

CENTER FOR DRUG EVALUATION AND RESEARCH

Office of Surveillance and Epidemiology

Detecting, Assessing, Preventing,
and Managing Drug Risks

Responding to Public Health Issues

2025 ANNUAL REPORT



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Director's Message

Greetings,

I am pleased to share the 2025 Annual Report of the Office of Surveillance and Epidemiology (OSE). This report highlights OSE's contributions to drug safety surveillance, epidemiology, medication error prevention, risk management, and modernization throughout the product lifecycle.

In 2025, OSE continued to apply technology and regulatory science to strengthen how FDA detects, assesses, prevents, and manages medication risks. The AI-enabled Information Visualization Platform (InfoViP) moved into production, and OSE advanced work with large language models to support AEMS report review, literature review and summarization, safety-related clinical concept extraction, report-quality classification, and signal detection.

OSE also helped build the next generation of real-world evidence infrastructure. The Real-World Evidence-Data Enterprise is now in operation, and OSE contributed to scientific work describing how large language models may improve postmarketing safety in the Sentinel System. In 2025, the Risk Evaluation and Mitigation Strategies (REMS) data standard was updated to include discussion of incorporating electronic routing of REMS data utilizing structured product labeling files. This functionality is currently in prototype and under active development, with the potential to reduce implementation burden for stakeholders once fully realized.

OSE supported 46 novel drug and therapeutic biologic approvals, processed more than two million AEMS reports, completed 59 Sentinel medical product assessments, supported opioid safety actions, advanced REMS releases and modifications, and contributed to public health communications on emerging drug safety issues.

As always, OSE's success is a direct result of staff expertise, judgment, and commitment to public health. I hope this report provides a clear view of the impact of OSE's work in 2025 and the strategic direction of our office.

Best regards,

Gerald Dal Pan, MD, MHS



Gerald Dal Pan, MD, MHS

Director

Office of Surveillance
and Epidemiology

2025 Signature Achievements

High-impact accomplishments that define OSE contribution and value

These achievements translate OSE work into enterprise-level outcomes: improved transparency, evidence-driven risk management, standards-based modernization, and stronger decision support for safety review.

HIGHLIGHT	2025 CONTRIBUTION
	Clozapine REMS released After a thorough analysis, FDA released the Clozapine REMS on June 13, 2025, ending more than three decades of restrictive distribution requirements while maintaining critical safety information in labeling and a Medication Guide.
	AEMS Public Dashboard daily refresh The AEMS Public Dashboard shifted to daily, near-real-time refresh and drew 2.71 million users and 2.84 million sessions in calendar year 2025.
	ICH M14 and E2D(R1) global standards leadership OSE contributed to finalizing international work on International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) M14 and E2D(R1), supporting harmonized approaches to real-world data, safety assessment, and post-approval safety reporting.
	Digital transformation and AI adoption OSE supported OneNexus Release 1.0, documented more than 100 Elsa use cases, moved InfoViP into production, and advanced Large Language Model (LLM) exploration for safety review workflows.
	REMS modernization OSE advanced REMS integration concepts, public dashboard transparency, and continued development of standards-based approaches that can reduce burden while preserving risk mitigation.
	Public health response OSE supported opioid safety actions, unapproved-drug communications, compounded-semaglutide safety messaging, and targeted surveillance for shortage-affected products.

Terminology Note*
In March 2026, FDA launched the Adverse Event Monitoring System (AEMS), a unified platform that replaces legacy adverse event reporting systems, including the FDA Adverse Event Reporting System (FAERS). Some 2025 activities described in this report as AEMS activities were previously conducted under FAERS, the system name in use at the time.

OSE By the Numbers



RISK MANAGEMENT – REMS
Approvals, modifications, and releases across CY 2025

PHARMACOVIGILANCE
CY 2025

2.05M
AEMS reports processed

79 potential signals posted to the AEMS Potential Signals webpage

110 Newly Identified Safety Signals opened with OSE as signal identifier or safety lead

32.4M+ reports total in the AEMS database to date >50% of reports contained serious AEs not in the product label

REVIEW ACTIVITY
Completed reviews across all application types

46 Novel drug & therapeutic biologic approvals OSE contributed to

504 Proprietary name reviews completed in CY 2025

9 Newly Identified Safety Signals medication error reviews — wrong drug, wrong route, confusion packaging

~2000 Proprietary name and nonproprietary name suffix, labeling, and human factors reviews completed

THE SENTINEL SYSTEM
Active surveillance – CY 2025

59 medical product assessments

1.5B person-years of longitudinal data

541.5M unique patient identifiers

138.7M patients actively accruing new data

25.2B prescription records in the system

13.5M live-birth deliveries linked to mother-infant outcomes

5 REMS with ETASU approved

53 REMS modifications

2 Shared system REMS approved

SPOTLIGHT
Clozapine REMS released June 13, 2025 — ending 35+ years of restrictive distribution after FDA reviewed 20 years of safety data in collaboration with the U.S. Department of Veterans Affairs, Brigham and Women’s Hospital, and through the FDA Sentinel System.

AEMS PUBLIC DASHBOARD
Daily refresh launched Aug 2025 → Nearly twelvefold increase in public usage

CY 2024
226K users

CY 2025
2.71M users

12 x growth in users YoY
2.84M sessions in CY 2025
120+ presentations • 2 guidances
3 MaPPs published

AI & MODERNIZATION
LLMs, InfoViP, and OneNexus

100+ Elsa platform use cases built by OSE staff

1.0 OneNexus Release 1.0 launched in 2025

AI InfoViP deduplication platform now in production

6 REMS released

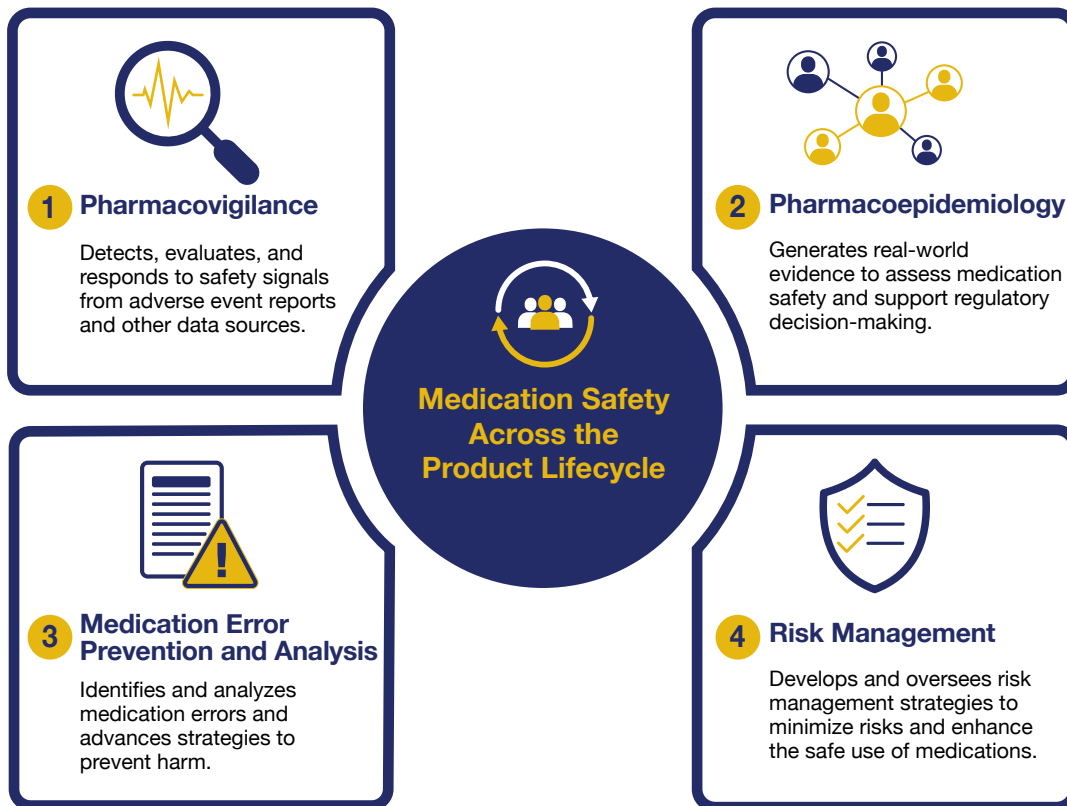
12,774 REMS Dashboard users

OSE at a Glance

Medication safety across the drug product lifecycle

OSE works to detect, assess, prevent, and manage drug risks. OSE participates before products reach patients and continues monitoring after products are marketed, using complementary data sources, regulatory review disciplines, and risk mitigation tools.

OSE's Four Core Functions



OSE's public health responsibilities

- Identify and evaluate emerging adverse events and medication errors.
- Generate real-world evidence to support regulatory decisions.
- Prevent use-related errors through naming, labeling, packaging, and human factors review.
- Design, assess, and modernize risk management strategies.

How OSE works

- Integrates pharmacovigilance, pharmacoepidemiology, medication error prevention, and risk management.
- Partners across FDA offices to evaluate benefit-risk evidence.
- Uses AEMS, Sentinel, labeling reviews, human factors, and REMS data to inform action.
- Supports clear communications to industry, health care professionals, patients, and the public.

Organization and Leadership

Multidisciplinary structure supporting OSE's public health mission

OSE operates through integrated offices and divisions with expertise in pharmacovigilance, epidemiology, error prevention, risk management, regulatory science, regulatory affairs, project management, and communications.

Leadership



Gerald Dal Pan
Director



Robert Ball
Deputy Director



Vasantha Ayalasomayajula
Deputy Director, Operations

Immediate Staff



Jana McAninch
Associate Director,
Public Health
Initiatives



Grace Chai
Associate Director,
Special Initiatives



Amarilys Vega
Director, Regulatory
Science Staff



**Germarie
Sanchez-Pomales**
Director, Project
Management Staff



Tracy Salaam
Director, Regulatory
Affairs Staff



Richard Forshee
Associate Director,
Benefit-Risk
Assessment

Office of Pharmacovigilance and Epidemiology



David Moeny
Acting Director



Monica Munoz
Director,
Division of
Pharmacovigilance I



Chris Jones
Director,
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Wei Hua
Director,
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Monique Falconer
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Office of Medication Error Prevention and Risk Management



Irene Chan
Director



Mishale Mistry
Director
Division of
Medication Error and
Prevention and Analysis I



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Division of
Medication Error and
Prevention and Analysis II



Laura Zendel
Director,
Division of
Risk Management



Sevan Kolejian
Director,
Division of
Mitigation Assessment and
Medication Error Surveillance

2025 Impact Dashboard

Key indicators of review support, surveillance, risk management, and modernization

46 Novel approvals supported Drug and biologic approvals	13 Human Factors reviews for novel approvals Premarket human factors support	2 Novel approvals requiring REMS Risk mitigation at approval	2.05M AEMS reports processed CY 2025
59 Sentinel assessments Medical product assessments	37 Real World Evidence (RWE) consults Effectiveness-focused consults	53 Risk Evaluation and Mitigation Strategies (REMS) modifications CY 2025	100+ Elsa use cases OSE-documented use cases

A total of around 2000 medication error reviews and 552 safety evaluations make up the breadth of OSE’s 2025 portfolio: Premarket review support, postmarket surveillance, real-world evidence, risk mitigation, public dashboard transparency, and practical adoption of emerging tools.

Area	2025 Results	Why it Matters
Premarket review support	Around 2000 Proprietary name and nonproprietary name suffix, labeling, and human factors reviews completed 2 required REMS	OSE contributes before approval by identifying safety, use-related, labeling, and risk mitigation considerations before products reach patients.
Postmarket surveillance	2,048,059 AEMS reports processed; 59 Sentinel medical product assessments completed	OSE uses complementary passive and active surveillance systems to detect, assess, and characterize safety issues after products are marketed.
Evidence and risk management	37 RWE effectiveness-focused consults; 53 REMS modifications approved	OSE helps determine whether real-world evidence is fit for regulatory use and adjusts risk management programs as evidence and implementation needs evolve.
Modernization	100+ OSE-documented Elsa use cases	OSE is applying modern tools to support review efficiency, knowledge synthesis, and safety-related analytical workflows.

Product Lifecycle Contributions

Continuous vigilance from premarket review through postmarket learning



OSE contributed to reviews of labels and labeling for rare disease and emergency-use products, including drug options for Niemann-Pick disease and hypoparathyroidism, and human factors data for epinephrine nasal spray for emergency treatment of allergic reactions, including anaphylaxis.

2 REMS for novel drug products Novel and biologic approvals requiring REMS	3 REMS for non-novel drug products Additional non-novel products requiring REMS	11 REMS for biosimilar drug products Biosimilar approvals requiring REMS	3 REMS for generic drug products Generic approvals requiring REMS
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OSE impact begins before approval and continues through postmarket surveillance, signal evaluation, risk mitigation, and continuous learning.

OSE Contributions to Novel Drug and Biologic Approvals in 2025

46 novel drug and biologic approvals – filled cells indicate OSE involvement

Trade Name	Packaging	Labeling	Proprietary Name Review (PNR)	Human Factors Review	REMS	Postmarketing Requirement (PMR)	Postmarketing Commitment (PMC)	Real World Evidence	Biologic Suffix Review
Andembry	●	●	●	●					
Anzupgo	●	●	●						
Avmapki Fakzynja Co-Pack	●	●	●						
Blujepa	●	●	●			●			
Brinsupri	●	●	●						
Cardamyst	●	●	●	●					
Datroway	●	●	●						●
Dawnzera	●	●	●	●					
Ekterly	●	●	●						
Emrelis	●	●	●						●
Enflonsia	●	●	●	●					
Exdensur	●	●	●	●		●			
Forzinity	●	●	●	●					
Gomekli	●	●	●						
Grafapex	●	●	●				●		
Hernexeos	●	●	●						
Hyrnuo	●	●	●						
Ibtrozi	●	●	●						
Imaavy	●	●	●			●			●
Inluriyo	●	●	●						
Jascayd	●	●	●						
Journavx	●	●	●			●			●
Keytruda Qlex	●	●	●						
Komzifti	●	●	●						
Kygevvi	●	●	●	●					
Lerochol	●	●	●	●					
Lynkuet	●	●	●						
Lynozyfic	●	●	●		●				●
Modeyso	●	●	●						
Myqorzo	●	●	●		●				
Nereus	●	●	●			●			
Nuzolvence	●	●	●	●		●			
Palsonify	●	●	●						
penpulimab-kcqx	●	●	●						●
Qfitlia	●	●	●	●					
Redemplo	●	●	●	●					
Rhapsido	●	●	●			●			
Romvimza	●	●	●			●			
Sephience	●	●	●						
Tryptyr	●	●	●	●					
Vanrafia	●	●	●						
Vizz	●	●	●	●					
Voyxact	●	●	●			●			●
Wayrilz	●	●	●			●			
Yartemlea	●	●	●			●		●	●
Zegfrovy	●	●	●						

Controlled Substances and Overdose Crisis

2025 actions to reduce risk and expand evidence-based response

OSE supported FDA work on opioid medication safety, safe disposal, potentially dangerous unapproved products, buprenorphine dosing, pediatric unintentional exposure prevention, and emerging risks involving controlled substances.

Timing	Action	Public health impact
Mar 31	Opioid analgesic mail-back envelopes available	OA REMS changes enabled pharmacies and other dispensers to provide free, pre-paid disposal envelopes to patients and caregivers.
May 5	Joint advisory committee meeting on ER/LA opioid PMR studies	Evidence from long-term opioid analgesic studies informed later labeling and regulatory actions.
May 8	Tianeptine Dear Healthcare Provider Letter	OSE data supported communication on serious harms linked to an unapproved drug sold in consumer settings.
Jul 29	7-OH integrated assessment action as a critical step in the fight against opioid addiction	OSE contributed to an 8-factor analysis and HHS scheduling recommendation for a highly potent kratom-derived alkaloid.
Jul 31	Safety labeling changes for opioid analgesics	OSE collaborated on SLC letters and a Drug Safety Communication for all opioid analgesics.
Dec 22	ER/LA observational PMRs fulfilled	OSE's review of postmarketing epidemiologic studies on long-term opioid use resulted in safety labeling changes for all opioid analgesics and fulfillment of all observational PMRs (3033-1 through 3033-10).



Public Health Response

Targeted surveillance and rapid coordination when safety issues emerge

Weather-related drug shortage response

- Participated in a multidisciplinary Intravenous Fluids Shortage Task Force after a major manufacturing disruption.
- Performed heightened surveillance of adverse events involving affected intravenous fluids and products granted regulatory discretion.
- Collaborated with the Office of Product Quality to rapidly identify potential new safety issues.

Consumer and clinical communications

- Supported warnings about unapproved epinephrine nasal solutions.
- Contributed to public communications on compounded injectable semaglutide dosing errors.
- Supported communications on tianeptine and copycat delta-8 THC food products.

Rapid surveillance activation Heightened monitoring for shortage-affected products	Cross-office coordination Safety + quality integrated response	Public communications Evidence to action practical safety messages
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The common thread across these actions is operational readiness: OSE uses surveillance, clinical review, data interpretation, and coordinated communications to identify and respond to public health threats.



Pharmacovigilance and AEMS

Detecting, assessing, and communicating drug safety issues

AEMS remains a core source for adverse event reports, medication error reports, and product quality complaints involving drugs and therapeutic biologics. OSE reviewers use AEMS with other evidence sources to evaluate safety signals and inform regulatory action.

Selected 2025 safety outcomes supported by OSE work	Regulatory or public health significance
Withdrawal of obeticholic acid approval for marketing	Evidence supported significant safety actions, including product withdrawal, new and strengthened warnings, and public communications addressing serious and life-threatening risks.
Serious liver injury associated with fezolinetant use	Safety findings informed prescribing information and public communication.
New Boxed Warning for anaphylaxis with glatiramer acetate	Labeling strengthened risk communication for serious hypersensitivity.
Tranexamic acid injection warnings strengthened	Warnings emphasized intravenous administration only.
Dosing errors with compounded injectable semaglutide	Public warnings addressed medication-use safety concerns.



AEMS Public Transparency

Making safety data more accessible and actionable

2,712,641 Total users	7,432 Average users per day	5.29 Average session duration minutes	2,844,780 Sessions
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What changed in 2025

- The AEMS Public Dashboard shifted from quarterly refreshes to daily, near-real-time data refresh.
- Public interest grew substantially after the AEMS Public Dashboard data refresh cycle change, with total users increasing nearly twelvefold from 226,271 in CY 2024 to 2,712,641 in CY 2025.
- Dashboard functionality helps users search for adverse events, medication errors, and product quality issues.

Why it matters

- Improves transparency for FDA stakeholders and the public.
- Makes safety data easier to query and interpret.
- Supports informed engagement with postmarketing safety information.

Faster public access to current safety data strengthens trust, improves stakeholder understanding, and supports more informed engagement with drug safety information.

Pharmacoepidemiology and Real-World Evidence

Using real-world data to strengthen regulatory decision-making

In addition to spontaneous adverse event and medication error reports, FDA maintains a robust pharmacoepidemiology program to evaluate drug safety and effectiveness using real-world data (RWD). OSE epidemiologists guide pre- and post-approval assessments of real-world evidence (RWE) including sponsor submissions, observational studies, literature reviews, and FDA’s Sentinel System — to inform regulatory decision-making. OSE also leads reviews of RWE submitted as part of marketing applications, ensuring the appropriate use of RWD and RWE in support of regulatory decisions.

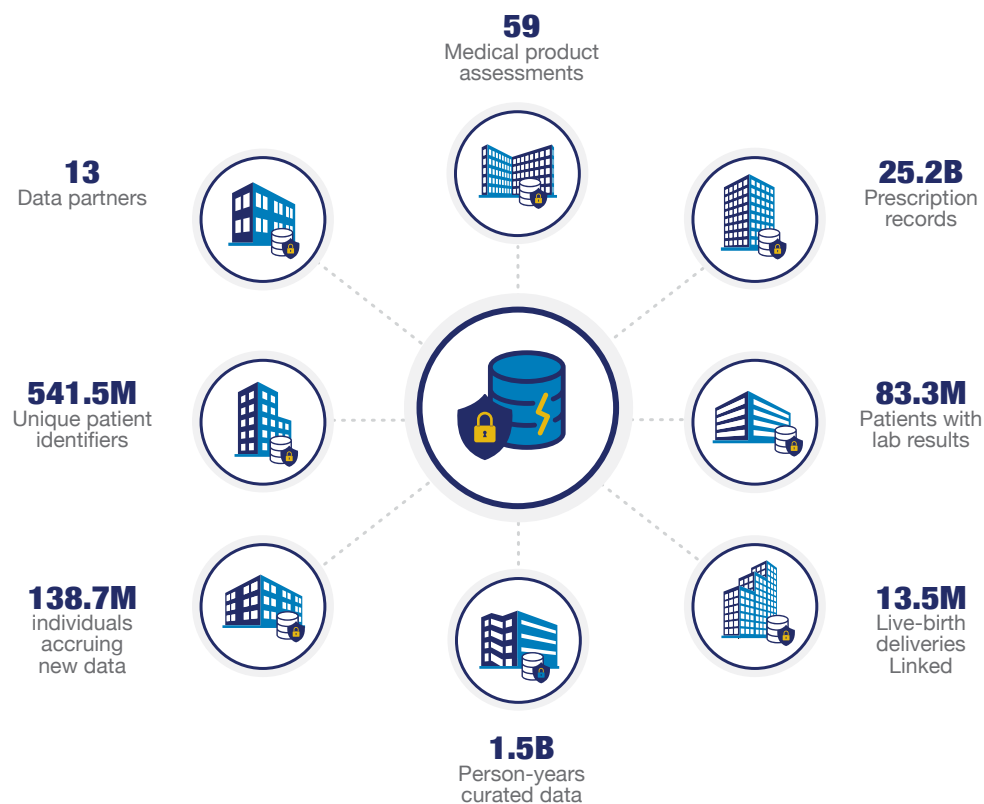
37 RWE consults Effectiveness-focused consults in 2025	2 Advancing RWE proposals OSE-led scientific review and guidance for sponsor proposals	M14 ICH guideline finalized General principles for pharmacoepidemiological studies using real-world data	RWE-DE data enterprise in operation Linked claims and EHR infrastructure for drug safety causal inference studies
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2025 Contribution	Focus
Drug safety evaluations	Reviewed safety issues, PMR protocols, statistical analysis plans, interim and final study reports, and literature-based signals — including as part of FDA’s multidisciplinary integrated reviews. Led reviews of safety signals in support of NISS evaluations, labeling supplements, and prior approval supplements. Responded to external inquiries including Executive Orders, congressional requests, Citizen’s Petitions, and foreign regulatory agency inquiries. Acquired novel psychedelic data sources to support anticipated pre-market application reviews and eight-factor analyses.
Effectiveness submissions	Assessed whether RWD and RWE were appropriate for regulatory decisions and labeling support. Responded to approximately 37 RWE effectiveness consults in 2025, providing timely regulatory guidance prior to application submission. RWD are data relating to patient health status and/or health care delivery routinely collected from sources such as EHRs and medical claims. RWE is the clinical evidence about the use and potential benefits or risks of a medical product derived from analysis of RWD.
Advancing RWE Program	Under PDUFA VII, OSE served on the Leadership Team and conducted scientific reviews for the Advancing RWE Program, which allows early meetings between sponsors and FDA to improve the quality and acceptability of RWE-based approaches for new labeling claims, including new indications or post-approval study requirements. In 2025, OSE led scientific review and provided study design and data source guidance for two selected sponsor proposals. OSE also created the first public report on RWE submissions to CDER under PDUFA VII.

2025 Contribution	Focus
RWE guidance and policy	Served as both Rapporteur and FDA Technical Lead on ICH M14 (finalized September 2025) and co-led ICH E2D(R1) (finalized September 2025). Continued to support FDA research demonstration projects and grants aimed at improving data reliability, RWE tools, and novel epidemiology methods.
International harmonization	Provided technical leadership for ICH M14 — “General Principles on Planning, Designing, Analyzing, and Reporting of Non-interventional Studies That Utilize Real-World Data for Safety Assessment of Medicines” — and ICH E2D(R1) on post-approval safety data definitions and standards. Both were adopted September 2025.

Sentinel complements AEMS by enabling FDA to conduct targeted analyses using large healthcare administrative claims and electronic health record data. It provides a privacy-preserving infrastructure for evaluating safety issues in real-world populations.

Sentinel infrastructure also supports methods development, including computable phenotypes, causal inference frameworks, and active surveillance approaches that can be applied to safety and effectiveness questions.



The FDA Sentinel System

The FDA's active drug safety surveillance system, advancing real-world evidence for regulatory decision-making

Mandated by the Food and Drug Administration Amendments Act of 2007, FDA established the Sentinel Initiative, a national medical product safety surveillance system. A core program of the Sentinel Initiative is the Sentinel System, which includes one of the world's largest multi-site, privacy-preserving healthcare databases dedicated to medical product safety. Using the Sentinel System, FDA proactively monitors the safety of FDA-regulated drugs, biologics, and other medical products, complementing spontaneous adverse event reporting from AEMS and other surveillance activities.

The cornerstone of the Sentinel System is the Active Risk Identification and Analysis (ARIA) system, which draws on the Sentinel Distributed Database (SDD) — a collection of harmonized electronic healthcare datasets from multiple Data Partners, formatted in the Sentinel Common Data Model. As of 2025, the SDD contains over 1.5 billion person-years of data covering more than 541 million unique patient identifiers, with more than 138 million members actively accruing new data. The Sentinel Innovation Center's Real-World Evidence Data Enterprise (RWE-DE) further extends Sentinel's capabilities by incorporating linked electronic health record (EHR) data with claims data to enable FDA to conduct drug safety studies not possible with claims data alone.

Between 2022 and 2024, 59 Sentinel studies informed regulatory decision-making or otherwise contributed to FDA's public health mission. Specifically, Sentinel was used to conduct postmarket safety monitoring for 12 drugs planned at approval, evaluate Newly Identified Safety Signals, support premarket drug evaluations, inform REMS assessments — including the Clozapine REMS elimination — and respond to public health events. These achievements were detailed in a report assessing the Sentinel System from 2022–2024 that was published by FDA in September 2025, fulfilling a core PDUFA VII commitment to analyze and report on Sentinel's use for regulatory purposes. Looking ahead, the Sentinel website continues to serve as the primary forum for sharing information about the Sentinel System's activities, including regulatory contributions, innovations in methodology, and AI integration, with the broader scientific community.

541.5M

unique patient
identifiers in
the Sentinel
Distributed
Database spanning
2000 to 2025

1.5B

person-years of
curated healthcare
data across 13 Data
Partners

59

Sentinel studies
contributed to
FDA's regulatory
and public health
mission from
2022–2024

Sources: [FDA.gov](https://www.fda.gov) • [sentinelinitiative.org](https://www.sentinelinitiative.org) • PDUFA
VII Assessment of the Sentinel System (2022–2024),
September 2025

Preventing Medication Errors and Use-Related Risks

Premarket prevention and postmarket feedback loops

OSE reviews product names, nonproprietary name suffixes, labels, labeling, packaging, product design, and human factors submissions to minimize or eliminate hazards that can contribute to medication or use-related errors.

504 PNR reviews CY 2025 Proprietary name reviews completed	58 Suffix reviews CY 2025 biological product suffix reviews completed	60 Human factors validation protocols CY 2025 reviews completed	983 Carton & container labeling reviews CY 2025 reviews completed
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95 Use-Related Risk Analyses CY 2025 URRA reviews completed	124 Other Human Factors Reviews Reports, consults, and meeting requests	9 Medication error NISS reviews Postmarket medication error signal reviews
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Risk Management and REMS

Targeted programs to ensure benefits outweigh serious risks

OSE plays a critical role in protecting public health by developing and evaluating strategies that support the safe and effective use of medications. Through the application of scientific evidence, risk assessment, and stakeholder engagement, OSE works to identify, communicate, and mitigate medication risks across the product lifecycle.

A key component of these efforts is the REMS program. A REMS is a drug safety program that FDA may require for certain medications with serious safety concerns to help ensure that the benefits of a medication outweigh its risks. REMS programs are designed to prevent, monitor, and manage specific serious risks through targeted risk mitigation measures that extend beyond product labeling alone.

5 REMS with ETASU approved	2 Shared system REMS approved	53 REMS modifications approved
6 REMS released	12,774 REMS dashboard users	2,884 Dashboard hours viewed

2025 REMS Action	Products / program	Impact
Eliminated	Clozapine REMS	Ended 35+ years of mandatory documentation requirements for prescribers and pharmacies. Elimination of the REMS is expected to improve access to clozapine and decrease the burden on the health care delivery system as labeling is sufficient to mitigate the risk.
Eliminated	Ambrisentan Shared System REMS, Macitentan-containing Products Shared System REMS, and Tryvio REMS	The elimination of the ERA (endothelin receptor antagonists) REMS streamlines patient access and reduces healthcare system burden without compromising public health as the risk is now considered to be adequately managed through labeling.
Modified	Bosentan Shared System REMS and Filspari REMS	These REMS were updated to remove the risk of embryo-fetal toxicity, reducing the documentation requirements to comply with the REMS as the risk is now considered to adequately be managed through labeling.

Clozapine REMS Elimination

Reducing burden on the health care system and improving access to clozapine.

“Although the risk of severe neutropenia with clozapine still exists, FDA has determined that the REMS program for clozapine is no longer necessary to ensure the benefits of the medicine outweigh that risk.”

Source: FDA Drug Safety Communication, “FDA removes risk evaluation and mitigation strategy (REMS) program for the antipsychotic drug Clozapine,” Aug. 27, 2025

Clozapine is an antipsychotic drug used to improve symptoms of schizophrenia in patients who do not respond adequately to standard antipsychotic treatment. Because of the risk of severe neutropenia, clozapine had been available only through a REMS program that imposed enrollment and Absolute Neutrophil Count (ANC) monitoring requirements on prescribers, pharmacies, and patients.

Following a comprehensive reevaluation that began in September 2023 — informed by three concurrent real-world studies: a Brigham and Women’s Hospital study (clozapine utilization and ANC monitoring adherence), a Veterans Health Administration study (incidence and severity of neutropenia), and a Sentinel System study (ANC monitoring adherence). FDA convened a joint meeting of the Drug Safety and Risk Management Advisory Committee and the Psychopharmacologic Drugs Advisory Committee on November 19, 2024. The committees’ advice informed FDA’s determination that the REMS was no longer necessary.

On February 24, 2025, FDA announced its determination that a REMS was no longer necessary for Clozapine. Prescribers, pharmacies, and patients were no longer expected to participate in the Clozapine REMS.

On June 13, 2025, the Clozapine REMS was formally eliminated. Information about severe neutropenia — including the existing Boxed Warning — remains in the prescribing information for all clozapine medicines. FDA still recommends that prescribers monitor patients’ ANC according to the frequencies described in the prescribing information.

Source: FDA.gov·Frequently Asked Questions | Clozapine REMS Modification·Last updated February 25, 2025

35+

Years of mandatory documentation requirements for prescribers and pharmacies ended in 2025

3

Concurrent real-world studies (Brigham & Women’s, VA, Sentinel) informing the decision

20

Years of data from different health systems and insurance coverage evaluated in the real-world studies informing the decision

Drug Safety Modernization

Modern tools, standards, and workflows for faster, stronger safety review

OSE advanced modernization through production deployment, AI exploration, regulatory process harmonization, and updated policy infrastructure.

InfoVIP Moved into production AI-enabled decision support for case series evaluation	100+ Elsa use cases documented Priority areas include AEMS case summaries and Sentinel concept briefs	Large Language Models Tested across safety workflows Causality, duplicates, adverse event extraction, literature screening, and case definitions	OneNexus Release 1.0 supported Unified regulatory platform implementation
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Modernization area	2025 contribution	Expected value
AEMS and LLMs	Explored clinical concept extraction, report-quality classification, duplicate detection, and case summarization.	Supports efficiency and consistency in high-volume safety review.
Sentinel and LLMs	Explored concept briefs and protocol development support.	Helps determine where AI can increase efficiency in study development.
OneNexus	Contributed workflow harmonization, user acceptance testing, and launch support.	Improves regulatory review process consistency and cross-office coordination.
MaPP 6700.9	Published revised process for posting new safety information or potential signals from AEMS.	Clarifies responsibilities, aligns procedures with NISS, and adds process maps.

Modernization is a mission enabler, and OSE modernization investments help reviewers manage volume, improve consistency, reduce burden, and translate safety evidence into action more efficiently.

InfoViP

An AI-Enabled Tool for Postmarket Safety Surveillance
— Now in Production

“InfoViP is a decision-support tool, not a replacement for reviewers. Safety evaluators can verify AI output against source ICSRs, ensuring interpretability and accountability.”

What is InfoViP? CDER’s Office of Surveillance and Epidemiology developed the Information Visualization Platform (InfoViP), an AI-enabled decision-support tool for postmarket drug and biologic safety surveillance. InfoViP is now in production.

The Challenge It Addresses — AEMS receives over 2 million adverse event reports per year (over 32.4 million in the AEMS database as of December 2025). Manual review and analysis of Individual Case Safety Reports (ICSR) is time consuming and labor intensive.

Key AI Capabilities — InfoViP’s Natural Language Processing (NLP) automatically extracts clinical concepts and builds timelines of events from ICSR narratives. The deduplication algorithm identifies potential duplicate ICSR records. The NLP and ML-based assessability classifier evaluates ICSR by information quality, enabling priority triage of high-quality reports.

Strategic Impact — Supports CDER’s strategic goal of modernizing drug and biologic operations through AI. Future integration of Large Language Models (LLM) will further enhance InfoViP to support safety reviewer workflows.

2 M +

adverse event
reports received by
AEMS annually

32.4 M

total AEMS reports
as of December
2025

3

core AI capabilities:
NLP extraction,
deduplication, and
ML assessability
classification

Botsis T, et al. Drug Saf. 2020;43(9):891–901.
doi:10.1007/s40264-020-00945-0 · PMID: 32445187
FDA/CDER Office of Surveillance and Epidemiology



Stakeholder Engagement and International Collaboration

Sharing evidence, strengthening methods, and supporting harmonization

OSE engages stakeholders through scientific meetings, workshops, public communications, interagency workgroups, international collaborations, and conference presentations. These activities improve understanding of OSE tools and strengthen regulatory science across FDA and partner communities.

Domestic and interagency engagement

- Scientific meetings and public workshops on Sentinel, AEMS, REMS, and emerging safety issues.
- Quarterly collaboration with the Department of Defense, Veterans Affairs, and Indian Health Service on medication error findings and risk-control strategies.
- Collaboration with the Centers for Disease Control and Prevention to monitor medication errors related to nirsevimab.

International scientific leadership

- Advanced RWE use for safety and effectiveness through CIOMS Working Group XIII.
- Led rare disease RWE engagement through the International Society for Pharmacoepidemiology (ISPE) scientific channels.
- Contributed to final ICH M14 and E2D(R1) work supporting harmonized safety evidence and post-approval reporting standards.

AEMS Public dashboard engagement Daily refreshes improve stakeholder access	REMS Dashboard transparency Users can visualize program trends and details	Sentinel Active surveillance community Methods and findings support broader learning
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ICH M14 and E2D(R1)

Setting the global standard for real-world evidence and post-approval safety reporting

“OSE served as FDA Technical Lead on both — as Rapporteur on M14 and as Regulatory Chair on E2D(R1) — playing a central role in their development from concept through finalization.”

In September 2025, two landmark ICH guidelines — M14 and E2D(R1) — reached Step 4 adoption simultaneously, representing a major milestone in the global harmonization of post-marketing drug safety science.

ICH M14 — “General Principles on Planning, Designing, Analyzing, and Reporting of Non-interventional Studies That Utilize Real-World Data for Safety Assessment of Medicines” — is the first internationally harmonized guideline for non-interventional pharmacoepidemiological safety studies. Endorsed at Step 2 in May 2024 and generating approximately 1,600 stakeholder comments during public consultation, the final guideline recommends a stepwise, iterative approach: from articulating the research question and assessing data fitness-for-use, through study design, feasibility, bias and confounding control, analysis, and regulatory submission. It applies to drugs, vaccines, and biological products across the post-marketing lifecycle and is designed to improve efficiency and transparency in the development, reporting, submission and review of non-interventional studies and resultant regulatory actions, as well as improve the ability of the study protocol and report to be accepted across regulatory authorities. M14 was implemented in the U.S. as a Final FDA Guidance on 3 March 2026.

ICH E2D(R1) — “Post-Approval Safety Data: Definitions and Standards for Management and Reporting of Individual Case Safety Reports” — updates the foundational 2003 E2D guideline to reflect two decades of evolution in pharmacovigilance practice. The revision addresses new sources of post-approval safety information including social media, patient support programs, and market research programs. The Expert Working Group consisted of 12 regulatory authorities and five industry organizations. The updated guideline harmonizes definitions, reporting timelines, and case management standards across all ICH regions and was implemented in the U.S. as a Final FDA Guidance on 4 March 2026.

ICH M14 Final Guideline, adopted 4 September 2025 ·
ICH E2D(R1) Final Guideline, adopted 15 September 2025
· FDA/CDER OSE served as Rapporteur on M14 and as
Regulatory Chair on E2D(R1).

Sept. 2025

Both M14 and E2D(R1) reached Step 4 adoption simultaneously

12+5

regulatory authorities and industry organizations on the E2D(R1) Expert Working Group

2025 Scientific Impact Snapshot

A broader view of OSE scientific and regulatory output

OSE’s 2025 scientific portfolio reflects the breadth of the office’s public health and regulatory science mission. In 2025, OSE staff contributed to 55 unique scientific outputs, including 40 peer-reviewed journal publications and scientific correspondence, 11 conference abstracts, 3 preprints, and 1 collaborative scientific report. These outputs advanced evidence generation across pharmacovigilance, pharmacoepidemiology, REMS and risk management, medication safety, controlled substances, real-world evidence, and emerging analytic methods.

Output type	2025 count	Enterprise value
Peer-reviewed journal publications and scientific correspondence	40	Advances methods, evidence, and interpretation for drug safety and regulatory decision-making
Conference abstracts	11	Shares emerging findings with scientific, regulatory, and public health communities
Preprints	3	Accelerates dissemination of methods and analytic approaches before journal publication
Collaborative scientific report	1	Supports international scientific consensus and cross-organizational regulatory science

Inclusive lens Publications + policies + tools and collaborations	Impact over activity Emphasize decisions Emphasize how outputs change decisions and practice	Portfolio structure Supports full inventory Supports full publication inventory
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For a full list of OSE publications in 2025, please find details at the following [link](#).



Looking Ahead

Strategic priorities for the next phase of OSE work

OSE will continue to broaden its pharmacovigilance, pharmacoepidemiology, medication error prevention, and risk management capabilities while modernizing the systems and methods that support regulatory decision-making.

	Fulfill user fee commitments	Fulfill user fee commitments and streamline review of human factors protocols, use-related risk analyses, REMS methods, proprietary name reviews, and premarket labeling reviews.
	Address nonmedical use and emerging risks	Continue addressing nonmedical use of prescription medicines and emerging drug-related risks through evidence generation and targeted safety actions.
	Modernize REMS and reduce burden	Modernize REMS and reduce implementation burden through development and testing of standards-based integration into health care workflows.
	Expand pharmacovigilance capabilities	Implement the Pharmacovigilance Strategy Program and coordinate cross-disciplinary safety assessment processes.
	Scale advanced analytics	Apply machine learning, natural language processing, and advanced analytics to improve signal evaluation, data quality, and efficiency.
	Strengthen collaboration	Strengthen collaboration with international regulators and federal partners to support emerging safety concerns.



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