U.S. FOOD & DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

DRUG SAFETY PRIORITIES 2020

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Introduction

The past year was an unprecedented one. With the SARS–CoV–2 coronavirus (COVID–19) pandemic, major aspects of people's lives were impacted and disrupted, and life as we knew it completely changed. Here at the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA), we collaborated closely with colleagues across the Agency as well as other federal and international partners to engage in activities to respond to the COVID–19 situation and to protect our nation's public health during these challenging times.

Although significant effort in 2020 was spent battling the COVID–19 pandemic, CDER continued to complete its critical work to ensure the safety of the medicines on which millions of patients rely. Our successes were many, thanks to our incredible workforce. I am honored and proud to serve alongside them.

CDER Drug Safety Priorities 2020 describes the wide range of safety work the Center undertook and provides updates on the year's safety-related achievements and milestones. From the Food and Drug Act of 1906 through legislation enacted over the years, the FDA's regulatory authorities and resources have been progressively enhanced, allowing the Agency to consistently strengthen and modernize its drug safety initiatives and programs. This includes work with the Sentinel System, our electronic safety surveillance system; the Safe Use Initiative that works to minimize preventable harm from medications; ongoing activities to help address the national opioid crisis; work to address unexpected — and potentially cancer-causing — impurities in medicines; and the use of a broad range of communications tools and technologies to transparently communicate drug safety to the public. This year's report also details the many ways in which CDER has been involved in promoting and protecting public health during the pandemic, including assessing the safety of products used to treat and prevent COVID–19, monitoring the medical supply chain to prevent supply disruptions or shortages of the medicines patients need, and taking action against fraudulent unapproved and potentially harmful products for COVID–19.

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COVID–19

In December 2019, an outbreak of respiratory illness caused by a novel coronavirus (SARS–CoV–2) was first identified in China and quickly spread to other countries, including the United States, where the first confirmed case of COVID–19 was reported on January 21, 2020. People infected with the virus reported a wide range of symptoms, from mild indications such as fever and cough that could have been associated with many other conditions to severe illness. But there were no tests that could detect it, no medications to treat it, no vaccines to prevent it, and many people died. By mid-March, transmission had become widespread, and by the Fall, there were more than 8 million confirmed and probable COVID–19 cases in the United States and almost 42 million worldwide. Amid all the challenges of the pandemic, the FDA has tackled these new demands and worked to ensure minimal disruptions in our efforts to fulfill the Agency's critical public health mission of ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation.

The FDA's CDER is engaged in critical work to ensure medications are safe and effective for their intended purposes, including during the pandemic. These COVID–19-related efforts included identifying and assessing the safety of products that might be able to be used to treat or prevent the disease, maintaining and securing drug supply chains, testing for and warning about contaminated hand sanitizers, taking actions against fraudulent unapproved products for COVID–19, and keeping the public informed. Getting timely information to those who

need it most has remained among CDER's highest priorities during this pandemic. The latest COVID–19 news from the FDA can be found here.

The highlights below detail key COVID–19 drug safety actions taken through mid-November 2020.

Assessing the Safety of Products used to Treat or Prevent COVID–19

At the onset of the COVID–19 pandemic, SARS–CoV–2 was a new virus, and as such, there were no FDA-approved medications to treat or prevent the disease. The FDA engaged in efforts to determine the safety and potential effectiveness of certain antiviral and other medications to treat patients suffering from this virus. CDER researchers began studying medications that were already approved for other health conditions as possible treatments for COVID–19, and they are continuing to undertake this important work. The FDA created a special emergency program for possible coronavirus therapies, the Coronavirus Treatment Acceleration Program (CTAP). The program uses every available method to move new treatments to patients as quickly as possible, while at the same time finding out whether they are helpful or harmful.

To protect and promote public health during the pandemic, the FDA:

- Reviewed safety data including adverse event reports and observational studies, as part of the overall benefit-risk assessment for products submitted for Emergency Use Authorization and new drug application (NDA) approval
- Conducted surveillance on case reports in the FDA Adverse Event Reporting System (FAERS), medical literature, National Poison Data System, prescription and non-retail sales, and other data sources, and evaluated newly identified safety concerns and medication errors related to products used to treat or prevent COVID–19
- Conducted searches and reviews of observational study literature on the impact of drugs used to treat or prevent COVID–19
- Reviewed and provided feedback on the quality and feasibility of proposals for Real World Data (RWD) analyses to inform the effectiveness of COVID–19 therapies
- Responded to Congressional and media inquiries related to the safety of products used to treat or prevent COVID–19
- Developed pandemic-related guidances such as the Policy for Certain REMS Requirements During the COVID–19 Public Health Emergency and Postmarketing Adverse Event Reporting for Medical Products and Dietary Supplements During a Pandemic

During public health emergencies, the FDA may in certain circumstances authorize through an Emergency Use Authorization (EUA) use of unapproved drugs or unapproved uses of approved drugs for serious or life-threatening conditions when there are no adequate, approved, and available options and other legal criteria are met. In determining whether to issue an EUA, the FDA evaluates the totality of scientific evidence available and carefully balances any known or potential risks with any known or potential benefits of the product for use during an emergency.

- Responded to multiple inquiries on individual approved Risk Evaluation and Mitigation Strategy (REMS) requirements during COVID–19
- Reviewed proprietary names (commonly known as brand names) and container labels for multiple COVID–19 therapies
- Reviewed multiple 'Dear Health Care Professional' letters and drug labels/labeling for imported products, and changes to U.S. marketed products for COVID–19 therapies
- Responded to multiple inquiries on the feasibility of conducting remote human factors studies during COVID–19
- Undertook an in-depth research project exploring the effects the COVID–19 pandemic was having on opioid use and addiction
- FDA's Sentinel System also initiated numerous activities designed to:
  - Monitor critical drugs to assess changes in utilization over time and by geography to inform CDER's response to national or regional drug shortages
  - Describe the course of illness among hospitalized COVID–19 patients, including their characteristics, health care utilization, disease progression, and outcomes
  - Evaluate the use of computable phenotypes to help identify COVID–19 positive patients in real-world data
  - Develop an adaptable protocol design to support a variety of on-demand queries and support subsequent studies of the safety or effectiveness of treatment in COVID–19 patients, including special populations of interest such as pregnant women and pediatric patients
  - Establish a framework to efficiently design and execute epidemiological studies of COVID–19 patients at the Sentinel Data Partners
  - Assess the occurrence of coagulopathy and its risk factors among hospitalized COVID–19 patients

Hydroxychloroquine sulfate and chloroquine phosphate

Early in the pandemic, preliminary research data showed that the antimalarial drugs chloroquine and hydroxychloroquine may be effective in treating COVID–19, however, the data had significant limitations.

MARCH 28 | Based on the scientific information available at the time, FDA issued an EUA for hydroxychloroquine and chloroquine to be used to treat certain hospitalized patients with COVID–19 when a clinical trial was not

available or feasible. FDA continued to urge the conduct of clinical trials to determine whether the benefits of the medications outweighed any potential risks to patients of this new use.

APRIL 24 | FDA issued a Drug Safety Communication cautioning against the use of hydroxychloroquine or chloroquine for COVID–19 outside of a hospital setting or clinical trial due to risk of serious heart-rhythm problems.

JUNE 15 | FDA revoked the EUA for chloroquine and hydroxychloroquine. Based on continued review of the scientific evidence available — including results from a large, randomized clinical trial in hospitalized patients that found that these medications showed no benefit — the Agency determined that chloroquine and hydroxychloroquine were unlikely to be effective in treating COVID–19 for the authorized uses in the EUA. Additionally, in light of ongoing serious cardiac adverse events and other serious side effects, the known and potential benefits of these medications no longer outweighed the known and potential risks for the authorized use.

Veklury (remdesivir)

The investigational antiviral drug was shown to shorten the time to recovery in a randomized, double-blind, placebo-controlled clinical trial in hospitalized patients.

MAY 1 | FDA issued an EUA for investigational antiviral drug Veklury (remdesivir) for hospitalized patients with severe COVID–19 disease.

JUNE 15 | FDA warned that coadministration of Veklury (remdesivir) and chloroquine or hydroxychloroquine was not recommended as it may result in reduced antiviral activity of Veklury (remdesivir).

AUGUST 28 | FDA broadened the EUA for Veklury (remdesivir) to include all hospitalized patients for treatment of COVID–19.

SEPTEMBER 10 | The Institute for Safe Medication Practices (ISMP) published FDA Advise-ERR: Reported Medication Errors with Veklury (Remdesivir) Emergency Use Authorization. FDA received numerous medication error reports related to incorrect preparation, administration, and storage of Veklury (remdesivir), which is supplied in two formulations for intravenous administration.

OCTOBER 22 | FDA approved Veklury (remdesivir) as the first treatment for COVID–19. It was approved for use in adult and pediatric patients 12 years of age or older and weighing at least 40 kg (about 88 lb) requiring hospitalization. The Veklury (remdesivir) EUA was also revised to continue to authorize Veklury (remdesivir) for emergency use by licensed health care providers to treat suspected or laboratory-confirmed COVID–19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients younger than 12 years of age weighing at least 3.5 kg.

Olumiant (baricitinib)

Olumiant (baricitinib) is a prescription medicine that is FDA-approved to treat adult patients with moderately to severely active rheumatoid arthritis after treatment with at least one other medicine called a Tumor Necrosis Factor (TNF) antagonist has been used and did not work well enough or could not be tolerated. Olumiant (baricitinib) is not FDA-approved to treat COVID–19. Olumiant (baricitinib) was being studied for the treatment of certain people in the hospital with COVID–19 and there was limited information about its safety and effectiveness to treat people in the hospital with COVID–19.

NOVEMBER 19 | FDA issued an EUA for Olumiant (baricitinib) in combination with Veklury (remdesivir) to treat suspected or laboratory-confirmed COVID–19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

Monoclonal antibodies are laboratory-made proteins that mimic the immune system's ability to fight off harmful antigens such as viruses.

Bamlanivimab

Bamlanivimab is an investigational monoclonal antibody therapy. Bamlanivimab was shown in clinical trials to reduce COVID–19-related hospitalization or emergency room visits in patients at high risk for disease progression within 28 days after treatment when compared to a placebo.

NOVEMBER 9 | FDA issued an EUA for bamlanivimab to treat mild-to-moderate COVID–19 in certain adult and pediatric patients. Specifically, bamlanivimab was authorized for patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age or older weighing at least 40 kg and are at high risk of progressing to severe COVID–19 and/or hospitalization. Those at high risk include people 65 years of age or older or who have certain chronic medical conditions.

Warnings about Hand Sanitizers

In response to the demand for alcohol-based hand sanitizers, the FDA issued guidance to communicate its policies for the temporary manufacture or compounding of alcohol-based hand sanitizer products and ethanol for use in alcohol-based hand sanitizer by some companies and pharmacies during the public health emergency posed by COVID–19. Since the beginning of the public health emergency, the FDA observed an increase in reports of serious adverse events, including some associated or reported deaths, related to both unintentional and intentional ingestion of alcohol-based hand sanitizers.

The FDA warned consumers and health care professionals that the Agency had seen a sharp increase in hand sanitizer products that were labeled to contain the appropriate chemical ethanol (also known as ethyl alcohol) but that tested positive for contamination with the potentially harmful chemicals methanol, or in some cases 1-propanol. The FDA also found that some hand sanitizers

are labeled to contain methanol, which is not an approved ingredient for hand sanitizer products in the United States. Contaminated hand sanitizers were associated with deaths in the United States.

The FDA is also concerned about hand sanitizer products being packaged in a way that may encourage ingestion, and warned manufacturers to be vigilant about packaging and marketing these products to help mitigate any potential inadvertent use by consumers. The Agency discovered that some hand sanitizers are being packaged in beer cans, children's food pouches, water bottles, juice bottles, and vodka bottles. Some also contain flavors, such as chocolate or raspberry. These products could confuse consumers into accidentally ingesting a potentially deadly product.

Through early November, the FDA's work to protect the public from poor quality and unsafe hand sanitizers included:

- Advising consumers of hand sanitizer products they should not use
- Placing more than 35 hand sanitizer firms from Mexico and one firm each from Turkey, Guatemala, and China on import alert, thereby preventing products from those firms entering the United States
- Requesting the voluntary recall of more than 150 hand sanitizer products, including six for products with methanol listed as an ingredient on the labels, products labeled as being "edible alcohol," and packages that resemble food containers
- Issuing seven warning letters to hand sanitizer manufacturers
- Collaborating with the U.S. Pharmacopeia to update the monograph for ethyl alcohol to specifically include a description of a test that could identify methanol contamination

JUNE 19 | FDA advised consumers not to use any hand sanitizer manufactured by Eskbiochem SA de CV in Mexico due to the potential presence of methanol that led to serious problems, including blindness, hospitalizations, and death.

JULY 2 | FDA warned of additional hand sanitizers contaminated with methanol and that it was aware adults and children were ingesting these products.

JULY 2 | A new import alert, 66-78, was issued to include detention without physical examination of drugs considered at risk for adulteration that pose a health risk due to contamination, substandard quality or ingredient substitution.

JULY 27 | FDA took additional action to help prevent certain hand sanitizers from entering the United States by placing them on an import alert, proactively working with manufacturers and distributors to recall all potentially dangerous products and encouraging retailers to remove these products from store shelves and online marketplaces.

Methanol, or wood alcohol, is a substance that can be toxic when absorbed through the skin and can be life-threatening when ingested; 1-propanol can cause skin irritation or serious damage to the eyes, and may be harmful if inhaled and life-threatening when ingested.

JULY 31 | FDA announced test results showing certain hand sanitizers had low levels of the active ingredients ethyl alcohol or isopropyl alcohol and later found sub-potent levels of benzalkonium chloride. FDA continued to add certain hand sanitizers to import alert to stop these products from legally entering the U.S. market.

AUGUST 7 | FDA updated guidances to provide additional clarification on testing of alcohol used in hand sanitizers manufactured under FDA's temporary policies to help ensure that harmful levels of methanol were not present in these products.

AUGUST 11 | FDA placed one firm on import alert, 66-41, for marketing products labeled as "edible alcohol."

AUGUST 12 | FDA expanded warnings about certain hand sanitizer products that were labeled to contain ethanol or isopropyl alcohol but tested positive for 1-propanol contamination.

AUGUST 24 | FDA provided a laboratory testing method to assess the quality of finished hand sanitizer products.

AUGUST 27 | FDA warned about alcohol-based hand sanitizers that were being packaged in containers that may appear as food or drinks and may put consumers at risk of serious injury or death if ingested.

A more complete timeline of FDA announcements, statements, and actions related to hand sanitizers, including those consumers should not use, can be found online.

Monitoring of Medical Product Supply Chain

During the COVID–19 pandemic, the FDA closely monitored the medical product supply chain expecting that it may be impacted, potentially leading to supply disruptions or shortages of some drug products needed by U.S. patients. The Agency understood the significant impact that this could have on patient care and did everything within our authority to help prevent and alleviate shortages.

The FDA worked to increase patient access to critically needed medications in shortage during the pandemic, including:

- Issuing 38 enforcement discretion decisions through early November to increase supplies of heparin, albuterol, etomidate, midazolam, propofol, and many other critically needed medications
- Issuing temporary enforcement discretion policies via two guidances on the compounding of drugs needed to treat hospitalized COVID–19 patients

- Issuing an EUA to permit the emergency use of the unapproved product, Fresenius Propoven 2% (propofol 20 mg/mL) Emulsion, to maintain sedation via continuous infusion in patients older than 16 years who require mechanical ventilation in an intensive care setting during the pandemic

The FDA continued to work closely with manufacturers to mitigate and prevent shortages as the COVID–19 situation evolved. U.S. shortages, including those related COVID–19, were posted online.

FEBRUARY | FDA actively monitored medical product supply chain, including potential disruptions to supplies or shortages of critical medical products.

MARCH | FDA provided proactive surveillance of more than 40 high-priority generic drugs to reinforce the continued supply of these safe and effective products.

Taking Actions Against Fraudulent Unapproved Products for COVID–19

While the FDA worked at a record pace with vaccine and drug manufacturers to find drugs to treat COVID–19 and develop vaccines, some companies and individuals sold unproven and illegally marketed products that made false claims, including that they effectively diagnosed, treated or prevented the coronavirus or COVID–19. Fraudulent products came in many varieties, including foods and dietary supplements, drugs, vaccines, tests, and other medical devices. The Agency actively monitored for firms marketing such products, and issued warning letters or pursued seizures or injunctions against people, products, or companies that violated the law. The Agency also increased enforcement at ports and borders to help ensure that fraudulent products did not enter the United States.

The FDA's work to protect patients from fraudulent and unapproved COVID–19 products included:

- Issuing 90 warning letters to companies marketing products fraudulently claiming to diagnose, cure, mitigate, treat or prevent COVID–19. More than 80 percent of the recipients of these letters complied with these warnings.
- Issuing 11 warning letters to internet pharmacies selling unapproved drugs claiming to treat COVID–19
- Working with the Department of Justice and Office of Chief Counsel to successfully obtain a court order against three companies that continued to market COVID–19 cures after receiving FDA warning letters
- Issuing a warning letter against a generic drug company for promoting a drug approved to treat asthma in children as an effective treatment for the symptoms of COVID–19

Postmarketing Drug Surveillance

Once a medication is available for prescription or over-the-counter use, FDA continues to monitor its safety, efficacy, and quality so the Agency can take action if needed.

Manufacturers must evaluate received adverse event reports associated with their marketed products and report certain serious adverse health effects to FDA for evaluation.

FDA periodically inspects drug manufacturing plants and continues to monitor drug quality.

FDA monitors the FDA Adverse Event Reporting System (FAERS) and reviews MedWatch reports submitted by health care professionals, patients, and drug manufacturers to investigate concerns related to drug product quality and safety.

To help FDA track safety issues with medicines, FDA urges patients, consumers, and health care professionals to report side effects involving medicines to the FDA MedWatch program by completing and submitting the report Online or calling 1-800-332-1088 to request a reporting form that can be mailed or faxed.

Visit www.fda.gov/drugs to learn more.

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Safety Surveillance and Oversight of Marketed Drug Products

Pharmacovigilance

The FDA maintains a wide-ranging practice of postmarketing surveillance and risk evaluation programs to identify and evaluate new adverse events that did not appear during the drug development and approval process or to learn more about known adverse events. These reviews and evaluations are based on detailed assessment of a variety of data. For example, the FDA Adverse Event Reporting System (FAERS) database is comprised of more than 20 million adverse event reports that have been submitted to the Agency by patients, family members, and health care providers through the MedWatch program, as well as by regulated industry. More than two million reports are submitted every year. In addition to adverse event reports, FAERS contains reports of medication errors and product quality complaints that result in adverse events, allowing identification of safety concerns, and recommendations to improve product safety and protect the public. The risk evaluation program includes:

- Surveillance, assessment, and review of epidemiologic data using various data sources, including Sentinel
- Review of protocols and studies submitted by industry

FDA maintains other searchable safety-related databases available to the public, including REMS (REMS@FDA), Drug Safety-related Labeling Changes (SrLC), Medication Guides (MedGuides), and Postmarket Requirements and Commitments.

- Surveillance and review of the published scientific literature

When information is uncovered that may change the benefit-risk profile of a product, the FDA will investigate the issue and consider appropriate action, including requesting or requiring labeling changes, issuing drug safety communications, requiring postmarketing studies, requiring a REMS, or rarely, requesting a market withdrawal of the product. The FDA continuously monitors the safety of all drug products while they are being marketed, even if the Agency has determined that one of these actions is not necessary at a specific point in time.

Selected updates

- FDA publicly posted a Draft of the "Best Practices in Drug and Biological Product Postmarket Safety Surveillance for FDA Staff" document as mandated by the 21st Century Cures Act, providing context and a general overview of the Agency's approach for timely postmarketing safety analyses of drugs and biological products. FDA established a public docket and solicited public comments on the draft document (see Docket No. FDA–2019–N–3768). FDA has reviewed public comments and is working on the final version of the document.
- As part of CDER's multidisciplinary approach to evaluating nitrosamine contamination in products, the Office of Surveillance and Epidemiology (OSE) continued to collaborate with international regulators to evaluate the potential impact of this issue and undertook a safety study in the Sentinel System to evaluate whether this contamination poses an increased risk of cancer in some antihypertensive products. FDA also assessed the use patterns of ranitidine and a comparator agent, famotidine, within the Sentinel distributed database.
- As a consequence of the Agriculture Improvement Act of 2018 (Public Law 115-334), colleagues from OSE and other CDER offices and FDA centers collaborated to evaluate multiple data sources that describe adverse experiences from cannabidiol (CBD) products in an effort to inform the safety of this now widely available substance. The law removed hemp (defined as the Cannabis sativa L. plant and any part of that plant with a THC concentration of not more than 0.3 percent) from the Controlled Substances Act.

FDA Adverse Event Reporting System Public Dashboard

Improving data access and transparency are core concepts underlying the FDA's work and driving development of the FAERS Public Dashboard, an interactive, user-friendly, web-based tool that allows the public to access information about adverse drug event reports received by FDA and contained in the FAERS database. Data may be searched and viewed in a customizable format.

Dashboard users can view a summary of the adverse event reports received on specific drugs during time periods dating from 1968 to the present. The data in the FAERS Public Dashboard is updated quarterly.

Medication Error Prevention and Analysis

The FDA works to increase the safe use of drug products by minimizing use errors related to product naming, labeling, design, and packaging. This includes a focus on how proprietary names (commonly known as brand names) can contribute to confusion in the marketplace.

Phonetic and Orthographic Computer Analysis (POCA) Updates

OSE made changes to its Phonetic and Orthographic Computer Analysis (POCA) program, a software tool that uses an advanced algorithm to determine the orthographic and phonetic (spelling and sound) similarity and thus potential confusion between two drug names. The program can compare a drug name against multiple drug names found in several different data sources contained in the software. The modernized POCA application, now cloud-based, provides the public with a search capability similar to the current POCA while eliminating the complex download processes currently required as well as the need for users to request access to the program and related software from the FDA.

Risk Management

Risk management is a critical consideration in assessing the benefit-risk balance of a drug, including:

- Development of strategies to minimize risks while preserving benefits
- Evaluation of the effectiveness of such strategies and reassessing benefit-risk balance
- Adjustments to risk minimization strategies when appropriate to further improve the benefit-risk balance

The FDA's primary risk management tool is communicating through FDA-approved product labeling, often referred to as the "package insert" or the "prescribing information," or the required "Drug Facts" labeling of nonprescription drugs, which includes a summary of the essential information needed by health care providers or nonprescription drug consumers for the safe and effective use of the drug.

Labeling is sufficient for most drugs to ensure that the benefits outweigh the risks. In a limited number of cases, the FDA may determine that a REMS will also be needed to ensure that a prescription drug's benefits outweigh its risks.

A REMS is a drug safety program that the FDA can require for certain drugs with serious safety concerns to help ensure the benefits of the drug outweigh its risks. REMS are designed to reinforce drug use behaviors and actions that support the safe use of that drug. While all drugs have labeling that informs health care stakeholders about drug risks, a relatively small number of drugs require a REMS.

Modernizing and Improving REMS Assessments

In 2020, the FDA launched an initiative to modernize and improve REMS Assessments. The FDA is focusing on four workstreams: 1) improving REMS assessment planning by developing and using a theory-based approach and incorporating REMS assessment planning into the design of the REMS; 2) clarifying FDA expectations by expanding the review of specific assessment metrics or study protocols; 3) improving the efficiency of our reviews; and 4) enhancing our enforcement actions and tools.

Other REMS Activities

MARCH | New Guidance for Industry: Policy for Certain REMS Requirements During the COVID–19 Public Health Emergency Guidance for Industry and Health Care Professionals

JUNE | MAPP 6702.2 — Determination of the Need for and Review of a New REMS

New REMS Approvals:

CDER approved a REMS with each of 3 new drug applications in 2020:

JUNE 25 | Fintelpa (fenfluramine hydrochloride) NDA 21202 approved

AUGUST 5 | Blenrep (belantamab mafodotin-blmf) BLA 761158 approved; priority review, orphan drug designation, breakthrough therapy designation, and accelerated approval

JULY 21 | Xywav (calcium, magnesium, potassium, and sodium oxybates) NDA 212690 approved. This joined the Xyrem REMS; orphan drug designation

OCTOBER 30 | A shared-system REMS for pomalidomide approved

The Sentinel System

The Sentinel Initiative, launched in 2008, began as a Congressional mandate for the FDA to establish a public-private partnership to develop an electronic medical product safety surveillance system using existing data. The principal operational component of the Sentinel Initiative is the Sentinel System, a network of databases (technically known as a distributed database) that, as of October 2020, included 14 partner institutions.

Sentinel collaborators include data and academic partners that provide access to health care data and scientific, technical, and organizational expertise. Distributed data networks allow secure access to multiple data sources, achieving far larger sample sizes than could ever be achieved through a single source, while assuring that data is collected securely with full patient privacy safeguards in place.

Sentinel monitors drug safety by analyzing emerging risks associated with FDA-regulated medical products, enabling product safety assessment under real-world conditions and providing unparalleled capabilities for investigation of new safety signals that arise from spontaneous reporting systems like FAERS and other sources of safety information. Sentinel can also be used to detect unsuspected potential safety concerns using new approaches that scan thousands of health outcomes, looking for unexpected safety signals after product exposure. Such analyses mine large amounts of health care data without prespecifying a specific target. While promising, the results of these data mining approaches need to be corroborated by further studies. Sentinel also supports inquiries on many different questions, including those related to medication errors, risk mitigation strategies, generic drugs, biosimilars, and drug safety in specific patient groups such as pediatrics and pregnant women.

The Sentinel System has transformed the way researchers monitor FDA-regulated medical products. Now one of the FDA's leading evidence-generation platforms, Sentinel proactively monitors medical product safety and serves to advance the science of RWD and RWE. The FDA now routinely uses RWD made available through the Sentinel System to generate evidence about drug safety, drawing on data from insurance claims, hospital stays, outpatient doctor visits, and pharmaceutical dispensing data. Sentinel has also begun querying data from partners with electronic health record information to address questions in the context of the COVID–19 pandemic. By making it possible to analyze emerging risks associated with FDA-regulated medical products and to study medical care more broadly, Sentinel enables the FDA to assess medical product safety, describe medical product utilization and characterize medical events under real-world conditions.

The FDA released the Sentinel System Five-Year Strategy 2019–2023, a roadmap charting the development of the Sentinel System through five strategic aims intended to expand the Sentinel System's operational foundation, augment the System's safety analysis capabilities and signal detection, and leverage the System to accelerate access to and broader use of RWD for real world evidence (RWE) generation. To advance these aims, the FDA established three centers as part of the Sentinel System: the Sentinel Operations Center (SOC), the Sentinel Innovation Center (IC), and the Community Building and Outreach Center (CBOC). The SOC will continue to focus on enhancing the infrastructure of the Sentinel System, while the IC will carry out work to advance analytic tools and accelerate novel data source acquisition and evaluation, and the CBOC will focus on building the community and engaging stakeholders.

2020 Highlights

APRIL | FDA's Sentinel System initiated numerous activities to protect and promote public health during the COVID–19 pandemic. These included 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, health care utilization, disease progression and outcomes; evaluating the use of computable phenotypes to help identify COVID–19 positive patients in real world data; developing an adaptable protocol design to support a variety of on-demand queries and support subsequent studies of the safety or effectiveness of treatment in COVID–19 patients in special populations such as pregnant women and children; and assessing the occurrence of coagulopathy and its risk factors among hospitalized COVID–19 patients. Sentinel is also collaborating with the Reagan-Udall Foundation and Friends of Cancer Research COVID–19 Evidence Accelerator.

JULY | Sentinel launched the newly redesigned Sentinel Initiative website. The new website was designed to improve organization and usability, and better provide the Sentinel community with up-to-date information on Sentinel assessments, tools, and news.

OCTOBER | The Twelfth Annual Sentinel Initiative Public Workshop was held virtually on October 14, bringing together stakeholder communities on a variety of topics on active medical product surveillance and current and emerging Sentinel activities. Sessions featured key leads from each CDER Sentinel coordinating center to discuss plans to advance and transform Sentinel's data infrastructure into a national resource for evidence generation. Sessions also highlighted the past, present, and future of Sentinel and RWE.

NOVEMBER | A Sentinel public training was held virtually on November 2 focusing on how Sentinel assesses questions related to maternal health and pregnancy. It consisted of presentations on the Sentinel System's distributed database and broad analytic capabilities. Among the presentations were sessions on cohort identification approaches for assessing medical product use during pregnancy, a case study employing a new inferential analysis tool, and pregnancy-related analyses, including how Sentinel links and uses mother and infant data.

Drug Safety Modernization

CDER established the Drug Risk Management Board (DRMB) in January 2020 as a cross-CDER board responsible for three key objectives: 1) facilitating and coordinating decisions around major product safety issues across all relevant Center stakeholders, 2) providing clear and consistent guidance enabling an appropriate response to major safety issues, and 3) systematically communicating decisions and resulting actions across the Center and to other stakeholders as appropriate. In addition, the DRMB facilitates and coordinates all new and existing marketed product safety initiatives across CDER, including the modernization of the Center's framework capabilities for safety surveillance of marketed products.

A major modernization initiative was achieved in April 2020, when CDER launched the Newly Identified Safety Signal (NISS) process, which allows for a standardized, interdisciplinary approach to systematically identify, evaluate, and resolve both clinical- and quality-related safety signals. The Lifecycle Signal Tracker (LiST) workflow tool was developed to support the NISS process, providing the ability to capture and manage all CDER safety signals for marketed drugs. The NISS MAPP and LiST not only support CDER's commitment to drug safety, but also its commitment under Prescription Drug User Fee Act (PDUFA) VI for timely and effective evaluation and communication of postmarketing safety. The NISS MAPP and LiST also address recommendations made in the 2015 Government Accountability Office report.

CDER continues to modernize and improve our postmarketing safety management processes, by working to better standardize and make a consistent approach to managing drug safety throughout the lifecycle of a drug, based on learnings from the NISS implementation. A key component of this modernization initiative is the use of interdisciplinary, team-based approaches that optimize utilization of safety expertise, promote information sharing from all CDER offices with scientific safety responsibilities, and facilitate a robust decision-making process.

Nitrosamine Impurities in Medicines: FDA's Continuing Multidisciplinary Response

In June 2018, the FDA learned that certain generic versions of valsartan, a high blood pressure and heart failure medication, contained unexpected impurities that posed a potential safety concern. These impurities, known as nitrosamines, are probable carcinogens that may increase the risk of cancer in humans. They include N-Nitrosodimethylamine (NDMA), N-Nitrosodiethylamine (NDEA), N-nitroso-N-methyl-4-aminobutanoic acid (NMBA), N-nitrosoisopropylethyl amine (NIPEA), N-nitrosomethylphenylamine (NMPA), 1-methyl-4-nitrosopiperazine (MNP), and 1-cyclopentyl-4-nitrosopiperazine (CPNP). There are many reasons why nitrosamines can be present in medications, including a drug's manufacturing process, its chemical structure, or the conditions in which it is stored or packaged.

Since the initial discovery of NDMA in valsartan, FDA scientists and regulators have investigated nitrosamine impurities in other products, including the heartburn medications ranitidine and nizatidine, the type 2 diabetes medication metformin, and the tuberculosis medications rifampin and rifapentine. The Agency has developed appropriate test methods for testing for these impurities in specific drug products, has tested drug products and drug substances, sent information requests to applicants and manufacturers of drug products suspected of containing nitrosamine impurities, and evaluated the information received from industry. It has assisted industry in initiating voluntary recalls of products when nitrosamines have been found above an acceptable level, and worked with industry when changes to manufacturing processes were appropriate. Throughout this process FDA has kept industry, health practitioners and the public informed of our investigation and regulatory actions. Timely

communication of this information has provided health care professionals, patients, consumers and other interested persons with access to the most current information concerning the potential risks and benefits of marketed drugs, helping them to make more informed treatment choices.

Ranitidine

All of FDA's 2020 updates and actions on ranitidine are available online. On April 1, FDA announced it was requesting manufacturers withdraw all prescription and over-the-counter (OTC) ranitidine medications from the market immediately. The Agency determined the NDMA impurity in some ranitidine products increases over time and when stored at higher than room temperatures and may result in consumer exposure to unacceptable levels of this impurity.

Metformin

The full timeline of announcements, statements, and actions related to metformin products is available online. Key 2020 actions addressing NDMA impurities in metformin products include:

FEBRUARY 3 | FDA announced that it posted laboratory results showing NDMA levels in some metformin products approved in the United States. The Agency determined that the levels of NDMA in the metformin products tested ranged from not detectable to low levels.

MAY 28 | FDA alerted patients and health care professionals that laboratory testing revealed levels of NDMA above the Agency's acceptable intake limit in several lots of the extended release (ER) formulation of metformin.

JUNE 11 | FDA named five companies that voluntarily recalled certain ER metformin and updated the Agency's laboratory test results showing the levels of NDMA it found in samples of metformin to date. FDA also posted a second liquid chromatography-electrospray ionization-high resolution mass spectrometry (LC-ESI-HRMS) testing method to provide an option for regulators and industry to detect eight different nitrosamine impurities in metformin drug substances and products.

JULY 2 | The AAPS Journal, an official journal of the American Association of Pharmaceutical Scientists, published FDA's manuscript titled, "A Cautionary Tale: Quantitative LC-HRMS Analytical Procedures for the Analysis of N-Nitrosodimethylamine in Metformin." This article assessed the cause for the discrepancy between the NDMA values FDA found in its testing of metformin drug products and the values a private laboratory reported. In summary, FDA found the private laboratory method to be inappropriate for quantifying NDMA in metformin drug products due to presumptive overestimation of NDMA caused by the presence of a substance that interfered with the testing results. This article emphasized the importance of the use of appropriate test methodology. If FDA relied upon the data from inappropriate test methods, drug products approved

NDMA is a common contaminant found in water and foods, including cured and grilled meats, dairy products, and vegetables. Everyone is exposed to some level of NDMA. The FDA does not expect NDMA to cause harm when ingested at low levels. Nitrosamines may increase the risk of cancer if people are exposed to them above acceptable levels and over long periods of time.

Small Business and Industry Assistance (SBIA) is often the first stop for a small pharmaceutical business interested in working with the FDA. SBIA's goal is to help small pharmaceutical business and industry navigate the wealth of information that the FDA offers and to provide assistance in understanding the regulation of human drug products.

by FDA may have been removed or voluntarily recalled from the market causing unnecessary disruption to patients and health care providers.

JULY 13 | FDA announced that several companies voluntarily recalled ER metformin medications due to the possibility they could contain NDMA above the acceptable intake limit. FDA also published a recalled metformin list that included details about metformin products that had been recalled, which has since been updated.

Rifampin and Rifapentine

AUGUST 26 | FDA announced it was aware of nitrosamine impurities in certain samples of rifampin and rifapentine, which are antibacterial medications used to treat tuberculosis. The Agency identified rifampin containing MNP and rifapentine containing CPNP above the acceptable intake limits. FDA has been investigating this problem and is working with manufacturers to permit temporary distribution of these drug products to avoid shortages and to help ensure patients continued to have access to these necessary medications, until manufacturers can reduce or eliminate the impurities. FDA announced it would not object if certain manufacturers temporarily distributed rifampin containing MNP below 5 parts per million (PPM), and rifapentine containing CPNP below 14 ppm.

SEPTEMBER 2 | FDA published a LC-ESI-HRMS testing method to provide an option for regulators and industry to detect nitrosamine impurities in rifampin and rifapentine.

OCTOBER 29 | To continue to mitigate or avoid a shortage, FDA announced it would not object to certain manufacturers temporarily distributing rifapentine containing CPNP at or below 20 ppm to help ensure patients had continued access to the medication.

FDA Guidance for Industry

On September 1, FDA announced the publication of the guidance "Control of Nitrosamine Impurities in Human Drugs." The guidance recommends steps manufacturers of active pharmaceutical ingredients (APIs) and drug products should take to detect and prevent unacceptable levels of nitrosamine impurities in their drugs. The guidance also describes conditions that may introduce nitrosamine impurities. On October 2, FDA held a Small Business and Industry Assistance webinar to explain the guidance.

Continued Efforts to Address the Misuse and Abuse of Opioid Drugs and Controlled Substances

The misuse and abuse of illicit and prescription opioids and the risks of addiction, overdose, and death are a public health crisis in the United States. In 2019, an estimated 1.6 million Americans had a substance use disorder involving prescription pain relievers and 400,000 had a substance use disorder involving heroin. From 1999 to 2019, approximately half a million people died from an overdose involving any opioid, including prescription and illicit opioids. Opioids were involved in more than 50,000 deaths in 2018, and provisional data for 2019 suggest those numbers are rising. The FDA has continued to prioritize addressing the opioid crisis even as the Agency has been thrust to the forefront of efforts related to the global COVID–19 pandemic. Actions, activities, and updates through mid-November 2020 are highlighted below.

Support Recovery from Opioid Use Disorder and Reduce Overdose Deaths

JULY 23 | FDA issued a Drug Safety Communication announcing several recommendations concerning increasing access to naloxone, the opioid overdose reversal medication, to help reduce the risk of death from opioid overdose. FDA required the manufacturers of all opioid pain relievers and medications to treat opioid use disorder (OUD) to add new recommendations about naloxone to the prescribing information to help ensure that health care professionals discuss its availability and assess each patient's need for

Currently, most states allow pharmacists to dispense naloxone with a standing order from the state's health department. This allows a pharmacist to dispense naloxone without a prescription for any individual patient.

the medication when opioid pain relievers or OUD medications are being prescribed or renewed. The prescribing information further recommends that health care professionals consider prescribing naloxone when they prescribe medicines to treat OUD and when they prescribe opioid pain medications to patients who are at increased risk of an opioid overdose. A naloxone prescription should also be considered for patients prescribed opioids who have household members, including children, at risk for accidental ingestion or opioid overdose.

AUGUST 6 | FDA approved a Supplemental New Drug Application (sNDA) that provides for a shelf life extension for Narcan (naloxone hydrochloride) nasal spray from a 2-year shelf-life to 3 years and updates to the prescribing information.

OCTOBER 2 | FDA published the final Guidance for Industry, Opioid Use Disorder: Endpoints for Demonstrating Effectiveness of Drugs for Treatment, which is intended to help sponsors develop drugs for treatment of OUD. This guidance addresses clinical endpoints acceptable for demonstrating effectiveness of such drugs.

Foster Development of Novel Pain Treatment Therapies

The FDA continued to engage the Advisory Committees on novel pain treatments and convened several meetings to discuss new drug applications. On September 10–11, the FDA convened a joint meeting of the Drug Safety and Risk Management Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee to discuss the results of required postmarketing studies that evaluated the effect of the reformulation of OxyContin (oxycodone extended release tablets) on abuse, misuse, and fatal and non-fatal overdose. The product was formulated with properties intended to deter non-oral abuse. The committees discussed whether these studies, in addition to other information from the published literature, have demonstrated that the reformulated OxyContin product has resulted in a meaningful reduction in these outcomes. The committees also discussed the broader public health impact of OxyContin's reformulation.

FDA Continues to Examine the Potential Role of Prescription Opioids with Abuse-deterrent Formulations (ADFs) in Helping to Combat the Opioid Crisis

- Opioids with ADFs are designed to prevent—or make more difficult—actions such as crushing tablets to enable snorting, smoking, or intravenous (IV) injection.

- ADFs have physical or chemical properties intended to either hamper manipulation of a tablet or make abuse of a manipulated product less rewarding.
- "Abuse-deterrent" does not mean a product is impossible to abuse or that abuse-deterrent properties fully prevent addiction, overdose, and death, but ADFs may be a step toward helping to reduce abuse.
- The science of abuse deterrence is relatively new, and both the formulation technologies and the methods for evaluating those technologies are rapidly evolving.
- FDA has been supporting the development of opioid medications with progressively better abuse-deterrent properties, which has included working with individual drug makers, developing testing methods for both innovator (often known as "brand name") and generic products, and publishing guidance on the development and labeling of abuse-deterrent opioid products.

Prior research conducted by CDER's Office of Communications (OCOMM) found misunderstanding and low levels of ADF opioid prescribing among health care providers. As a result, the office undertook a three-phase project exploring and assessing the knowledge, attitudes, and understanding regarding ADF opioids among prescribers and dispensers/pharmacists, including the ADF terminology. Based on findings from focus groups with opioid prescribers and pharmacists in the first project phase, development and testing of a follow-up survey was undertaken in 2020 to obtain more representative data, related to the terminology. The finalized survey will be fielded in 2021, to be followed by an experimental study.

Strengthen Enforcement Against Illicit Opioids

JUNE 8 | FDA and the National Telecommunications and Information Administration (NTIA) announced a new 120-day pilot program to help reduce the availability of unapproved opioids illegally offered for sale online.

Other Opioid Activities

The FDA posted and submitted the following reports to Congress to fulfill the requirements of various sections of the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities (SUPPORT) Act, which provided the FDA with new authorities for confronting the opioid crisis:

- Report on Evidence-Based Opioid Analgesic Prescribing Guidelines
- Report on Abuse-Deterrent Opioid Formulations and Access Barriers Under Medicare

Activities Related to Other Controlled Substances

SEPTEMBER 23 | FDA issued a Drug Safety Communication requiring updates to the Boxed Warning and the addition of other information to the prescribing information of all benzodiazepine medications to describe the risks of abuse, misuse, addiction, physical dependence, and withdrawal reactions consistently across all the medicines in the class.

OCTOBER 6 | FDA hosted a public meeting on Patient-Focused Drug Development for Stimulant Use Disorder. This meeting provided the opportunity to obtain input from individuals who are struggling or have struggled with the use of cocaine, crystal meth, methamphetamine, or misuse of prescription stimulants such as Adderall or Ritalin. In particular, FDA was interested in hearing perspectives on the health effects and daily impacts of their conditions, of opioid and polysubstance use on their conditions, treatment goals, and decision factors considered when selecting a treatment.

OCTOBER 8 | FDA convened a joint meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee to discuss a new drug application for amphetamine sulfate immediate-release oral capsules for the treatment of attention deficit hyperactivity disorder (ADHD). The product was formulated with properties intended to deter non-oral abuse. The committees discussed the overall risk-benefit profile of the product, including the potential public health impact and whether the product demonstrated abuse-deterrent properties. They also discussed whether developing prescription stimulants with abuse-deterrent properties in general is likely to have a positive public health impact. Ultimately, the committees unanimously voted against approval of this drug.

Ensuring Quality, Safety, and Effectiveness of Generic Drugs

The FDA's generic drug program continued to substantially increase the availability of affordable, high-quality drugs in the United States. More than 10,000 generic drugs are currently approved, and nine of 10 prescriptions filled in the United States are for generic drugs. Generic drugs have saved the health care system more than a trillion dollars in the past decade.

Increasing the availability of generic drugs helps to create competition in the marketplace, which helps reduce the cost of treatment and increase access to health care for more patients. The Office of Generic Drugs (OGD) follows a rigorous review process to ensure that, compared to the brand-name drug, a generic drug has the same:

- Active ingredients (the ingredients that treat your condition or symptoms)
- Strength
- Dosage form (for example: tablet, capsule, cream, patch or liquid)
- Route of administration (for example: oral, topical, inhalation or injection)
- Conditions of use
- Labeling (with certain exceptions)

OGD evaluates generic drug safety before these drugs are approved and continues to monitor and evaluate generic drug safety after a generic drug product is approved for marketing through the time it is no longer available for sale in the United States.

Effective postmarket surveillance is essential to making sure that FDA-approved generic drugs provide the same therapeutic effect and safety as brand-name drugs.

Communicating Safety Surveillance Activities to Stakeholders in 2020

In 2020, OGD presented its scientific approach to conducting safety evaluations and postmarketing surveillance, and engaged with several major stakeholder audiences.

JANUARY 29 | *Challenges in Generic Drug Surveillance: Proactive Approaches for Complex Generic Drug Products* presented at the Drug Information Association (DIA) Pharmacovigilance and Risk Management Strategies Conference.

FEBRUARY 2 | Participated in several panel discussions with industry, health care provider and pharmacist stakeholders at the Duke Margolis Center for Health Policy Meeting — Understanding How the Public Perceives and Values Pharmaceutical Quality.

APRIL 16 | *The Physician Reviewer's Role in Premarket Safety Review of Generic Drugs, Post-market Pharmacovigilance Data Analysis and Decision Making, and Emerging Trends in Postmarketing Safety Surveillance for Generic Drugs* presented at the CDER Small Business and Industry Assistance Generic Drugs Forum.

MAY 4 | Presented *Postmarket Surveillance of Generic Drugs: Opportunities for GDUFA Research* and led a break-out session at the FY 2020 Generic Drug Regulatory Science Initiatives Public Workshop.

OCTOBER 20 | Co-led *Challenges and Opportunities in Post Marketing Pharmacovigilance and Lifecycle Management for Complex Generic Drug-Device Combination Products* session at the DIA/FDA Complex Generic Drug-Device Combination Products Conference.

NOVEMBER 10 | Presented and participated in panel discussions on *Nitrosamines, Past, Present, and Future; and Pharmacovigilance: The Same Requirements for All* at the Association for Accessible Medicines (AAM) GRx + BioSims 2020 Virtual Conference.

Safety Surveillance of Generic Drugs—OGD's Clinical Safety Surveillance Staff

OGD's Clinical Safety Surveillance Staff (CSSS) performs and facilitates broad preapproval and postapproval generic drug safety and surveillance activities with an interdisciplinary team of physicians, pharmacists, epidemiologists, chemists, and other scientists. The CSSS analyzes postmarketing generic drug adverse event reports and trends, follows generic drug distribution patterns, and reviews serious adverse events from bioequivalence studies and periodic safety reports submitted by generic drug companies. The CSSS also identifies emerging safety issues through published literature, direct contact from patients or health care professionals to the FDA's Division of Drug Information, or information shared by pharmacies and drug safety-focused organizations.

JANUARY | CSSS supported the voluntary market withdrawal of all bacitracin injection products because the risks of harm to the kidneys and serious allergic reactions outweighed the benefits of the drug. Bacitracin injection was FDA-approved to treat infants with pneumonia and empyema, a collection of pus in the space between the membranes lining the lungs, caused by staphylococci bacteria shown to be susceptible to the drug.

SEPTEMBER | CSSS engaged with FDA surveillance groups on a voluntary recall of Perrigo albuterol sulfate inhalation aerosol due to possible clogging of the inhaler resulting in patients not receiving enough or any medicine.

Throughout 2020, the CSSS led a cross-CDER effort to evaluate the need for regulatory action regarding fatal neurologic injury or death related to the accidental spinal rather than intravenous administration of vinca alkaloid drugs, a group of chemotherapy agents that includes vincristine sulfate, vinblastine sulfate, and vinorelbine tartrate. This issue was included in the April-June 2020 Potential Signals of Serious Risks/New Safety Information Identified by the FDA Adverse Event Reporting System (FAERS).

The CSSS also continued to participate in the FDA task force addressing issues related to the presence of nitrosamine impurities in ranitidine, metformin, and rifampin and rifapentine products.

NTI drugs are those where small differences in dose or blood concentration may lead to serious therapeutic failures and/or adverse drug reactions that are life-threatening or result in persistent or significant disability or incapacity.

Generic Substitution and Safety of Generic vs Brand-Name Drugs—OGD's Office of Research and Standards

OGD's Office of Research and Standards (ORS) funded a series of extramural grants through the Generic Drug User Fee Amendments (GDUFA) to study generic drug substitution and compare the effectiveness of brand-name versus generic drugs, particularly narrow therapeutic index (NTI) drugs. Because generic NTI drugs were largely approved based on bioequivalence studies in healthy adult subjects, postmarketing surveillance can be useful for verifying there are no unexpected issues when these drugs are used in patient populations.

Two studies compared the generic drugs and their brand-name counterparts for the thyroid medicine levothyroxine and the blood thinner warfarin. In the first study, the heart-related outcomes and rates of falls and fractures were not significantly different in adults who started treatment with brand-name versus generic levothyroxine between 2008 and 2018. The second study showed a comparable safety profile and risk of all-cause death for brand-name versus generic warfarin products started by patients in the Medicare population. These studies provide real-world evidence that could increase public confidence in generic NTI drugs.

Postmarketing evaluations of generic drugs are often complicated by product use and prescribing patterns, as well as perceptions of their therapeutic effects. GDUFA-funded studies were conducted in senior Medicare and Medicaid populations treated with the thyroid medicine levothyroxine, the antidepressant escitalopram, or the transplant medicine tacrolimus. These studies suggested that patient demographic factors and health service utilization are associated with the initiation and substitution of these generic drugs.

ORS also collaborated with OSE to use Sentinel to conduct postmarketing evaluations of generic versus brand-name product performance.

Safe Use Initiative: Collaborating to Reduce Preventable Harm from Medications

Millions of Americans depend on prescription and OTC medications to sustain their health on a daily basis, with more than four billion prescriptions written annually. Too many people suffer unnecessary injuries—and some die—as a result of preventable medication errors, which can include medications dispensed in error, medications taken for too long or not long enough, or inappropriately mixed with other medications or with foods that can increase the risk of side effects.

The FDA believes that many of these risks are manageable if partners committed to the safe use of medications work together. The FDA's Safe Use Initiative (SUI) works to create and facilitate public and private collaborations within the health care community that can help to reduce preventable harm by identifying specific, preventable medication risks and developing, implementing, and evaluating interventions along with partners and collaborators.

Current and potential partners in Safe Use programs and projects include federal agencies, health care professionals, and their professional societies; pharmacies and hospitals; and patients, caregivers, consumers, and their representative organizations. SUI enables many of its collaborations through funding as well as actively participating in research projects that seek to reduce preventable harm from drugs, and it maintains an open and continuous announcement to solicit research proposals. SUI projects target many kinds of preventable medication-related harm using a range of approaches.

Projects Completed in 2020

Evaluation of an Educational Resource for the Effective Communication between Health Care Professionals and Patients about Impairing Risks of Medication in Relation to Driving. This project developed a communication

resource to help prescribing health care professionals talk to patients about the risks of driving when taking pain medication. Patients using the developed smartphone app demonstrated increased knowledge and were less likely to drive within 2 hours of taking pain medication; however, the results were not statistically significant. The project was presented at the 30th Canadian Association of Road Safety Professionals Conference and the 14th La Prévention Routière Internationale World Congress in June 2020.

National Standardization of Intravenous (IV) and Oral Liquid Medication. This study included the standardization of concentrations for both IV medications and oral compounded liquid medications. The standardized formularies will be disseminated through multiple avenues, including direct mail, email, educational programs, and a website. The adoption of these formularies will also be assessed. Standardized concentration lists for Adult IV Continuous Infusion Standard Concentrations and Compounded Oral Liquid Standard Concentrations have been published.

Identifying Best Practices for the Safe Use of Pediatric Cough and Cold Medications. This study identified health literacy-informed strategies to improve parental understanding of age restriction information on OTC labels for children's cough/cold medication. Errors were reduced when the packaging contained both the standard warning and an explicit warning.

Small Dispenser Pilot Study — Understanding the Impact of the Oncoming Track and Trace Legislation on Small Dispensers. The Drug Supply Chain Security Act (DSCSA) was enacted by Congress on November 27, 2013, to improve the security of the U.S. drug supply and protect U.S. patients from illegitimate products such as counterfeit medications. This project assisted the Office of Compliance in understanding how the DSCSA requirements affect small dispensers in terms of operations and resources. The project examined the process to scan and collect serialized data present within barcodes on individual prescription drug packages in retail, hospital, long-term care, and specialty pharmacies, and compare the data with the human-readable information on respective packages. The study found that most small dispensers in the project were unaware of DSCSA requirements, expressed a desire to be compliant, needed assistance with implementation, and were ultimately able to comply with these requirements with some assistance from equipment and training.

Projects Published or Presented in 2020

Safe Stimulant Medication Prescribing for Adult ADHD.

Improving Safe Use of Fluoroquinolones through Development of an Innovative Educational Program.

Core Elements of Anticoagulation Stewardship. The Stewardship Guide and a Checklist for health care centers to assess their progress are now available.

Projects Ongoing in 2020

A Scalable, Patient-centered Approach to "Right-sizing" Opioid Prescriptions. Patient-reported data on the actual use of opioid pain medications after specific procedures are lacking, and many studies have found that more pills are prescribed than are actually needed. This project aims to collect data from patients undergoing elective orthopedic and neurosurgical procedures, as well as those seen in an Emergency Department for acute pain. Information on the number of doses of opioid pain medication used, the number of days of medication used, and how patients feel about their ability to treat their pain is being collected. Understanding how much medication most patients actually used can enable updating standard orders for surgeries to reflect actual patient need. The project's findings will help ensure patients are provided enough medication to treat their pain while minimizing the number of pills that could be diverted, misused, or abused.

Suicide-related Risks Associated with Prescription Opioid Deprescribing. Concerns exist that abrupt discontinuation or rapid/unsupported tapering of opioid pain medication may result in unintended consequences including suicides, and in 2019 FDA required label changes guiding prescribers on how to safely taper patients off these medicines. However, the scope of suicides and suicide attempts after opioid deprescribing, as well as which patients are most vulnerable, are largely unknown. This project assesses overdose and suicide-related outcomes associated with prescription opioid deprescribing in a large, multi-site, nationally representative, observational study using data from six health systems. This study is further designed to identify factors that can reduce associated risks and reduce preventable harm related to opioid deprescribing.

Manganese Contamination in Neonatal Parenteral Nutrition. Parenteral nutrition (PN), which is the administration of nutrition through a vein, has become standard and essential to the care of preterm newborns in the neonatal intensive care unit. Health benefits of PN include positive nitrogen balance, weight gain, and reduced neurodevelopmental impairment. However, the daily provision of PN to preterm newborns involves numerous safety risks, including side effects from ingredient formulations not ideally suited for this vulnerable population. The trace element manganese is one example. This project evaluates the sources of manganese in approved products by testing a variety of PN components. Work from this part of the project was published. The second part of the project will determine whether preventing potential harm from PN manganese overexposure can be done reliably and safely through creative product selection during the PN compounding process.

Perioperative Medication Safety Self-Assessment for Hospitals and Ambulatory Surgical Centers (ASCs) and Targeted Risk-Reduction Tool Development. Preventable harmful medication errors in perioperative settings are a common cause of morbidity and mortality in the United States. The frequency of medication errors reported in perioperative settings varies widely depending on detection and measurement strategies. Systematic identification and characterization of perioperative medication errors is essential to enable targeted interventions to reduce preventable harm. This project involves the development, testing, and implementation of a perioperative medication safety

self-assessment instrument for systems and practices in U.S. hospitals and ambulatory surgical centers. Additionally, the Institute for Safe Medication Practices (ISMP) will apply findings from this project to create a self-assessment tool for general use by health care providers and institutions to enable reduction of preventable harm from perioperative medication errors.

New Projects Initiated in 2020

Leveraging the Electronic Health Record (EHR) to Promote Pharmacy Adoption of Dosing Best Practices and Reduce Parent Errors in Administering Pediatric Liquid Medications. This project examines whether an instruction to pharmacists incorporated into the EHR as part of the electronic prescription will reduce errors in administering pediatric liquid medications. The instructions will specify that the prescription should be in "mL only" units and that an appropriate-sized dispensing device should be given to the patient. Follow-up with patients will assess the effectiveness of the instructions to the pharmacist and if the intervention reduces dosing errors made by parents.

Evaluation of Stimulant Abuse in the United States: A Mosaic Epidemiology Study. Stimulant abuse is increasing dramatically; however, little is known about this emerging public health issue. This project will use several databases to characterize stimulant abuse. It will examine demographics, drugs of interest, motivations, behaviors, and trajectories of use.

Mentored Implementation and Dissemination of Anticoagulation Stewardship (MIDAS) Program. Anticoagulants are essential medicines to reduce the risk of blood clots and strokes, but they are also a major source of preventable harm due to the risk of excessive bleeding and because they can be challenging for health care professionals to manage. This project examines the ability of an anticoagulation stewardship program to reduce preventable harm using a Mentored Implementation Program in five diverse hospitals. A Stewardship Guide and Self-assessment were developed in a previous FDA-funded project. In this new effort, paired physician-pharmacist teams serve as mentors for five different hospitals, each of which conduct a self-assessment at the beginning of the program, create an interdisciplinary team, and work with the mentors to create an individualized implementation plan. Monthly mentoring will take place over a year-long period. The hospitals will share lessons and provide updates quarterly. A content development committee will use the implementation plans and lessons to create a "playbook" that can be used by other institutions to create and carry out their own Anticoagulation Stewardship Implementation Programs.

Preventable Harm from Pediatric Outpatient Medication Errors: Measure Development. This project seeks to develop an understanding of current measures in outpatient pediatric medication safety and assess the gap between current measures and needs. Measure development is a necessary step in defining and establishing quality improvement programs. Quality measures in pediatrics have lagged behind measure development in other areas. The project will include both a systematic literature review and input about measure development from stakeholders, including health care providers, parents, and patients.

Compounded Drugs: Continuing Oversight and Stakeholder Outreach

Human drug compounding is generally a practice in which certain health care professionals combine, mix, or alter ingredients of a drug to create a medication tailored to the needs of an individual patient. The health care professionals who may be involved in human drug compounding are licensed pharmacists, licensed physicians, or, in the case of an outsourcing facility, a person under the supervision of a licensed pharmacist. Although compounded drugs can serve an important medical need for certain patients, they also can present a risk to patients.

Compounded drugs do not undergo FDA premarket review for safety, effectiveness, and quality, and therefore may present a greater risk of harm to patients than FDA-approved drugs. To help mitigate these risks, the FDA has developed a novel approach to engage outsourcing facilities and other compounders to improve the overall quality of compounded drugs.

The Compounding Quality Center of Excellence is designed to enhance collaboration with, and provide educational programs for, outsourcing facilities with the goal of improving the overall quality of compounded medications.

Through the Compounding Quality Center of Excellence, the FDA is engaging and collaborating in new ways, including in-person and online trainings on current good manufacturing practice (CGMP) requirements. These requirements for outsourcing facilities are particularly important because their compounded drugs reach many patients across the country.

FDA's compounding program aims to protect patients from unsafe, ineffective, and poor-quality compounded drugs, while preserving access to lawfully marketed compounded drugs for patients who have a medical need for them.

In 2020, the FDA advanced the development of the framework for the Compounding Quality Center of Excellence through the following initiatives, including:

- Developing and holding in-person, virtual, and online CGMP and compounding policy trainings for outsourcing facilities
- Hosting a virtual conference in September 2020 to engage industry, the Agency, and stakeholders to bolster the quality of compounded drugs

In August, the FDA issued a compounding risk alert to inform compounders, ophthalmologists, and other health care professionals about risks associated with the intraocular administration of moxifloxacin drugs that contain more than 0.3 mL of 0.5% moxifloxacin or that contain certain potentially harmful inactive ingredients such as xanthan gum. The Agency also cautioned health care professionals to carefully consider the concentration and inactive ingredients of any moxifloxacin drug before intraocular administration.

In October, the FDA issued the final standard memorandum of understanding (MOU) for signature between state boards of pharmacy or other state agencies and the FDA. These collaborative efforts will enhance communication and maximize federal and state resources for oversight of compounded drugs produced by traditional compounding pharmacies.

In November, the FDA issued a final guidance to enhance our efforts to help compounders identify and prevent insanitary conditions at their facilities. The final guidance provides recent examples of insanitary conditions that inspectors have observed at compounding facilities and details corrective actions that facilities should take when they identify these conditions.

Other resources related to human drug compounding can be found online at FDA.gov:

- Compounding inspections, recalls, warning letters, and related information
- Compounding risk alerts
- Consumer and health care professional information
- Common questions and answers related to drug compounding

Communicating Drug Safety: Global Outreach Through Diverse Tools and Technologies

CDER's Office of Communications (OCOMM) supports the FDA's mission to protect and promote public health through a broad range of communication tools and technologies. Throughout 2020, OCOMM continued to develop and expand this mission through the expertise and efforts of a multidisciplinary staff of health care professionals, science and medical communications specialists, researchers, web and graphic designers, and senior strategists and advisors. These professionals enable OCOMM to:

- Provide strategic communication advice to FDA leadership
- Develop and coordinate overarching public communication initiatives and educational activities
- Devise and deploy comprehensive communication strategies that ensure consistent branding, messaging, and direction of communication initiatives and tools
- Offer expertise on communication products across a variety of media
- Respond to inquiries from the public about a range of topics related to human drugs
- Conduct social science and risk communications research

Communicating Drug Safety Across Multiple Audiences

Drug Safety Communications (DSCs) provide new and/or emerging information for patients, caregivers, health care professionals, and the public about safety risks and adverse events associated with prescription and over-the-counter drugs. DSCs may communicate safety issues affecting a large number of patients, describe potentially serious or life-threatening adverse events or other cautions related to use of a drug or class of drugs, and contain actionable recommendations for patients and health care professionals.

The DSC home page is consistently one of the most visited pages on the FDA's web site. This key safety information is also broadly circulated through many other channels, including large email listservs, social and traditional media, podcasts, as well as targeted outreach to media, health care professionals, advocacy groups, and other stakeholders. Throughout 2020, DSC information was widely reported, including by ABC News, the Associated Press, Bloomberg News, CBS News, CNN, Forbes, FOX News, the Hill, NBC News, New York Times, New York Post, Newsweek, NPR, Reuters, U.S. News, USA Today, Washington Post, and Washington Times.

Drug Safety Communications (DSCs) support more informed decision making by patients and health care professionals and help prevent or mitigate drug-related harm.

Ten DSCs were issued in 2020, generating more than 2.3 million unique pageviews on the DSC website. Among the DSCs issued, several involved high-profile issues or medications, including:

- Hydroxychloroquine and chloroquine: Serious risks with the use of the malaria and autoimmune conditions medications to treat COVID-19 in certain hospitalized patients
- Benzodiazepines: Requiring updates to the *Boxed Warning* to address the serious risks of abuse, addiction, physical dependence, and withdrawal reactions
- Diphenhydramine (Benadryl and generics): Serious problems and death when misusing higher than recommended doses of this common over-the-counter allergy medication
- Nonsteroidal anti-inflammatory drugs (NSAIDs): Recommendations to avoid using NSAIDs such as ibuprofen at 20 weeks or later in pregnancy due to rare but serious kidney problems in the unborn baby, leading to low levels of amniotic fluid
- Belviq, Belviq XR (lorcaserin): Withdrawal of the weight-loss medication from the market due to an increased occurrence of cancer
- Montelukast (Singulair and generics): Strengthening warnings about serious behavior and mood-related side effects with the allergy and asthma medication

Across all DSCs issued during 2020, visitors spent an average of 4 minutes on DSC content. In comparison, most users generally stay on websites for less than 15 seconds.

To further expand the outreach of the DSC information, in September 2020, the OCOMM launched a distribution listserv that allows health care professionals, patients, and consumers to sign up to receive email alerts about DSCs on medications and medical specialties of specific interest to them. Through the end of the year, the listserv had more than 4,700 subscribers across the 75 different DSC medication and medical specialty topics offered. DSCs issued in 2020 were also widely shared via social media on FDA's Facebook page, Twitter feed, and LinkedIn page. LinkedIn—which has greater potential for targeting health care professionals—saw more than 9,300 "click-throughs" to the full DSCs.

Drug Safety Podcasts were issued in conjunction with each DSC, providing an additional platform to find emerging safety information about drugs. The 10 podcasts issued in 2020 are available online and in Apple Podcasts as FDA Drug Information Updates.

Drug Information Webinars offer free live online continuing education for physicians, physician assistants, nurse practitioners, nurses, pharmacists, and pharmacy technicians. The webinars often center on drug safety or safety-related topics. These webinars remain online and are available to interested professionals.

- **JUNE 30 |** Role of FDA and ISMP in Preventing Medication Errors webinar

- **SEPTEMBER 29 |** An Overview of Naloxone and FDA's Efforts to Expand Access webinar.

Responding to Public Inquiries

OCOMM responds to public inquiries about all human drugs. These inquiries are received via phone, email, letters, and through social media platforms such as Facebook and Twitter. Expert responses are developed and facilitated by a team of pharmacists, nurses, and other health professionals who field questions from consumers, health care professionals, journalists, research organizations, non-profits, regulated industry, other government agencies, and academia, as well as queries from international stakeholders in government and research institutions.

Online Communications

Drug safety news, announcements, and information are distributed to multiple audiences using a variety of digital and electronic media supported by a broad portfolio of services, including video production and photography, web graphics, online publications, custom-designed flow-charts, posters, infographics, illustrations, and other materials. The online communications team also maintains web content, including drug safety information and safety-related regulatory policy documents on FDA web pages; manages public databases; and develops web and mobile applications, including optimizing applications for viewing formats such as smart phones and tablets.

Between January 1 and September 30, 2020, the traffic to CDER's web pages amounted to more than 96 million individual sessions. The metrics below depict the extent of this online engagement, including the platforms from which the traffic is coming, the 10 most-viewed CDER web pages—collectively accounting for more than five million online visits—and the topics, questions, and documents generating the most online traffic for the period. Also tracked are trending topics on social media, as well as the leading subjects of news stories and other informational outlets, and those carried via newsfeeds and social media.

Social Media Engagement

The OCOMM Social Media team has significantly expanded CDER's communications outreach by 'meeting people where they already are' on numerous social media platforms, including Facebook, Twitter, YouTube, and LinkedIn.

Drug safety information is now actively pushed to more than 700,000 FDA Facebook followers and nearly 300,000 Twitter followers, facilitating exponential growth in the distribution of FDA's public health messages, safety communications, and drug safety warnings. In addition to posting content and engaging in two-way communication, the social media team also performs social listening, monitoring the comments and questions users post on FDA's social media channels to obtain real-time feedback on FDA actions and decisions.

OCOMM received and managed more than 60,000 public inquiries between October 1, 2019, and September 30, 2020.

PUBLIC INQUIRIES MANAGED BETWEEN OCTOBER 1, 2019– SEPTEMBER 30, 2020

Phone	41,808
Email	20,296
Letters	379
Social Media	892*
TOTAL	**63,375**
**Facebook and LinkedIn*	

TOP 10 PUBLIC INQUIRIES

COVID-19	15,966
Nitrosamines	5,678
Opioids	1,791
Personal Import	1,508
Electronic Registration and Listing	1,291
Investigational New Drugs (IND)	1,218
Expanded Access/ Right to Try	1,108
Recalls	963
Clinical Trials	914
Import/Export	789

WEB TRAFFIC BETWEEN JANUARY 1– SEPTEMBER 30, 2020

TRAFFIC VOLUME	SESSIONS*
Mobile	55,847,361
Desktop	37,650,351
Tablet	3,250,453

* *Number of individual online sessions initiated by all users with periods of inactivity less than 30 minutes.*

TRAFFIC SOURCES	% OF SESSIONS
Search Engines	55
Direct (URLs)	21
Referrals	4
Email	3
Social Media	3

The team also oversees 'live' tweeting of discussions occurring at meetings and workshops, providing real-time highlighted content to many more people than those able to attend in person. Live tweeting, including through Twitter Chats, also positioned FDA's drug and drug safety subject matter experts at the top of trending topics on social media platforms.

Between October 1, 2019, and September 30, 2020, the Social Media Team:

- Actively pushed FDA information to followers on Twitter through 833 tweets and Facebook through more than 280 posts
- Provided information to more than 100,000 subscribers on our Drug Information Listserv through 304 messages sent, generating more than 745,000 URL "click-throughs" to FDA content
- Gained more than 39,000 new followers on Twitter and 75,000 new followers on Facebook
- Leveraged expanded social media outreach for COVID-19 communications, and the Remove the Risk opioid disposal campaign, BESAFE Rx online pharmacy campaign relaunch, Biosimilars campaign, and Sunscreen campaign

TEN MOST VIEWED CDER PAGES

	Unique Pageviews*
1. FDA Updates on Hand Sanitizers with Methanol	10,118,102
2. FDA updates on hand sanitizers consumers should not use	3,981,856
3. FDA advises consumers not to use hand sanitizer products manufactured by Eskbiochem	2,682,147
4. FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems	1,608,090
5. Drugs	1,567,011
6. Q&A for Consumers: Hand Sanitizers and COVID-19	1,015,861
7. Drug Approvals and Databases	804,473
8. FDA advises patients on use of non-steroidal anti-inflammatory drugs (NSAIDs) for COVID-19	658,413
9. FDA Updates and Press Announcements on NMDA in Zantac (raniditine)	594,797
10. FDA Updates and Press Announcements on NMDA in Metformin	492,954

* *Number of sessions during which the page was viewed one or more times.*

TOP 10 GOOGLE SEARCHES

1.	Hydroxychloroquine
2.	Hand sanitizer recall
3.	Metformin recall
4.	Zantac
5.	Ranitidine
6.	Coronavirus/COVID–19
7.	N95 masks
8.	Benzalkonium chloride
9.	FDA warning letters
10.	Drug recalls

SOCIAL MEDIA OUTREACH

FACEBOOK	
Facebook followers	707,320
Posted content	280
Replied to comments	473
Public Likes/Shares	81,900
LINKEDIN	
Total followers	390,501
Small Business and Industry Assistance (SBIA) Showcase page	10,336
Global Alliance of Drug Information Specialists (GADIS)	934
TWITTER	
Total followers	298,437
Tweets	833
Retweets	23,151
Likes	29,854

A hand sanitizer quiz was launched on Twitter and Facebook as a fun and engaging way to educate stakeholders on the safety and proper use of hand sanitizers. Through this informal quiz, FDA was able to identify areas where additional education was needed, which will help inform future hand sanitizer communications. Areas for future focus include:

- **Expiration date:** 86 percent of respondents incorrectly answered the number of years after which hand sanitizers should be considered expired if they don't have an expiration date. The correct answer is three years.
- **Product classification:** 69 percent of respondents voted that hand sanitizer is not a drug. The correct answer is that hand sanitizer is a drug.
- **Prevention:** 61 percent of respondents voted that hand sanitizers have been proven to prevent COVID-19, which is false. The same percentage responded that hand sanitizer should always be used to disinfect hands to prevent the spread of COVID-19, when the correct answer is that washing hands is the best way to prevent its spread.

Drug Safety-related Labeling Changes

Not every safety concern can be identified at the time a drug product is approved for marketing. If new safety concerns emerge after a drug is marketed, the FDA may require a Drug Safety-related Labeling Change. The drug safety-related labeling changes (SrLCs) database includes safety labeling changes required or ordered by the FDA, as well as labeling changes that are voluntarily submitted by product sponsors.

- The database makes safety information available in near real time and can be easily searched through a user-friendly portal by stakeholders such as health care professionals, patients, and health IT and information vendors. Stakeholders accessing the database provide valuable feedback that assists the FDA in continually upgrading how safety labeling information is organized and presented.

SAFETY-RELATED LABELING CHANGES*

Adverse Reactions	782
Boxed Warnings	193
Contraindications	290
Drug Interactions	425
Patient Counseling information and/or Medication Guides	774
Use in Specific Populations	790
Warnings and Precautions	783
TOTAL	**4,037**

**Between October 1, 2019-September 30, 2020*

Risk Communications Research

OCOMM undertakes a range of social and behavioral science research studies to gather real-world data and evidence related to numerous drug and drug safety-related issues.

- The goal of this research is to enhance understanding of our stakeholders' knowledge, perceptions, needs, desires, and behaviors.
- Findings from these studies provide detailed and comprehensive evidence to inform policy, regulatory, and communication decisions aimed at enabling health care professionals, patients, and the public to make informed health decisions.
- These studies involve both qualitative and quantitative methodologies, including testing of materials and messages, and exploratory pharmacovigilance studies conducted through monitoring and analysis of open-source data available online and through social media.

Highlights of 2020 Research Programs and Projects

Proactive pharmacovigilance through social media monitoring and analysis is aimed at obtaining an understanding of the social contexts and trends surrounding opioids and other prescription drugs, particularly their use for non-medical or recreational purposes, being discussed in publicly available online discussion forums and on social media. In addition to developing monthly social media research reports concerning prescription opioids, OCOMM undertook an in-depth project exploring the effects the coronavirus pandemic is having on opioid use and addiction. OCOMM also awarded a contract in late 2020 for access to a social conversation network that will enable its social scientists to access physician-specific discussions about these and other topics of interest.

Exploration of substances that may be used as adjuncts or alternatives to prescription opioids. Two separate studies are underway investigating such substances among both consumers with opioid use disorder and health care professionals who prescribe these substances. Among the substances being explored are benzodiazepines (among patients undergoing treatment and among prescribers) and gabapentinoids, kratom and CBD (among patients undergoing treatment).

Studies to Enhance FDA Communications Addressing Biosimilar Products focuses on assessing educational materials FDA developed to most efficiently and effectively communicate with patients about biological products that are demonstrated to be "biosimilar" to an FDA-licensed biological product. The educational materials consist of an infographic, fact sheet, and video public service announcements to be posted on FDA's website or disseminated to patients through other tactics. This study is a follow-up to a related study that collected information about knowledge, awareness, and understanding of biological products and biosimilars from patients and health care professionals.

Several message testing studies undertaken in 2020 assessed a variety of FDA materials, including prescription opioid packaging, a buprenorphine Medication Guide template, CBD web content, draft naloxone drug labeling recommendations, usability of FDA's Purple Book database of approved biological products and two opioid outreach campaigns: A consumer-focused effort called Remove the Risk concerning proper opioid storage, and an opioid prescriber awareness and education campaign FDA is sponsoring called Search and Rescue.

Results from several OCOMM research projects were presented at peer-reviewed conferences in 2020, including the American Public Health Association annual convention; the Health Communication, Marketing and Media conference; and the International Conference on Risk Communications.

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