat	PhRMA
Annetta Beauregard	BIO

MEETING SUMMARY

This meeting focused on FDA's presentation of Sentinel's value and resource requirements for PDUFA VIII. FDA provided detailed information on Sentinel's contributions to safety, regulatory decision-making, and Real-World Evidence (RWE) methodology. FDA also presented Biologics Effectiveness and Safety (BEST) Initiative accomplishments. FDA proposed PDUFA VIII resource allocations for the maintenance of Sentinel. Industry raised questions about data access, transparency, and long-term sustainability of the proposed funding model.

Topic 1: Sentinel's Contributions to Regulatory Decision Making and Supporting the Use of Real-World Evidence

Regulatory Decision Making

FDA presented comprehensive data showing 784 completed analyses since 2016 and regulatory impacts including, but not limited to, 8 Advisory Committee presentations, 4 Drug Safety

Communications, 12 labeling changes, 8 NDA/BLA review contributions, 1 product withdrawal, 2 risk evaluation and mitigation strategy (REMS) removal contributions, and 46 post-market safety surveillance activities. FDA presented Sentinel studies conducted from 2022-2024, where the Active Risk Identification and Analysis (ARIA) system had been deemed to be sufficient in the determination required by the Food, Drug, and Cosmetic Act, Section 505(o)(3). FDA and Industry also discussed common reasons why ARIA has been found insufficient in some cases. Industry expressed that they would expect to see an increase in ARIA sufficiency determinations as Sentinel has and continues to mature to replace postmarketing requirements (PMRs) at the time of a product's approval. FDA highlighted that signal identification is now routine in Sentinel and was conducted on 8 products.

Real-World Evidence (RWE)

FDA presented on the Sentinel RWE Data Enterprise, a distributed data network utilizing linked claims-electronic health record data that covers more than 25 million lives. FDA presented improvements in outcome capture through computable phenotyping and machine learning methods, as well as development of a trial emulation framework for causal inference in non-interventional studies. FDA also presented on a process guide for inferential studies using healthcare data from routine clinical practice to evaluate the causal effects of drugs (PRINCIPLED). It was clarified this process could be applied to both post-market safety and efficacy.

Sentinel and the Biologics Effectiveness and Safety (BEST) Initiative

FDA shared that BEST Initiative accomplishments included shorter data lag times, the development of 10 algorithms for identifying adverse events of special interest (AESIs), linkages to 37 state/local Immunization Information Systems, and mother-infant linkages. FDA also shared that the Center for Biologics Evaluation and Research (CBER) evaluated COVID-19 treatments and vaccines, presented at 6 FDA Vaccines and Related Biological Products Advisory Committee Meetings (VRBPAC) or Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) meetings, and conducted vaccine effectiveness studies. From 2022-2025, 19 BEST studies contributed to regulatory decisions with 2 of those BEST studies contributing to safety labeling changes.

Topic 2: Resources Allocated for the Sentinel System under PDUFA VI and PDUFA VII and FDA Proposal for the Maintenance of Sentinel Capabilities

FDA reviewed the user fee resources allocated for Sentinel from PDUFA VI and PDUFA VII and proposed continuing the annual operational funding (i.e., direct costs) that was provided in PDUFA VI and PDUFA VII. FDA indicated that the agency would continue internal discussions about disclosing total or budget authority resources that were allocated to Sentinel during the PDUFA VII timeframe. FDA did not request continued funding for negative controls (\$2.25 million) and pregnancy safety initiatives (\$14 million) allocated in PDUFA VII, because those demonstration projects will be successfully completed. FDA also proposed that some of the

operational funding for PDUFA VIII could be reallocated to fund 10 full-time equivalents (FTEs) to support Sentinel 3.0's operational model where FDA staff will conduct analyses directly, replacing contractor staff.

Industry raised questions around sponsor access to data in Sentinel 3.0, reasons for ARIA insufficiency determinations, and long-term implications of FDA's proposal for funding the maintenance of Sentinel through PDUFA direct costs and FTEs.

Next Steps

FDA and Industry agreed to continue negotiations, with Industry providing formal responses to FDA's proposals and both sides working toward agreement on resource allocation and commitment language for PDUFA VIII reauthorization.

Future Discussions, FDA and Industry will review:

- Reasons for ARIA insufficiency
- Counterproposal to proposed draft commitment letter text