U.S. FOOD & DRUG ADMINISTRATION

Office of Surveillance and Epidemiology

Annual Report 2020

DETECTING, ASSESSING, PREVENTING, AND MANAGING RISKS

May 2021
www.fda.gov

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DIRECTORS MESSAGE

I am pleased to share with you the 2020 Annual Report for the Office of Surveillance and Epidemiology (OSE).

OSE has four core functions – pharmacovigilance, pharmacoepidemiology, medication error prevention and analysis, and risk management – and operates across multiple disciplines to review and assess the safety of medicines. Everything in OSE is tied to these four core functions. These core functions are supported by staff specializing in medicine, pharmacy, regulatory science, regulatory affairs, epidemiology, human factors engineering, social science, safety surveillance, information technology, clinical informatics, project management, administration, contracting, training, and communication.

The COVID-19 pandemic presented us with challenges that we could not have imagined when the year began, disrupting our personal and professional lives as well as society as a whole. It also required us to adopt new and innovative approaches to monitoring the safety of medicines and managing their risks.

OSE used its full array of tools to ensure the safety of products for COVID-19 and to monitor their performance, from hand sanitizers to monoclonal antibodies. We set up an office-wide COVID-19 team for the rapid and efficient review of pre-approval, pre-authorization, and postmarket safety data, focused primarily on adverse event analysis, medication error prevention, and drug utilization. We accessed new data sources and employed new analytic methods to understand patterns of drug use and to identify safety signals. Given the national and global reach of COVID-19, we actively participated in the Evidence Accelerator sponsored jointly by the Reagan-Udall Foundation and Friends of Cancer Research and in scientific collaborations with the International Coalition of Medicines Regulatory Authorities. Working beyond our office, our Commissioned Officers were deployed to various agencies and healthcare settings, while other staff picked up their work in OSE.

Staff not working specifically on COVID-19 kept the rest of our important work going – and there was lots of it, including our review work, hiring and onboarding new staff, budgeting and contracting activities to bring in new data sources, modernizing our regulatory programs, continuing implementation of the Drug Safety Teams, participating in outside meetings, and many other activities.

The keys to our success in 2020 were our staff's dedication to FDA's mission, its professionalism, and its commitment to robust science.

Best regards,

Gerald Dal Pan, MD, MHS
Director, Office of Surveillance and Epidemiology

WHO WE ARE AND WHAT WE DO

The Office of Surveillance and Epidemiology (OSE) within the Center for Drug Evaluation and Research (CDER) works to detect, assess, prevent, and manage the risks of medications so that they can be relied upon to treat disease and improve health. All medicines have risks as well as benefits; the risks of medicines are the chances that something unwanted or unexpected could happen when consumers use them. OSE participates in the safety analysis of drugs before they are marketed to patients and consumers. After the drugs are marketed, we utilize risk assessment tools to identify and assess adverse events and medication errors that did not appear during the drug development process as well as to understand better those risks observed in clinical trials. OSE also provides expertise on risk mitigation strategies to prevent medication errors, to improve the safe use of products, and to manage the risks associated with medicines after they are marketed.

OSE has four core functions – pharmacovigilance, pharmacoepidemiology, medication error prevention and analysis, and risk management – and operates across multiple disciplines to review and assess the safety of medicines. Everything in OSE is tied to these four core functions.

WHO WE ARE AND WHAT WE DO

Pharmacovigilance

- Detection and assessment of safety-related issues for all marketed drug and therapeutic biologic products.
- Use of surveillance tools such as the FDA Adverse Event Reporting System (FAERS) to identify new safety concerns with marketed products.

Pharmacoepidemiology

- Review of post-marketing study protocols and study reports submitted by manufacturers to inform drug safety and use .
- Conducting epidemiological studies to quantify risk and identify risk factors.
- Use of population-based data to evaluate the risks and uses of medications.

Medication Error Prevention and Analysis

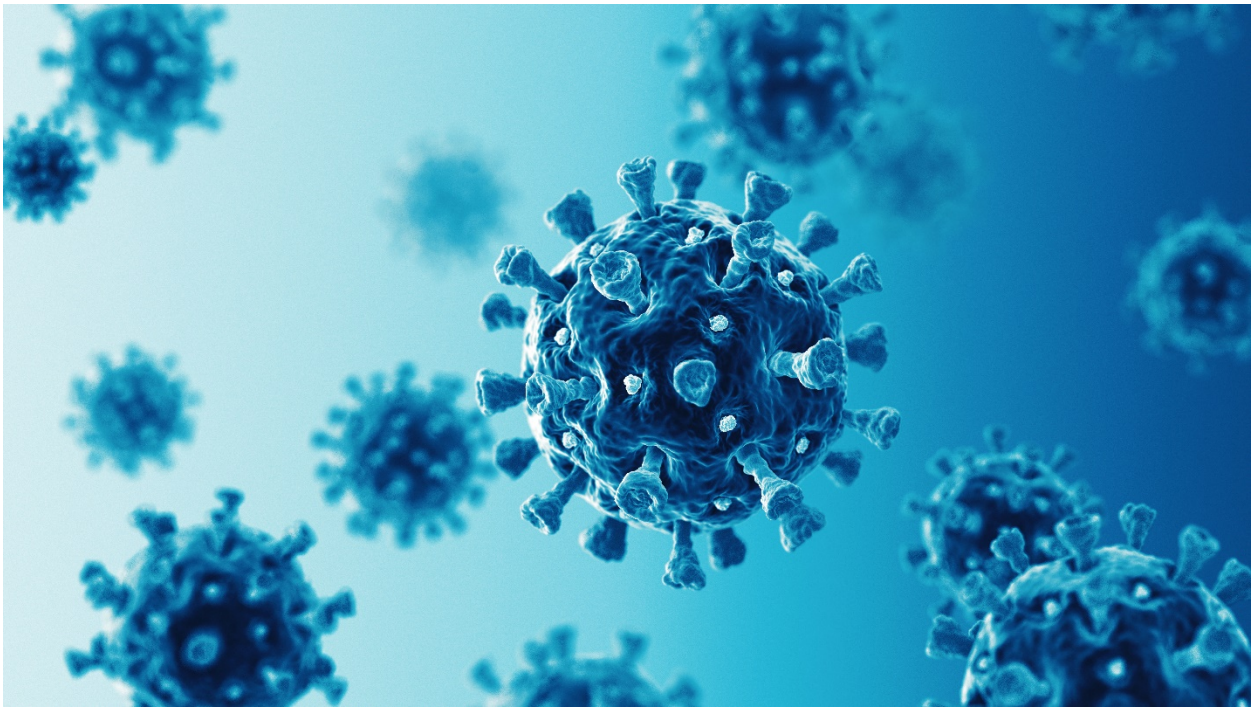
- Review of proposed proprietary names for drugs and biologics, nonproprietary name suffixes for biological products, labels, labeling and human factor studies to minimize user error.
- Review of medication error reports to identify trends in improper prescribing, dispensing, or usage of drug products.

Risk Management

- Evaluate the need for a risk mitigation strategy for all novel drugs.
- Review proposed risk evaluation and mitigation strategies (REMS), and modifications to approved REMS.
- Evaluate methods to assess the impact of mitigation strategies and reviews the results of those REMS assessments.

These core functions are supported by staff specializing in medicine, pharmacy, regulatory science, regulatory affairs, epidemiology, human factors engineering, social science, safety surveillance, information technology, clinical informatics, project management, administration, contracting, training, and communication. See organizational chart for 2020 in Appendix I.

RESPONDING TO COVID-19



OSE in Action: Responding to the COVID-19 Pandemic

On January 31, 2020, the Secretary of the Department of Health and Human Services (HHS) issued a declaration of a public health emergency (PHE) related to the Coronavirus Disease 2019 (COVID-19) and mobilized HHS Operating Divisions. On March 13, 2020, the President of the United States declared a National Emergency in response to COVID-19. This transformed the way we live and work. The FDA—and OSE–were critical to the nation's response to this pandemic. OSE's activities ranged from monitoring and assessing the safety and supply of novel and re-purposed medicines, including those under Emergency Use Authorization, used to treat COVID-19 to providing guidance on how to adapt Risk Evaluation and Mitigation Strategies (REMS) programs during a pandemic. We have shared our results of multiple safety and epidemiological analyses with colleagues in other FDA offices, as well as with the National Institutes of Health, the Centers for Disease Control and Prevention, and the COVID-19 Evidence Accelerator sponsored by the Reagan-Udall Foundation and Friends of Cancer Research. We have also collaborated with our international regulatory partners to develop common protocols to study the effects of drugs used to treat COVID-19.

OSE's pharmacovigilance activities included daily searches of the FDA Adverse Event Reporting System (FAERS) and the biomedical literature to identify adverse events and medication errors associated with the use of drugs to treat or prevent COVID-19; daily searches of the American Association of Poison Control Centers National Poison Data System (NPDS) for calls involving hydroxychloroquine and chloroquine; detailed analysis of several safety signals related to hydroxychloroquine, azithromycin, and other products; summary safety analyses for hydroxychloroquine and remdesivir; daily searches of FAERS and NPDS for adverse events related to hand sanitizers potentially contaminated with methanol; and expedited triage and entry of adverse event reports

related to COVID-19. These activities have contributed to the Agency's oversight of, and public communications concerning, Emergency Use Authorizations (EUAs) and the recall of methanol-containing hand sanitizers.

To expand data sources available to OSE, FDA awarded a Task Order Contract to the American College of Medical Toxicology (ACMT) for the development of a COVID-19 Adverse Drug Event Sub-registry for enhanced collection of safety data related to drug therapies used in patients with COVID-19.

FDA's Sentinel System, led by OSE, engaged in numerous activities to protect and promote public health during the COVID-19 pandemic, including:

- Monitoring critical drugs to assess changes in utilization over time and by geography
- Describing the course of illness among hospitalized COVID-19 patients, including their characteristics, healthcare utilization, disease progression, and outcomes
- Evaluating the use of computable phenotypes (i.e., a disease, clinical condition or event ascertained using a computerized query of Electronic Health Records) to identify COVID-19-positive patients in real world data
- Developing an adaptable protocol designed to support a variety of on-demand queries and subsequent studies of the safety or effectiveness of treatments for COVID-19 in special populations of interest such as pregnant women and children
- Assessing the occurrence of coagulopathy and its risk factors among hospitalized COVID-19 patients
- Collaborating with the Reagan-Udall Foundation and Friends of Cancer Research on the COVID-19 Evidence Accelerator initiative to share methods, information, and results to address key questions about COVID-19.

"The Sentinel Initiative has been leveraged to address public health crises, such as the opioid crisis and currently is being used in FDA's efforts to understand COVID-19."

Robert Ball, M.D., OSE Deputy Director

The use of Sentinel to respond to the COVID-19 pandemic has highlighted the need for improved and rapid access to electronic health records (EHRs) and linked claims-EHR data to address questions about drug treatment in hospital and especially intensive care unit settings. To address this issue, the Sentinel System incorporated new data sources, created a rapidly refreshed database, and adapted a pilot project that was originally designed for assessing performance of drugs for severely ill influenza patients to assessing drugs used to treat COVID-19 patients, including new insights on where in the EHR detailed information on oxygen use can be found. These lessons will be carried forward in furthering the Sentinel System's capabilities and preparedness for future public health emergencies.

RESPONDING TO COVID-19

Because of the disruption in healthcare delivery caused by COVID-19, OSE received several inquiries from external stakeholders regarding laboratory monitoring requirements in REMS and the impact that these requirements have on patient access to REMS drugs when patients self-isolate or are subject to quarantine due to COVID-19. On March 22, 2020, under OSE's leadership, FDA issued the temporary Policy for Certain REMS Requirements During the COVID-19 Public Health Emergency Guidance for Industry and Health Care Professionals to provide recommendations to sponsors and health care providers on REMS-related patient laboratory testing or imaging studies during the PHE. FDA advised healthcare providers prescribing and/or dispensing these drugs to use their best medical judgment in weighing the benefits and risks of continuing treatment in the absence of laboratory testing and imaging studies if there are compelling reasons not to complete these tests or studies during the PHE and to communicate with their patient regarding this assessment.

OSE conducted expedited proprietary name evaluations submitted for multiple COVID-19 therapies under EUAs, Investigational New Drug Applications (INDs), and New Drug Applications (NDAs). OSE reviewed container labels and carton labeling for multiple COVID-19 therapies under EUAs to minimize the risk of medication errors. In collaboration with other FDA offices, OSE reviewed multiple Dear Healthcare Provider letters regarding labels and labeling for imported products and changes to US marketed products to prevent medication errors with COVID-19 therapies.

Through OSE's surveillance efforts, we identified medication errors related to Veklury (remdesivir) that resulted in updating the EUA Fact Sheets to address reported medication errors. OSE also collaborated with Institute of Safe Medication Practices (ISMP) to publish on reported medication errors with Veklury (remdesivir) EUA. OSE also identified reports of wrong drug, incorrect dose, and other medication errors with Regen-Cov (casirivimab and imdevimab); in response, we updated the EUA Fact Sheet and revised the labeling and packaging. The vial labels and carton labeling were revised to clearly state the product names and strength. A new packaging configuration, dose packs containing vials of casirivimab and imdevimab to make one treatment dose, was introduced to help ensure the product was prepared correctly for administration.

OSE also provided scientific leadership on drug supply chain data and started developing a data-driven, evidence-based approach to refine and validate signals of drug shortages. OSE has been instrumental in assessing, acquiring, and analyzing data sources for the US drug supply chain in collaboration with others in CDER and the Office of the Commissioner, and is analyzing and monitoring use of critical drugs used in the treatment of COVID-19 and its complications to inform CDER's response to national or regional drug shortages.

Detecting And Assessing Risks

Multiple approaches to detecting and assessing risks in the postmarket setting

FDA uses several approaches for post-marketing surveillance and risk assessment to identify adverse events and medication errors that may not have appeared during the drug development process. FDA maintains two major systems for postmarketing drug safety surveillance, a "passive" system known as the FDA Adverse Event Reporting System (FAERS), and an "active" system known as the Sentinel System.

2x

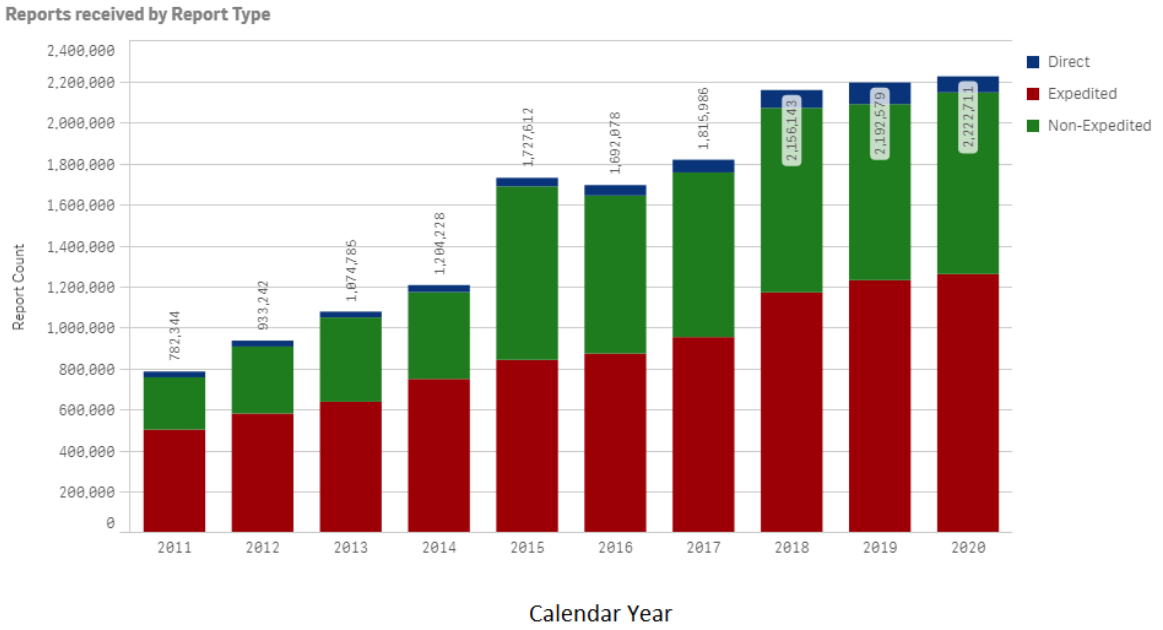
FAERS reports more than doubled since 2013

FDA Adverse Event Reporting System (FAERS)

For over 50 years, FDA's primary source of medical product safety data has come from adverse event reports from patients, health care professionals, the pharmaceutical industry, and others. These reports, collectively part of a "passive surveillance" system in FAERS, still serve a critical purpose for safety researchers.

FAERS reports have continued to increase over time. Since 2018, we have received over 2.1 million reports annually. OSE uses the FAERS reports to identify and evaluate drug safety concerns and recommend actions to

improve product safety and protect public health. Of the over 2.2 million reports received in 2020, more than 1.2 million were described as serious adverse events not mentioned in the product label.



Systematic data mining (or looking for patterns in large data sets) of FAERS allows OSE to generate medication and adverse event pairs that are disproportionately reported. OSE reviewers conduct disproportionality analyses of FAERS data at intervals for newly approved products (such as new molecular entities (NME); original biological products; and products without NME designation but having a newly approved dosage form, route of administration, indication, or patient population that may result in increased safety concerns), and yearly, at minimum, for all products approved more than three years. Once we identify a signal, we may develop a case series built upon those cases meeting the criteria in the case definition and assessed as causally associated.

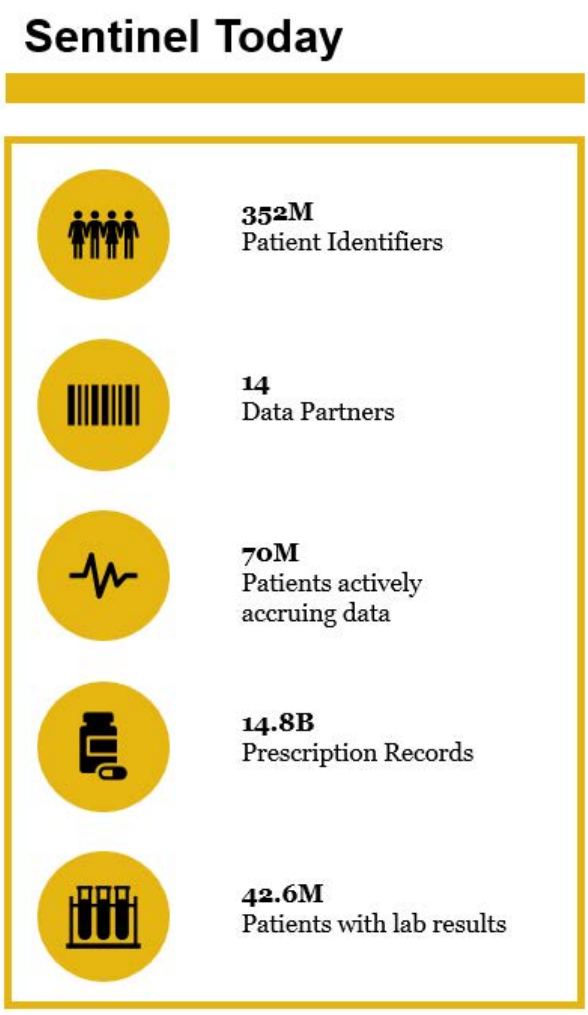
Sentinel: Strengthening surveillance and detection

The Sentinel System was developed to analyze large quantities of electronic healthcare data to monitor the safety and effectiveness of medical products, and to turn any resulting signals and other findings into information that can help patients and providers make more informed decisions. Sentinel has access to medical, pharmacy, and laboratory records, primarily from the insured population. OSE utilized the Sentinel System in 78 medical product assessments in 2020.

DETECTING AND ASSESSING RISKS

The “active surveillance” capabilities of Sentinel are an important complement to FAERS data. Instead of waiting to receive safety data, it enables FDA to search for it when needed. Safety signals coming from FAERS or elsewhere can be used to query the Sentinel database to assess risk in a larger patient population.

Sentinel proactively monitors medical product safety and serves to advance the science of real-world data (RWD) and real-world evidence (RWE). Real-world ***data*** are data that are routinely collected to inform on individuals’ health, such as electronic health records, claims and billing, product and disease registries, and patient-generated data, for example using mobile technologies. Real-world ***evidence*** is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD. RWE can be generated by different study designs or analyses, including but not limited to, randomized trials, large simple trials, pragmatic trials, and observational studies (prospective and/or retrospective).



In September 2019, a new five-year Sentinel contract was awarded to two consortiums, one led by Harvard Pilgrim Health Care and the other by Deloitte Consulting, which created three distinct coordinating centers: Sentinel Operations Center, Innovation Center and Community Building and Outreach Center. This was the third five-year contract awarded since Sentinel’s establishment. The new Sentinel structure widens participation to a broader array of scientific expertise, seeks to translate new technologies from data science and big data, creates laboratories to develop new approaches to using EHRs and cultivates a robust scientific community to uncover novel ways to leverage the system’s core capabilities beyond drug safety.

The new contract retains and builds upon the core innovations that were responsible for many of the achievements in the prior decade: the participation of data partners who bring their knowledge and expertise to the Sentinel network, the re-useable analytic tools that run against data formatted in the Sentinel Common Data Model, the multifaceted data quality and curation process and the ability to trace important clinical information back to the medical record. Sentinel remains one of the world’s largest multi-site, privacy-preserving, medical product safety surveillance systems available.

DETECTING AND ASSESSING RISKS

As an example of how new technologies are being applied in Sentinel, the Innovation Center launched a comprehensive effort to develop a framework to use natural language processing (NLP) and machine learning (ML) to improve Health Outcome of Interest (HOI) identification. A recently completed project showed that using NLP and ML it is possible to develop an improved algorithm to identify anaphylaxis in EHRs.

A second project demonstrated the feasibility of developing and validating a claims-based HOI algorithm using ML techniques applied to a linked claims-EHR database. In addition to these examples, the Sentinel System has proposed a comprehensive set of innovation strategies in the Innovation Center master plan to address the full range of data, methods, and tools required to build a sustainable infrastructure that incorporates artificial intelligence methods to address FDA's needs.

Real-World Data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. Real-World Evidence (RWE) is the clinical evidence regarding the usage, and potential benefits or risks, of a medical product derived from analysis of RWD.

Preventing Risks

Increasing Safe Use through Human Factors Analysis

Human factors engineering (HF) is the is the scientific discipline concerned with the understanding of interactions among humans and other elements of a system. HF applies theory, principles, data and methods in order to optimize patient safety in the healthcare environment. OSE leads the review of HF for CDER. HF often applies when a drug requires a device for administration, such as an auto-injector or inhaler. If applicable, sponsors are required to submit HF protocols to study their product in real-world settings and evaluate the user interface of a product.

Evaluation of container labels and carton labeling

OSE works closely with other offices to review proposed labeling revisions to prevent medication errors, and to manage known risks associated with the use of certain drug products prior to approval. In addition to relying on labeling to manage the medication error risk, OSE also advises on product design changes, such as revisions in strength and container closure prior to approval.

PREVENTING RISKS

Using POCA to Prevent Risks by Avoiding Look-Alike, Sound-Alike Drug Names

OSE is CDER's lead office for review of proposed proprietary names during drug development and pre-market review of drug applications. First released to the public in 2009, the Phonetic and Orthographic Computer Analysis Program (or POCA) is a software tool that uses an advanced algorithm to determine the orthographic (look-alike) and phonetic (sound-alike) similarity between two drug names. The program can compare a proposed drug name against multiple existing drug names found in several different data sources contained in the software. This analysis helps avoid medication errors caused by look-alike or sound-alike names in the prescribing, transcription, and filling of drug orders.

With the recent increase in drug approvals, OSE completed 499 proprietary name reviews in fiscal year 2020. Despite the increased workload compared to previous years, OSE met its Prescription Drug User Fee Act (PDUFA) and Biosimilar User Fee Act (BsUFA) performance goals for proprietary name review .

> OSE met its PDUFA and BSUFA naming goals for greater than 99% of the time in fiscal year

OSE released a modernized, cloud based POCA

OSE changed POCA to a cloud-based program, which provides the public with a search capability that is easier to use than the current public version of POCA. This cloud-based version eliminates the complex download processes required in the existing POCA public version of the application. End users no longer need to request access to the program and related software from the FDA.

Proprietary Naming Guidance

FDA issued two guidance documents on proprietary naming: Best Practices in Developing Proprietary Names for Human Prescription Drug Products and Best Practices in Developing Proprietary Names for Human Nonprescription Drug Products. The first guidance document, for prescription drug products, is a final guidance. The second document which is focused on nonprescription drug products, is a draft guidance.


Best Practices in Developing Proprietary Names for Human Prescription Drug Products
Guidance for Industry


Best Practices in Developing Proprietary Names for Human Nonprescription Drug Products
Guidance for Industry

These documents provide guidance to sponsors on the development of proposed proprietary names. They describe best practices to help minimize proprietary name-related medication errors and otherwise avoid adoption of proprietary names that contribute to violations of the Federal Food, Drug, and Cosmetic Act and its implementing regulations. The documents describe the framework FDA uses in evaluating proposed proprietary names that the sponsors can use, if they choose to, prior to submitting names for FDA review.

Managing Risks

RISK EVALUATION AND MITIGATION STRATEGIES PROGRAMS

Product labeling is the cornerstone for risk management of drug and biological products. Among many other sections, product labeling includes *Boxed Warnings*, *Warnings and Precautions*, *Contraindications*, and *Adverse Reactions*. For a small number of drugs and biologics, additional measures beyond the product labeling are necessary to mitigate the risks and preserve the benefits of the product. Risk Evaluation and Mitigation REMS is a drug safety program that FDA can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks, and are designed to reinforce medication use behaviors and actions that support the safe use.

FDA maintains a website listing medications with approved REMS that are currently active and their associated materials at (REMS@FDA).

REMS may include one or more of the following components: a Medication Guide (or patient package insert) to provide risk information to patients, a communication plan to disseminate risk information to health care providers, and/or certain packaging and safe disposal technologies to reduce serious risk of abuse or overdose. FDA may also require certain elements to assure safe use (ETASU) when necessary to mitigate specific serious risks associated with a drug. ETASU may include, for example, requirements that health care providers who prescribe the drug have particular training or experience, that patients using the drug be monitored, or that the drug be dispensed to patients with evidence or other documentation of safe-use conditions. Certain REMS with ETASU may also include an implementation system through which the manufacturer is able to monitor and evaluate implementation of the ETASU and work to improve their implementation. Finally, a REMS generally must have a timetable for submission of assessments of the strategy.

DRUG SAFETY MODERNIZATION AND INNOVATION

In 2020, OSE had several notable accomplishments related to modernizing drug safety that were designed to improve the efficiency in adverse event reporting, expand our use of surveillance tools with Sentinel, and increase the safe use of medicines. To this end, OSE would like to highlight the following accomplishments:

Computerized Labeling Assessment Tool

FDA awarded a new contract for the development of a Computerized Labeling Assessment Tool (CLAT) which uses computer programming and artificial intelligence technology to automate portions of the drug product labeling review process. Computerized automation of the FDA drug product labeling assessment/review applies novel and rapidly evolving technologies to increase efficiencies and assist in standardizing reviews to ensure consistency across different products as part of the FDA's Technology Modernization Action Plan.

OSE Public Health Surveillance Study Evaluation and Management

We designed, implemented, piloted and rolled out OSE's Public Health Surveillance Study Evaluation and Management. This comprehensive process is designed to review potential projects to ensure they align with FDA and CDER priorities, do not duplicate ongoing efforts, and have the potential for regulatory impact. The process also includes expert consultation on technology transfer requirements,

data use agreements, IRB and public health surveillance requirements, and government-sponsored research requirements. The OSE Research Project Evaluation & Management process was adapted to allow the OSE COVID Core Scientific Team to review and prioritize proposed COVID-19 projects proposed by OSE staff.

Contractor Performance Assessment Reports

OSE developed, launched and enhanced a new informatics tool to handle Contractor Performance Assessment Reports (CPARs) Compliance Tracking System (CTS). The FDA CPARSCTS proactively tracks individual Contracting Officer's Representative (COR) compliance with completing the CPARS.gov contractor performance assessment within the evaluation process time. The improved tracking and reporting capabilities informs PMAP elements for CORs, and enables Senior Management to plan more accurately for future funding on existing contracts.

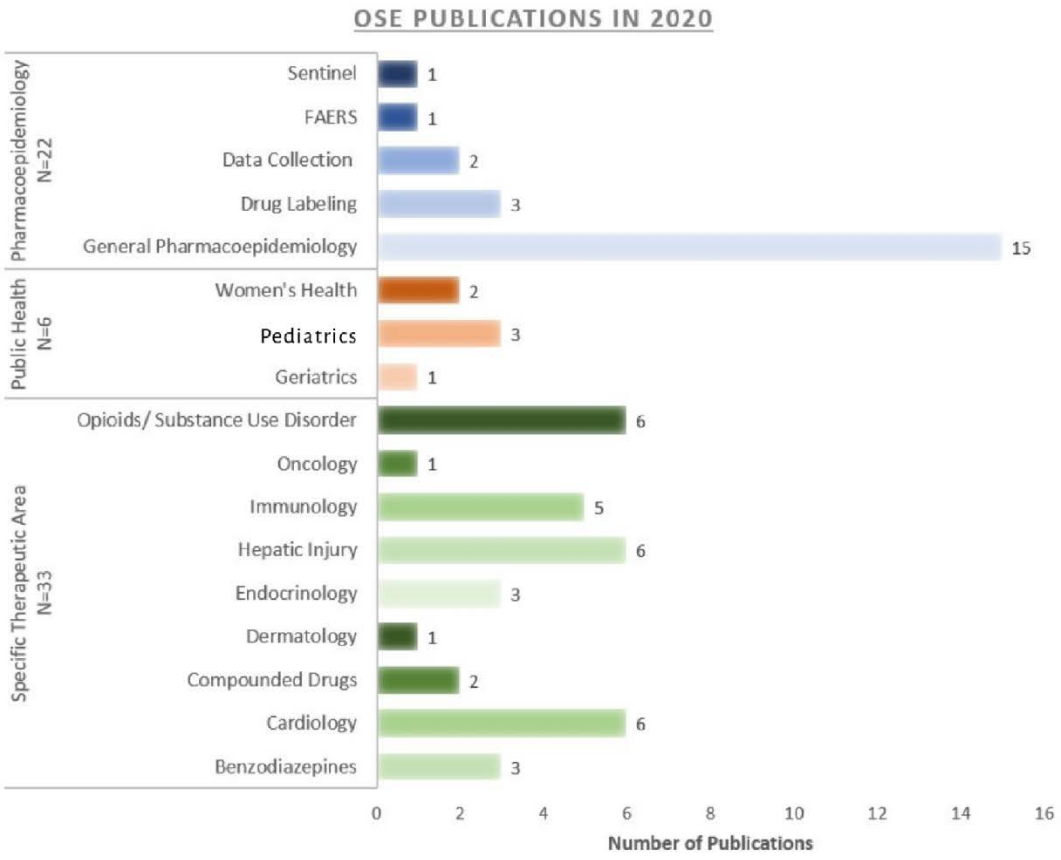
Research Activities

OSE researchers expanded their prior research on the association of expedited drug development and review programs (i.e., priority review, accelerated approval, and fast track designation) on changes to the safety information in a drug's label after approval by FDA. In addition to small-molecule, new-molecular-entity drugs, the analyses now include therapeutic biologics approved between October 2002 and December 2015. An additional 2½ years of label changes were also added to the review, with the new analyses including a withdrawal of the drug or biologic due to a safety issue or a change to a safety section of the label through June 2018. The additional data allowed researchers to do a detailed comparison of occurrence and timing of changes to the label of drugs and therapeutic biologics. The results of this study are published in Clinical Pharmacology & Therapeutics (CPT).

2020 PUBLICATION REPORT

A glance at the topics addressed by OSE's publications in 2020.

61 Total articles written by OSE staff



ENGAGING PUBLIC & INTERNATIONAL COMMUNITIES

OSE facilitated public engagement activities ranging from topical information sessions, to interactive workshops and training in 2020.

Engaging the Public

Sentinel Outreach

12th Annual Sentinel Public Workshop (October 2020)

In collaboration with the Duke-Margolis Center for Health Policy, OSE held the **12th Sentinel Annual Public Workshop** in October 2020. This was the first annual workshop held virtually. Day 1 was a gathering of the Sentinel community with over 500 attendees. Leading experts participated to share recent developments within the Sentinel Initiative. On Day 2, the Operations Center provided training on Sentinel's tools to evaluate questions related to maternal health and pregnancy.

To better serve FDA and engage industry stakeholders, the Sentinel Initiative website was redesigned, updated, and successfully launched on July 17, 2020, allowing all stakeholders to more easily stay up to date with Sentinel assessments, tools, and events.

ENGAGING PUBLIC & INTERNATIONAL COMMUNITIES

OSE communicated about the Sentinel System and its analyses to the scientific community in multiple ways:

- 25 presentations, posters, and symposia at the International Society for Pharmacoepidemiology meeting
- 16 presentations or posters in other scientific venues
- 17 Sentinel-related publications

Public Sentinel Training on Maternal Health and Pregnancy (November 2020)

On November 2, 2020, the FDA hosted the Sentinel Initiative Public Training on Maternal Health and Pregnancy. The training consisted of presentations on the Sentinel System's distributed database and broad analytic capabilities as they apply to maternal health. The training was conducted by Sentinel epidemiology investigators and 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.

OSE's Public Health Initiatives Program's Continued Response to the Opioid Public Health Crisis

In response to the opioid public health crisis, OSE recruited experts educated healthcare providers, and worked with the community to modify REMS to decrease use of prescription opioids and prevent new addiction. OSE's formation of the Public Health Initiatives program (PHI) has allowed for improved coordination of the resources of the pharmacovigilance, pharmacoepidemiology, medication error prevention and analysis, and risk management functions to address the full scope of the opioid crisis.

"All four of OSE's core functions have been called to action to address the opioid crisis."

Gerald Dal Pan, M.D., M.H.S., OSE Director

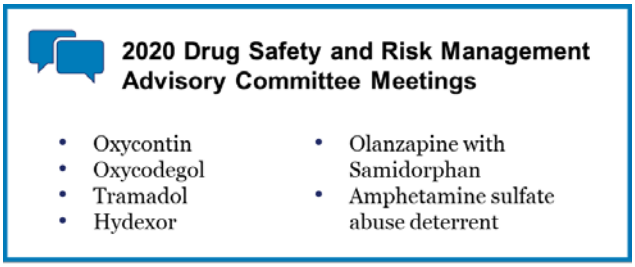
Drug Safety and Risk Management Advisory Committee (DSaRM) Meetings on Opioids

PHI was especially advantageous in addressing the opioid crisis in 2020 by recruiting experts across a wide range of disciplines addressing substance use disorders for the Drug Safety and Risk Management Advisory Committee (DSaRM).

The goal of DSaRM is to provide advice that will enhance FDA's decision making, increase transparency, and strengthen public confidence in the advisory committee program. FDA welcomes external advice on issues related to the safety of all FDA-regulated products. FDA's Advisory Committee (AC) program is governed by several federal laws and regulations that set forth standards for convening advisory committees and reviewing potential conflicts of interest.

ENGAGING PUBLIC & INTERNATIONAL COMMUNITIES

DSaRM reviews and evaluates information on risk management, risk communication, and quantitative evaluation of spontaneous reports for drugs and for any other product regulated by FDA. DSaRM also advises FDA on the scientific and medical evaluation of all information gathered by the Department of Health and Human Services (DHHS) and the Department of Justice with regard to safety, efficacy, and abuse potential of drugs or other substances, and recommends actions to be taken by the DHHS with regard to the marketing, investigation, and control of such drugs or other substances.



OSE collaborated with Office of New Drugs on six joint meetings of the Anesthetic and Analgesic Drug Products Advisory Committee and DSaRM to discuss opioid-related matters. Details on these meetings, including minutes and materials, may be accessed through the Advisory Committee section of FDA's website.

SUPPORT Act

As part of the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) Act to improve the safe use of opioids and to enhance the education of health care professionals and patients, OSE continues to work on providing data analyses and literature reviews to support using new authorities relating to packaging and disposal of opioids, as well as the development of evidence-based, indication-specific practice guidelines for treating acute pain. OSE also conducted assessments to support the requirement that all drug manufacturers of all opioid pain relievers and medicines to treat patients with Opioid Use Disorder add new recommendations about naloxone to the prescribing information. In July 2020, FDA required drug manufacturers of all opioid pain relievers to add new recommendations about naloxone to the prescribing information. This will help ensure that health care professionals discuss the availability of naloxone and assess each patient's need for a naloxone prescription.

Transmucosal Immediate-Release Fentanyl REMS

OSE collaborated with the Office of New Drugs to require a modification to the Transmucosal Immediate-Release Fentanyl (TIRF) REMS to address concerning use of these products in patients who are not opioid-tolerant. TIRF medicines are used to manage breakthrough pain in cancer patients who are already receiving and are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain. The TIRF medicines contain fentanyl, a potent opioid agonist that has the potential to cause serious morbidity and death due to respiratory failure if administered to an opioid non-tolerant person. The TIRF REMS, a restricted distribution program, was initially approved in 2011 to ensure that the benefits of the drug outweigh the risks of misuse, abuse, addiction, overdose, and serious complications due to medication errors. Despite the restrictions of the initial TIRF REMS program, FDA became aware that 35 - 55% of patients may not have been opioid-tolerant when they received an outpatient prescription for a TIRF medicine. The REMS modification includes a requirement that opioid tolerance be verified prior to dispensing each TIRF prescription and the addition of a patient registry which will enable the Agency to better monitor safe use in outpatients taking a TIRF medicine with respect to opioid tolerance and related serious adverse events including overdose and death.

ENGAGING PUBLIC & INTERNATIONAL COMMUNITIES

Evaluating the Effect of the Opioid REMS Education Program on Prescribing Behaviors and Patient Outcomes

OSE continues efforts to evaluate the opioid analgesic (OA) REMS. In December 2020, we hosted a workshop inviting scientific discussions about methods to evaluate the impact of the OA REMS on prescriber behavior and patient outcomes. The goal of the OA REMS is to educate prescribers and other health care providers (including pharmacists) on the treatment and monitoring of patients with pain. The public workshop served as a forum for public scientific discussion of innovative, multidisciplinary methods to consider when evaluating the OA REMS education program. The FDA will use these discussions to ensure that the methods ultimately used to evaluate the OA REMS are scientifically sound.

Effectively addressing the opioid crisis requires continued focus and collaboration across many different stakeholders. REMS are an important tool that provide safe access to drugs that would otherwise be unavailable. It is critical we ensure they are continuing to fulfill their purpose.

Engaging the International Community

OSE exchanges information with international regulators on safety surveillance topics, adverse event reporting, and other issues of common interest. The goal of these interactions is to collaborate on drug safety activities and support global harmonization on similar regulatory programs. The interactions with our international partners allow OSE to enhance our surveillance activities and inform emerging safety concerns.

LOOKING TO THE FUTURE

OSE Priorities in 2021 and beyond

In 2021, OSE will continue to modernize our programs in pharmacovigilance, pharmacoepidemiology, medication error prevention and analysis, and risk management, with a sustained focus on our many COVID-19 activities. Our strategic planning will focus on enhancing drug safety surveillance activities to inform emerging safety concerns.

We will advance our Best Practices in Pharmacovigilance as required under the 21st Century Cures Act, including the finalization of the draft Best Practices in Drug and Biological Product Postmarket Safety Surveillance for FDA Staff document.

In 2021, OSE looks forward to the continued implementation of the Drug Safety Teams (DSTs), a major modernization initiative.
Gerald Dal Pan, M.D., M.H.S., OSE Director

Exploring novel methods, including natural language processing and machine learning, to evaluate the growing number of adverse event and medication error reports received by the FDA Adverse Event Reporting System (FAERS) is a major priority for OSE.

In 2020, OSE provided pharmacoepidemiologic review of proposals and submissions that included real-world evidence to support effectiveness and developed tools and processes for an expanded review role in the future.

LOOKING TO THE FUTURE

In 2020, OSE launched several Sentinel training modules for FDA staff to help us prepare for 2021, the second year of Sentinel's awarded contract and five-year strategic plan. We will further enhance the foundation of the Sentinel system and its safety analysis capabilities; accelerate access to and broader use of real-world data to evaluate effectiveness; create a national and international resource by broadening the Sentinel user base; and disseminate knowledge and advance regulatory science to enable innovation.

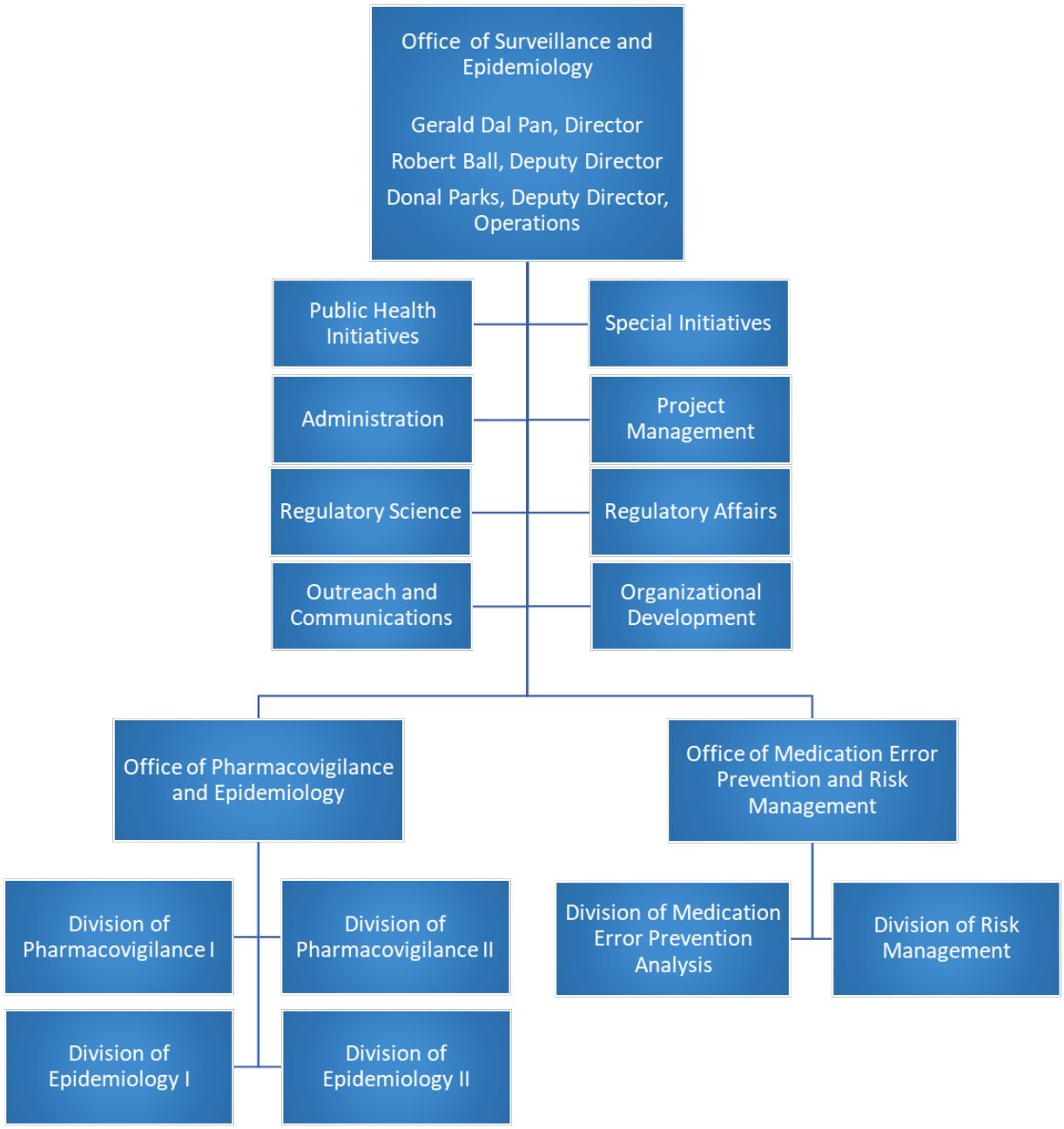
We will continue our efforts to modernize and improve REMS Assessments by improving the quality of the information used to assess the effectiveness of REMS, taking action on REMS that are not meeting their risk mitigation goals, and improving the efficiency of FDA's reviews. Additionally, we plan to seek external expertise to understand how existing and emerging health information technologies can be used to support greater integration of REMS into the healthcare delivery system.

In accordance with the SUPPORT Act, we will continue to evaluate our strategies to confront the nonmedical use of opioids, including regulatory actions, enhanced education to health care professionals and patients, and enhanced safety labeling.

OSE looks forward to the continued implementation of the Drug Safety Teams (DSTs), a major modernization initiative. DSTs are CDER's organizing principle for collaborative, interdisciplinary centralized scientific safety expertise and ownership for an assigned portfolio of drugs. The teams facilitate sharing of information about safety issues from all CDER Offices with scientific safety responsibilities, and increase efficient safety evaluations by eliminating workload redundancy and improving safety signal prioritization and evaluation.

We will continue interactions with our international regulatory partners to increase the exchange of information on pharmacovigilance activities and to support global harmonization on similar regulatory programs, including products to address the ongoing pandemic.

APPENDIX I: ORGANIZATIONAL ELEMENTS



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