

CENTER FOR DRUG EVALUATION AND RESEARCH  
**OFFICE OF COMPLIANCE**

**2021**

# **ANNUAL REPORT**

Shielding patients from poor quality, unsafe and ineffective drugs through proactive compliance strategies and risk-based enforcement actions.



# Table of Contents

Director’s Message .....	4
Re-Organization of CDER Compliance.....	6
COVID-19 Response .....	8
Implementing Alternative Tools.....	8
Shielding Consumers from Unsafe Hand Sanitizers .....	9
Increasing Access to Critically Needed Medications and Supporting Development of New COVID Therapeutics..	11
Protecting Consumers Against Unproven Drugs with Fraudulent Claims to Prevent or Treat COVID-19 .....	11
Human Subject Protection During the Pandemic .....	13
Compounding .....	14
Protecting Patients from Poor Quality Compounded Drugs.....	14
Partnering with State Regulators on Compounded Drug Oversight .....	16
Adverse Events Linked to Compounded Drugs.....	17
Reducing the Impact of the Opioid Crisis.....	19
Clinical Trial Oversight.....	22
Enhancing Our Clinical Trial Oversight .....	22
Protecting Patients in Clinical Trials .....	23
Implementing the Drug Supply Chain Security Act.....	24
Shielding Patients and Consumers from Unsafe Drug Products.....	26
Products with Hidden Drug Ingredients .....	26
Alerting Companies and Consumers About CBD Health Fraud .....	27
Alerting Patients and Health Care Professionals to Benzene and Nitrosamine-Related Recalls .....	27
Shielding Patients from Potentially Unsafe Homeopathic Medicines .....	28
Shielding Patients from Poor Quality Unapproved Porcine Thyroid Drug Products.....	28
Proactively Promoting Compliance .....	29
Cosponsoring the Annual Parenteral Drug Association (PDA)/FDA Joint Regulatory Conference .....	30
Hosting a Registration and Listing Workshop for Industry Stakeholders.....	30
Supporting Global Collaborations to Enhance Compliance .....	31
Risk-based Regulatory and Compliance Actions.....	32
Compliance by the Numbers .....	32
Proactively Keeping Dangerous Medicines from Entering the U.S. Supply Chain .....	33
Looking Ahead.....	34



**Donald D. Ashley, J.D.**  
Director, CDER Office of Compliance

## Director's Message

I am pleased to present the 2021 annual report for the Office of Compliance in FDA's Center for Drug Evaluation and Research.

This report provides a high-level overview of our efforts to shield patients and consumers from unsafe, ineffective and poor-quality drugs in 2021, including unsafe hand sanitizers and products fraudulently claiming to prevent, treat or cure COVID-19. The report further describes the many other ways we have responded to the pandemic, including our actions to increase access to critical medicines needed to treat patients with COVID-19, such as albuterol, oxygen and propofol, as well as to support the development of new therapeutics.

The ongoing COVID-19 pandemic required numerous operational innovations to allow us to continue to shield the public from potentially harmful and ineffective drug products. Mission-critical inspections continued throughout the pandemic, but we also made extensive use of alternative tools to support compliance and enforcement actions usually based upon on-site inspections, including sampling and testing drug products at the border, record requests in lieu of inspection and remote regulatory assessments.

Our efforts to address the COVID-19 pandemic do not neatly fit into a single calendar year, and neither do the results produced by our highly skilled and specialized staff across our many other drug compliance programs. Many of the achievements you will read about in these pages reflect efforts that began years ago or build on work by other FDA offices, other government agencies and academic institutions. Our work to ensure that compounded drugs are safe and available to patients whose needs cannot be met by an FDA-approved drug is a great example. With a reorganization in early 2021, the Office of Compliance added the Office of Compounding Quality and Compliance as an official suboffice within our larger organization. This is just the latest step in our long-standing commitment to strengthen federal oversight of drug compounding.

We continued to protect patients from poorly compounded drugs and to alert patients and health care professionals to nitrosamine-related recalls as well as recalls of benzene in hand sanitizer, sunscreen, antiperspirant and anti-fungal products. Our efforts to implement the Drug Supply Chain Security Act are moving forward to guide industry on meeting the enhanced drug distribution security requirements for electronic, interoperable package-level product tracing systems by November 2023 to identify and trace most prescription drugs as they are distributed within the United States. We also achieved significant milestones in ensuring compliance with [ClinicalTrials.gov](https://www.clinicaltrials.gov) registration and results information submission requirements.

In another major achievement, perhaps our most significant in 2021, we took action to remedy serious data integrity violations at two contract research organizations located in India — Panexcell Clinical Lab Pvt. Ltd., and Synchron Research Services Pvt. Ltd. We found that both these contract research organizations falsified data submitted to the FDA in support of more than 100 new and generic drug applications. CDER has requested new bioavailability and bioequivalence studies from sponsors as a result.

Our risk-based approach to compliance and enforcement actions allows us to have the greatest impact on patient health, keeping potentially harmful medicines from entering the U.S. drug supply chain. In 2021, we issued 149 warning letters across our compliance programs, obtained two injunctions, oversaw good clinical practice inspections and issued clinical inspection summaries for more than 122 new drug and biologic applications, and assisted in preventing or mitigating shortages for 59 different medications.

Our accomplishments in 2021 demonstrate the unwavering commitment by the Office of Compliance to our public health mission, and I want to thank each and every one of our talented, dedicated and hard-working staff members for their outstanding contributions.

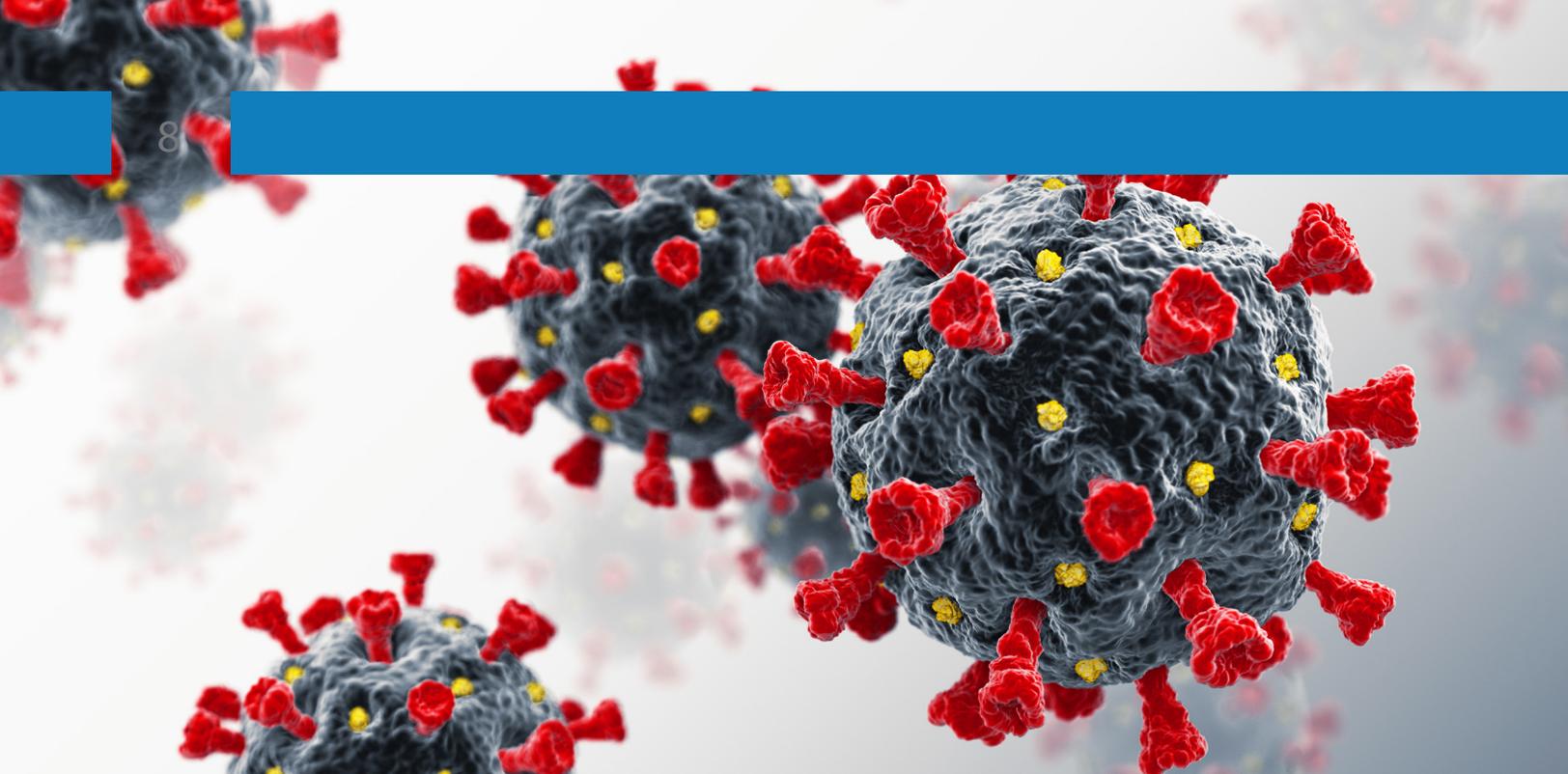
Donald D. Ashley, J.D.  
Director, CDER Office of Compliance



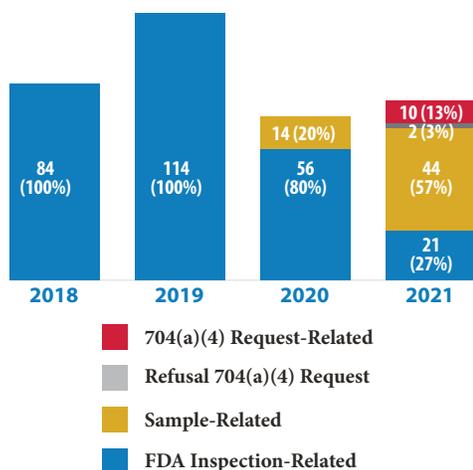
The Office of Compounding Quality and Compliance (OCQC) brings together staff from the Office of Unapproved Drugs and Labeling Compliance and the Office of Manufacturing Quality who work on the compounding program. This office is comprised of three divisions, each with two branches. Dr. Gail Bormel was selected to serve as the OCQC director.

While the creation of OCQC is certainly the most prominent change in the reorganization, other important changes included:

- The Office of Unapproved Drugs and Labeling Compliance (OUDLC) now combines functions of the Drug Registration and Listing Staff with similar functions of OUDLC, specifically the labeling component. This realignment establishes the Division of Labeling, Registration and Unapproved Drugs, which includes the Drug Registration and Listing Branch and the Over-the-Counter Drugs Branch. Additionally, the Division of Unapproved New Drugs is renamed the Division of Unapproved Drugs and Labeling and maintains the Fraud Drugs Branch and the Prescription Drugs Branch.
- The Office of Drug Security Integrity and Response is streamlining its functions by dividing the Import Export Compliance Branch into two branches — Imports Compliance Branch and Exports Compliance Branch — within the Division of Global Drug Distribution and Policy. This organizational change realigns functions for handling our response to public health incidents with a new Incidents, Recalls and Shortages Branch within the Division of Supply Chain Integrity. Additionally, within the Division of Supply Chain Integrity, the Supply Chain Strategy and Policy Branch is renamed to the Supply Chain Security Branch.
- The Office of Program and Regulatory Operations added a third staff to further strengthen our critical project and process management functions.
- Lastly, the Office of Manufacturing Quality now has two divisions with three branches each.



### Shift in Source of Drug Adulteration Warning Letters



Prior to 2021, the vast majority of our CGMP compliance warning letters were based solely upon observations made during on-site inspections. During the pandemic, when inspections were not always possible, we also relied on alternative tools to serve as the basis of our warning letters, including analytical testing of samples at the border and 704(a)(4) requests for information.

## COVID-19 Response

Responding to the COVID-19 pandemic remained our top priority throughout 2021. Developing and implementing alternative tools to support compliance and enforcement actions normally based upon inspections were a critical part of our COVID response efforts.

### Implementing Alternative Tools

Historically, a high percentage of our compliance and enforcement actions have been based upon inspection results. For example, prior to 2021, the vast majority of our CGMP compliance warning letters were based solely upon observations made during inspections. While mission-critical inspections continued throughout the pandemic, inspections were often not possible in many other cases. Consequently, we had to develop and implement numerous alternative tools to support compliance and enforcement actions, usually based upon on-site inspections, to allow us to continue to shield the public from potentially harmful and ineffective drug products. These tools include sampling and testing drug products at the border, record requests in lieu of inspection and remote regulatory assessments.

One alternative tool was collection of samples of imported drug products at our borders. FDA analyses of the collected samples identified products that contained contaminants or did not meet quality standards for potency. This tool proved to be very effective in identifying that 84 percent of hand sanitizers imported from Mexico from April through December 2020 were not in compliance with FDA regulations. As a result, in January 2021, we put in place an [import alert for all hand sanitizers from Mexico](#), marking the first time the FDA has issued a countrywide import alert for any category of drug.

We also turned to a provision in section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) that allows us to request records in advance of or in lieu of an inspection. The 2012 Food and Drug Administration Safety and Innovation Act added section 704(a)(4) to the FD&C Act. This led to our issuance of a precedent-setting warning letter in January 2021 — the first ever based on a review of records submitted in response to a request for records and other information pursuant to section 704(a)(4) of the FD&C Act. The letter was issued to [Yuyao Yijia Daily Chemical Co.](#) We sent nine more such warning letters in 2021.

Similarly, we used our 704(a)(4) authority to conduct remote regulatory assessments (RRAs) of clinical sites conducting biomedical research as part of our commitment to ensure that the rights, safety and welfare of individuals participating in clinical trials are protected. In 2021, we conducted more than 45 RRAs of clinical sites to ensure that they were not delayed due to COVID restrictions and the inability to conduct inspections in-person. These efforts protected trial participants and supported our commitments to review clinical sites named in new drug applications within established timeframes.

In addition to using existing authorities, the Office of Compliance worked with colleagues across the FDA to develop additional tools to evaluate industry compliance with regulations. One example is remote interactive evaluations, described in [Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities During the COVID-19 Public Health Emergency](#). This new draft guidance, published in April 2021, explains how FDA requests and conducts voluntary remote interactive evaluations at facilities where drugs are manufactured, processed, packed or held; facilities covered under FDA's bioresearch monitoring program; and outsourcing facilities.

The Office of Compliance and the Office of Pharmaceutical Quality (OPQ) collaborated on short videos to inform wider audiences about how FDA adapted to the challenges of the COVID pandemic. The [Office of Compliance](#) video is on the FDA YouTube channel, as is a complementary [video by OPQ](#).

In May 2021, FDA issued the [Resiliency Roadmap for FDA Inspectional Oversight](#) to inform manufacturers of FDA-regulated products about our alternative inspectional tools, the effect of the pandemic on our inspectional activities, our detailed plan for a more consistent state of operations and our priorities going forward. We updated the [Resiliency Roadmap for FDA Inspectional Oversight](#) in November 2021 to report on our progress and return to a more consistent state of operations.

## Shielding Consumers from Unsafe Hand Sanitizers

We continued to protect consumers from unsafe hand sanitizers throughout 2021, adding 46 products to the [FDA list of hand sanitizers consumers should not use](#). In 2020, we put more than 200 products on this list, most often for methanol and propanol contamination. In 2021, our continued vigilance and monitoring also identified hand sanitizer products contaminated with high

levels of bacteria that can cause serious infections as well as products contaminated with benzene.

In January 2021, FDA issued [guidance](#) outlining policies for drug manufacturers and compounders to test alcohol or isopropyl alcohol for methanol contamination prior to using the alcohol to produce drugs, including hand sanitizer products.

On March 25, 2021, FDA warned consumers and health care professionals not to use Durisan Antimicrobial Solutions Hand Sanitizer, due to microbial contamination with *Burkholderia cepacia* complex and *Ralstonia pickettii*. These bacteria can cause serious infections if they enter the bloodstream through a scrape or wound, especially in people with compromised immune systems. Durisan voluntarily [recalled](#) its hand sanitizer product on March 24, 2021, and [expanded the recall](#) on April 10, 2021.

Our Office of Unapproved Drugs and Labeling Compliance issued three warning letters in May to firms marketing and selling hand sanitizers or topical antiseptics with COVID prevention claims. Warning letters were issued on May 6 to [Covalon Technologies Ltd.](#) and [Disinfect & Shield](#) for hand sanitizer products with COVID prevention and extended efficacy claims. On May 19, we issued a warning letter to [BGP LLC](#) for its Biocence WS multi-use antibacterial/antiviral product, which made COVID prevention and other false claims.

We continued our efforts to protect people from accidental consumption of hand sanitizer from a container resembling a water bottle or other beverage container. We successfully secured a voluntary [recall](#) on June 21 of Prairie Wolf Spirits hand sanitizers in 16-ounce and 20-ounce containers resembling water bottles. Additionally, on July 1, we persuaded Ardil Comercial to [recall](#) its hand sanitizers in 4-ounce containers resembling water bottles.

In September, we added Bathletix Hand Sanitizers to [FDA's Hand Sanitizer Do-Not-Use list](#) for being packaged in containers that resemble water bottles. These products displayed the trademarked logos of Major League Baseball and National Basketball Association teams and were available for purchase at a Kohl's in Maryland. They were manufactured by Genesis Partnership Company SA, a firm in Guatemala.

Throughout the pandemic, we alerted consumers to newly discovered contaminants in hand sanitizers. In 2021, we discovered benzene in hand sanitizer products as well as certain sunscreen and anti-fungal products. In October, we warned consumers not to use any hand sanitizer products from artnaturals of Gardena, CA. FDA tested certain artnaturals scent-free hand sanitizer and found unacceptable levels of benzene, acetaldehyde, and acetal contaminants. The firm voluntarily [recalled](#) limited batches of 8-oz. bottles of Scent Free Hand Sanitizer.

Also in October, FDA announced that at the end of 2021 it would [withdraw](#) the March 2020 guidance outlining temporary policies for manufacturers, such as distilleries who were not traditional drug manufacturers, to produce certain alcohol-based hand sanitizer and alcohol for use in hand sanitizers during the COVID-19 public health emergency.

## Increasing Access to Critically Needed Medications and Supporting Development of New COVID Therapeutics

Another key aspect of our COVID-19 response activities relates to our response to COVID-related disruptions and shortages, a proactive effort we started in the early days of the pandemic. We knew that drug shortages would negatively affect not only care for COVID patients but also care for people with other serious conditions, cardiac problems and accidental injuries.

As we did during the first year of the pandemic, we continued to take action to increase patient access to critically needed medications in shortage for treating COVID-19.

- We issued 15 enforcement discretion decisions to increase supplies of albuterol, oxygen, propofol and many other critically needed medications. One urgent request covering the distribution of industrial grade oxygen for medical use due to significant shortages in Texas and increased demand due to COVID-19, was considered and approved in less than eight hours on the condition that oxygen distributors met several key quality and safety conditions, including testing for impurities prior to distribution and immediately reporting any serious adverse events.
- With the Office of Pharmaceutical Quality, we developed a framework for expediting assessment of manufacturing site quality and compliance for Emergency Use Authorizations (EUA) supporting new COVID-19 therapeutics. Along with OPQ, we conducted the manufacturing quality review for seven COVID-19 related EUAs, including for monoclonal antibodies. We ensured important conditions to protect patient health, including mandatory recall authority, were included in each EUA.
- During 2021, our Office of Drug Security, Integrity and Response (ODSIR) continued to diligently ensure the availability of lifesaving drugs. ODSIR collaborated across CDER, the Office of Regulatory Affairs, HHS and directly with industry to determine the appropriate import and export regulatory pathways for the development and availability of critical treatments for COVID-19.

## Protecting Consumers Against Unproven Drugs with Fraudulent Claims to Prevent or Treat COVID-19

As often happens in a public health emergency, numerous new products were introduced to the market with false claims they could prevent, treat or cure COVID-19. Many sellers started promoting fraudulent COVID products in 2020 and continued to do so throughout 2021. Our efforts removed hundreds of [unproven products](#) from the U.S. market and protected consumers from products that were at best ineffective and at worst downright dangerous. Here are some examples.

- In January, we worked with the Department of Justice and the Office of Chief Counsel to obtain a consent decree for permanent injunction against [Fusion Health and Vitality](#). The firm sold unapproved vitamin D and hordenine HCL products, called “CORE” and “IMMUNE SHOT,” with fraudulent claims that they prevent, treat, mitigate or cure COVID-19.
- When we learned that thymosin alpha-1 made by compounding pharmacies was being offered to patients to treat or prevent COVID-19, we informed the National Association of Boards of Pharmacy (NABP) and the Federation of State Medical Boards (FSMB) that thymosin is not approved to treat or prevent COVID-19 or any other condition. We also indicated we would take appropriate action against compounders that produce thymosin. Similarly, we alerted NABP and FSMB when we learned that compounded ivermectin was being offered for sale with claims that such products treat or prevent COVID-19. Ivermectin is also not approved for that purpose and poses significant risk to patients when taken inappropriately. Throughout the year, we updated the [FDA Compounding Activities | COVID-19 web page](#) with important COVID information for hospitals and compounding pharmacies.
- Experts in our Office of Unapproved Drugs and Labeling Compliance testified in the retrial of Richard Marschall in late October. Following the trial, he was found [guilty](#) of promoting and distributing Dynamic Duo for the prevention and treatment of COVID-19. The product, made from garlic and larch tree bark extracts, was also promoted to treat and prevent bacterial, viral, parasitic and fungal infections.
- In addition, we diligently pursued companies attempting to promote fraudulent products for COVID-19 by issuing 28 warning letters in 2021. Our consumer safety officers and regulatory counsels reviewed numerous websites and social media posts to identify sellers making false claims concerning treatments for COVID. Products being peddled included topical antiseptics, salt scrubs, nasal antiseptics, herbal oil sprays, mouth rinses, industrial bleach and more. The Federal Trade Commission jointly issued a dozen of these warning letters along with CDER Compliance.

## Human Subject Protection During the Pandemic

Biomedical research depends on clinical trials to evaluate the safety and effectiveness of new medical treatments. The COVID-19 pandemic underscores this reality as vaccines, monoclonal antibodies and antiviral drugs tested in clinical trials are lessening morbidity and mortality. We have come a long way in protecting people who voluntarily participate in clinical trials. Decades ago, some researchers conducted trials on prisoners and racial minorities without their consent or knowledge. Our role in clinical trial oversight is among the federal reforms implemented to protect trial participants. Today, established institutional review boards and FDA review of trial protocols are intended to ensure safeguards before the start of many clinical trials. When these safeguards are not followed, we take regulatory action. We took several actions in 2021, including these for trials of COVID treatments.

- In March, our Office of Scientific Investigations (OSI) issued a [warning letter](#) to HealthQuilt and Kimberly Dunn, M.D., Ph.D., for not complying with federal laws to protect people participating in clinical trials. HealthQuilt and Dr. Dunn were conducting a clinical trial on an investigational drug to treat COVID-19. HealthQuilt had not submitted an investigational new drug application (IND) to the FDA, had not obtained informed consent from trial participants in accordance with federal regulations, and had not retained records as required.
- In August, OSI issued a [warning letter](#) to Kaleido Biosciences for failure to submit an IND prior to conducting two clinical investigations of a trial product to treat COVID-19. FDA conducted a for-cause inspection after the data from these two studies was submitted to FDA in support of a planned follow-on clinical study. The sponsor had claimed the studies to be “clinical food studies.” OSI worked with colleagues across FDA to confirm that these clinical investigations required on an IND.
- In October, OSI sent a [warning letter](#) to RAAS Nutritionals for failure to submit an IND prior to conducting three clinical trials in which the firm tested investigational products on people. RAAS enrolled 100 participants in a trial to study dietary supplements for preventing and treating COVID-19 as well as many other viruses and bacteria.

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Issued 28 warning letters to companies and individuals selling unproven products with fraudulent claims to prevent or treat COVID-19. More than 89 percent of the recipients took voluntary compliance action in response to these warning letters.

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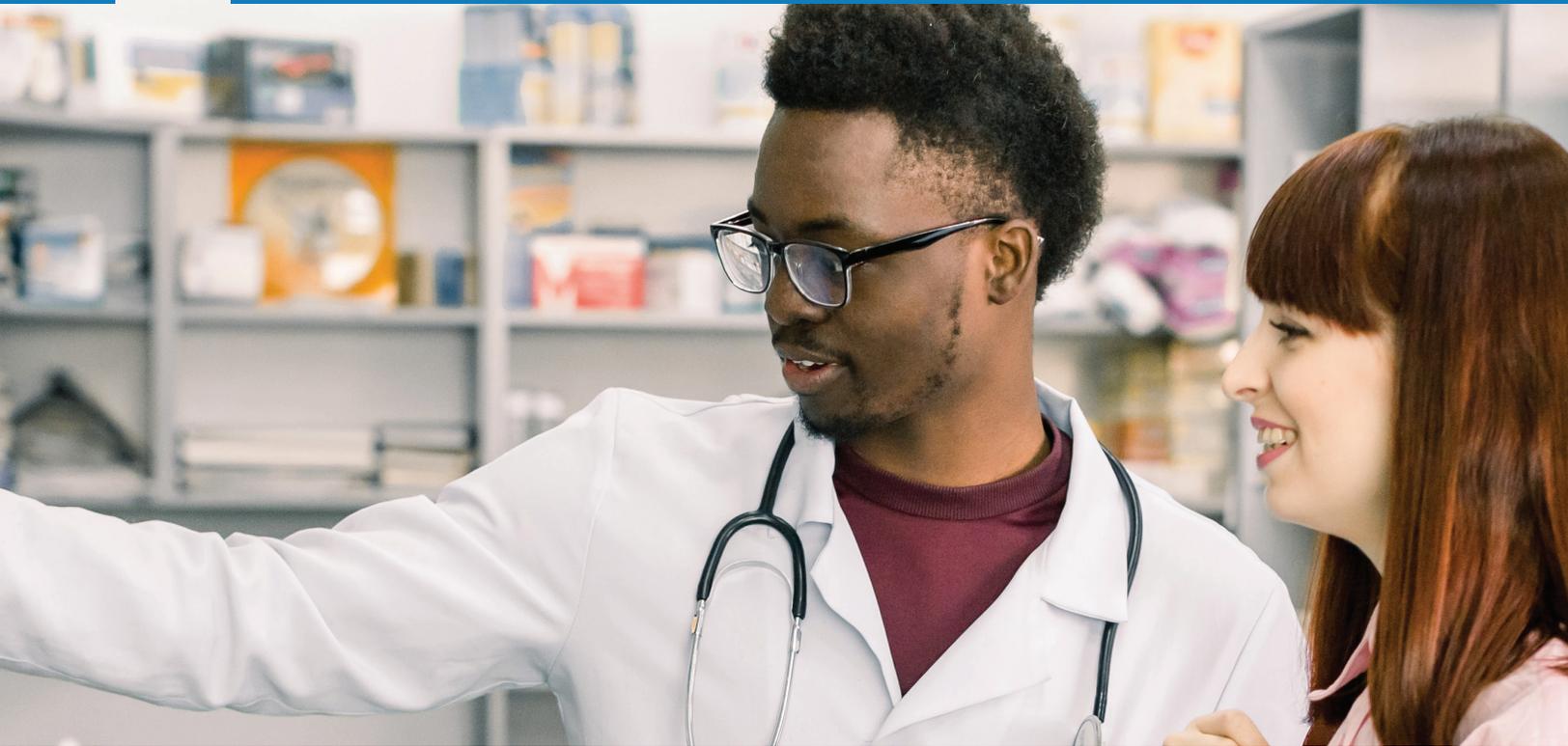
Issued six warning letters to internet pharmacies selling unapproved medications claiming to treat COVID-19.

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Worked with the Department of Justice and FDA Office of the Chief Counsel to obtain injunctive relief against Fusion Health and Vitality, a company that did not take appropriate action after receiving an FDA [warning letter](#).

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## Compounding

### Protecting Patients from Poor Quality Compounded Drugs

Compounded drugs can play an important role in patient care when a patient's medical needs cannot be met by an FDA-approved drug product, but they also bring risks because they are not subject to the same level of FDA oversight as FDA-approved drugs. Since Congress passed the Drug Quality and Security Act in 2013 following hundreds of cases of fungal meningitis associated with poorly compounded drugs, FDA has implemented statutory reforms and worked with industry to improve the quality and safety of compounded drugs.

Recognizing the increasing size and importance of the compounding program, we created our new [Office of Compounding Quality and Compliance](#) (OCQC) in January 2021 to lead our human drug compounding program. To accomplish this, we pulled all our compounding experts, including pharmacists, chemists and regulatory counsels, from throughout the Office of Compliance into a single entity under one leadership structure. This will allow us to better protect patients from the risks associated with compounded drugs and evidences our ongoing commitment to ensuring patient access to safe and quality compounded drugs.

One of the best ways to protect patients and minimize the risks presented by poor-quality compounded drugs is for the agency to work with compounders to foster higher quality products. Our Compounding Quality Center of Excellence was founded on this principle and celebrated its [second anniversary](#) in 2021.

One of the Center of Excellence's most important functions is providing training to compounding outsourcing facilities. To ensure that outsourcing facilities understand current good manufacturing practice requirements, our Center of Excellence offers training through virtual instructor-led courses and self-guided web-based training.

In 2021, the Center of Excellence delivered four instructor-led virtual training courses, three of which were offered more than once for a total of 10 training sessions on technical sterile drug compounding issues. The Center of Excellence also offers [nine self-guided web-based training sessions](#) on topics ranging from aseptic processing to insanitary conditions. Throughout 2021, more than 500 people took instructor-led training and self-guided web-based training courses. Nearly 80 percent of all outsourcing facilities have taken one or more of the Center of Excellence training courses.

The second [Compounding Quality Center of Excellence Conference](#), held virtually on Sept. 14–15, focused on the theme of “Culture of Quality” and drew more than 600 participants. Sessions this year were targeted towards outsourcing facilities with a focus on CGMP concepts and implementing quality practices. These included a keynote address on quality culture and sessions on quality management, systems, designing standard operating procedures, stability evaluation and analytical testing. Panel sessions with industry featured discussions on the relationship between outsourcing facilities and purchasers and the future of the outsourcing facility sector. This year, OCQC also offered a pre-conference session on Sept. 13, attended by 250 people, to provide background on compounding law and policy.

We also engaged with the compounding pharmacy regulators and the compounding industry through several listening sessions and our annual intergovernmental working meeting.

- OCQC hosted listening sessions with state government compounding pharmacy regulators on April 7, 8 and 9 to answer questions about the compounding [memorandum of understanding](#). From April 12 to 27, OCQC also held several small group listening sessions with outsourcing facilities. The outsourcing facilities have expressed that they highly value these opportunities to engage with FDA and were particularly complimentary about the courses offered by the [Compounding Quality Center of Excellence](#).

- OCQC held its annual listening sessions with representatives from outsourcing facilities on June 15, representatives from pharmacy, consumer and industry organizations on June 22, and medical and insurer organizations on June 23. The hospital and health system organizations session took place on July 8. OCQC received informative comments and feedback on several matters, including the standard compounding memorandum of understanding, adverse event reporting, the Compounding Quality Center of Excellence and oversight during the COVID-19 pandemic.
- On Oct. 26–27, OCQC convened its annual intergovernmental working meeting of state government officials on compounding. Attendees included officials from state boards of pharmacy and state health departments as well as representatives from the National Association of Boards of Pharmacy. The purpose was to discuss oversight of compounding, including implementation of the Compounding Quality Act (Title I of the Drug Quality and Security Act), and to identify opportunities to better protect the public health by strengthening oversight of compounders through improved federal-state collaboration. Sessions covered adverse event reporting, information sharing, oversight during the pandemic and policy updates. This year OCQC also held a pre-conference session on investigations and root cause analysis.

In response to comments from hospital and health system stakeholders, we issued revisions to our draft [Hospital and Health System Compounding Guidance to Help Preserve Patient Access to Compounded Drugs](#) on Oct. 6. To help preserve access to compounded drugs, we removed a geographic limitation known as the one-mile radius provision. While the revised draft guidance provides additional flexibility, we encourage hospitals and health systems to have procedures for obtaining non-patient-specific compounded drugs from outsourcing facilities and to consider registering their pharmacies as outsourcing facilities if they wish to distribute such products themselves.

## Partnering with State Regulators on Compounded Drug Oversight

In [October 2020](#), FDA made a [standard memorandum of understanding](#) (MOU) available for signature by states. The standard MOU is an agreement intended to address interstate distribution of inordinate amounts of compounded drugs and complaint investigation by a state regulator relating to compounded drugs distributed outside the state. Soon after issuing the standard MOU, FDA was sued by several compounding pharmacies in the U.S. District Court for the District of Columbia. In September 2021, the court remanded the standard MOU to FDA to engage in additional economic analysis.

FDA intends to undertake notice-and-comment rulemaking to address statutory provisions regarding certain distributions of compounded human drug products and to provide for a standard MOU between FDA and states. Before the court's decision, FDA had already [extended](#) the period before FDA intends to begin enforcing the statutory five percent limit on distribution of compounded human drug products out of the state in which they are compounded in states that do not sign the final standard MOU to Oct. 27, 2022. During the rulemaking process, FDA does not intend to enforce the statutory five percent limit.

FDA considers the standard MOU published in October 2020 to be suspended and not available for signature. FDA also considers the signed standard MOUs to be suspended and not operational. The standard MOU will be updated based on the content of a final rule and FDA intends to announce a new opportunity for all states to consider and sign.

FDA continues to encourage state regulators, pharmacies and consumers to voluntarily submit information on serious adverse events and serious product quality issues related to compounded drug products.

## Adverse Events Linked to Compounded Drugs

Our Compounding Incidents Program continued our work reviewing adverse events associated with compounded drugs. This team is dedicated to the surveillance, analysis and review of adverse events and complaints and follow-up actions related to safety risks associated with compounded drugs. To raise awareness of its work, the team published a paper in April 2021 in the *American Journal of Health-System Pharmacy*. The paper, *A pharmacist-driven Food and Drug Administration incident surveillance and response program for compounded drugs*, is available on the [journal website](#).

An example of the important work of the program is the [Compounding Risk Alert](#) we issued on Oct. 25 to ensure that medical offices and clinics were aware of the serious risks of compounded drug products, including intravenous (IV) infusion treatments, prepared under insanitary conditions, as well as their obligation to comply with federal and state regulations. Surveillance by the Compounding Incidents Program had identified several patients who experienced adverse events associated with compounded injectable drug products, including intravenous infusion treatments, prepared and/or stored under insanitary conditions. The program also became aware that sterile compounding activities, such as adding vitamins to IV infusion bags, were being performed by business entities such as IV hydration clinics, medical spas and mobile IV infusion companies.

We also issued a [Compounding Risk Alert](#) on Feb. 4 to alert health care professionals and compounders of the risks associated with compounding remdesivir (trade name Veklury), an anti-viral drug indicated for treating patients hospitalized with COVID-19. For a variety of reasons, remdesivir is particularly challenging to compound. We informed health care professionals and compounders in February that FDA cautions against compounding remdesivir and recommends using the FDA-approved drug for patients prescribed remdesivir.

## Opioid OVERDOSE KIT

### NASAL SPRAY



### INJECTION



### RESCUE BREATHING

1. Tilt the person's head back
2. Pinch nose



## Reducing the Impact of the Opioid Crisis

We continue to fight the opioid epidemic with every available tool in order to protect consumers from unapproved and misbranded drugs sold on internet pharmacies and other online platforms. In 2021, we expanded our focus to include other dangerous controlled substances sold illegally online on the same sites selling opioids.

Specifically, we have observed sites offering benzodiazepines for sale along with opioids. These drugs are frequently misused and abused together, heightening the risk for serious consequences including profound sedation, respiratory depression, coma and death. To address this emerging public health concern, we issued three warning letters in 2021 to operators of nine websites selling unapproved and misbranded opioids and benzodiazepines together.

We also issued two warning letters in 2021 to companies selling fraudulent opioid addiction treatments — [Umbrella Labs](#) and [Cannafyl](#). Including our 2021 warning letters, FDA has issued more than 50 warning letters targeting more than 500 websites unlawfully selling opioids over the internet to U.S. consumers since 2017.

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Prior to the COVID-19 pandemic, the ongoing opioid crisis was a complex and daunting public health emergency. Tragically, it has worsened during the pandemic with [deaths topping 100,000 annually, according to the CDC](#).

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A key component of the FDA's multipronged response to the opioid epidemic is reducing the volume of opioids entering the country outside of the legitimate supply chain, including through illegal online sales. Given the complexity of this issue, it is imperative that we include stakeholders from a variety of sectors in the conversation. To this end, we virtually hosted the [third Online Opioid Summit](#) on Sept. 9 which included internet stakeholders, government entities, academia and other partners. Acting Commissioner Janet Woodcock delivered [opening remarks](#), and Compliance Director Donald Ashley delivered a presentation on successes and continuing challenges.

Our Online Opioid Summit provides stakeholders a unique opportunity to collaborate, leverage expertise and explore meaningful ways to help reduce the availability of opioids online. In this year's summit, we discussed the evolving landscape of online opioid purchasing with younger and more vulnerable populations being exposed to dangerous opioids through social media and other online platforms. We also discussed ways to enhance cross-industry and global collaboration, successes and novel solutions implemented since previous summits, and new ways to continue to prevent the illegal sale of opioids through internet platforms and services.

In addition, internet domain name registries are a critical part of the solution to the illegal sale of opioids online. In February 2021, FDA announced the completion of a successful 120-day pilot program launched in June 2020 with the National Telecommunications and Information Administration and domain name registries Verisign, Public Interest Registry, and Registry Services (formerly Neustar).

Under the pilot, the FDA notified the participating registries of website operators who did not respond adequately within the required timeframe to FDA warning letters. The registries reviewed the FDA's notifications and assessed whether to take further voluntary action, including possible domain name suspensions or blocks. As result of the pilot, nearly 30 websites illegally offering opioids for sale became inaccessible to the public.

This program has proven to be an effective tool in maximizing the impact of FDA's efforts to limit the illegal sale of unapproved opioids online, and FDA has continued this collaboration to help prevent illegal online opioid sales. In addition, FDA is working with registries to extend the process we are using for opioids to other controlled substances, including benzodiazepines.

In addition, we partner with FDA's criminal investigators and the Department of Justice to enforce criminal statutes and bring perpetrators to justice. In 2021, we helped FDA's Office of Criminal Investigations pursue criminal enforcement cases to address counterfeit opioids. In May, we helped support the criminal sentencing of a couple from Alabama convicted of making dangerous and counterfeit pills containing a high-dose of fentanyl and a low-dose of heroin. The counterfeit pills were made to look like legitimate pharmaceutical products with markings such as "Lortab," "Adderall," "Soma," "Xanax," "Ecstasy," "Oxycodone" and "OxyContin." The intent was to fool buyers into thinking the products were safe FDA-approved drugs. In fact, they contained dangerous ingredients that are driving the upward trend in overdose deaths. A letter from our senior medical advisor to the District Court judge described the increased risk of the products. The judge noted that the letter was influential in the [sentence](#) of six and a half years' imprisonment.



## Clinical Trial Oversight

### Enhancing Our Clinical Trial Oversight

Transparency about results of completed clinical trials enables important advances in the development of drugs and other medical products. Transparency also helps ensure a safe, effective and efficient clinical research enterprise. Our Office of Scientific Investigations works with clinical trial responsible parties to encourage compliance with federal requirements to submit registration and summary results information to the [ClinicalTrials.gov](https://www.clinicaltrials.gov) data bank run by the National Institutes of Health.

While most responsible parties comply with these regulations, OSI takes regulatory action when they do not. In 2021, we achieved a significant milestone in issuing our first [notices of noncompliance](#) for failure to submit required results information to ClinicalTrials.gov. Our notice of noncompliance to Acceleron Pharma on April 27 marked a first for the FDA. The [notice](#) and a [statement](#) by acting FDA Commissioner Janet Woodcock were posted on [FDA.gov](https://www.fda.gov) on April 28. Subsequently, we issued notices of noncompliance to [Accuitis, Inc.](#) on July 26 and to [Dr. Andrey Petrikovets](#) on Aug. 31 for noncompliance with the [ClinicalTrials.gov](#) results information submission requirements. Dr. Petrikovets and Acceleron Pharma have since come into compliance.

Since 2017, OSI has worked with several other CDER offices on draft guidance to help clinical trial sponsors understand their responsibilities. FDA published the draft guidance, [Sponsor Responsibilities—Safety Reporting Requirements and Safety Assessment for IND and Bioavailability/Bioequivalence Studies](#), on June 25. It provides recommendations for sponsors and sponsor-investigators to comply with the safety reporting requirements for investigational new drug applications and for bioavailability and bioequivalence studies.

OSI collaborated with CDER's Office of Study Integrity and Surveillance (OSIS) to address significant instances of misconduct and violations of federal regulations by two India-based contract research organizations. On Sept. 15, OSI and OSIS jointly issued untitled letters to [Panexcell Clinical Lab Pvt. Ltd.](#) and [Synchron Research Services Pvt. Ltd.](#) for significant data integrity concerns for bioavailability and bioequivalence studies submitted in support of new and generic drug applications. Based on FDA inspections and subsequent data analysis, CDER determined that data from these two contract research organizations could not be considered in support of over 100 new and generic drug applications. These were among our most significant and impactful compliance actions of 2021. As a result, CDER posted information on [FDA.gov](#) for applicants, physicians and patients, and has engaged in discussions with all the applicants to require new bioavailability and bioequivalence studies.

## Protecting Patients in Clinical Trials

A key part of OSI's mission is to ensure that the rights, safety and welfare of individuals participating in clinical trials are protected. Throughout the year, OSI worked to protect patients in clinical trials through a number of actions. As discussed in the COVID-19 RESPONSE section of this report (see page 8), we also took action to protect people participating in clinical trials for COVID treatments.

For example, in May, we issued warning letters to two clinical investigators [Jon Cole, M.D.](#), and [Lauren Klein, M.D., M.S.](#), in a highly publicized case involving research at the Hennepin County Medical Center in Minnesota. The researchers failed to submit IND applications to FDA before testing investigational products on people.

OSI's action has proven to be influential in improving the conduct of clinical trials over times. An OSI study showed that 70 percent of investigators who received an FDA Official Action Indicated letter following an inspection between Oct. 1, 2010, and Sept. 30, 2015, were no longer conducting trials. The study was [published](#) on June 9 in the journal *Therapeutic Innovation & Regulatory Science*. This cross-sectional study analyzed inspectional data from CDER's good clinical practice inspections of clinical investigators, sponsors, contract research organizations and sponsor-investigators who received Official Action Indicated letters for good clinical practice violations during the conduct of CDER-regulated clinical trials.

As a part of FDA's efforts to be responsive to a rapidly evolving technological ecosystem, the agency in December issued new draft guidance, [Digital Health Technologies for Remote Data Acquisition in Clinical Investigations](#). This draft guidance provides recommendations to sponsors, investigators and other stakeholders on the use of digital health technologies to acquire data remotely from participants in clinical investigations evaluating medical products. OSI contributed to this effort.



## Implementing the Drug Supply Chain Security Act

In 2021, we reached several significant milestones in implementing the [Drug Supply Chain Security Act](#) (DSCSA), which significantly strengthens FDA's ability to protect consumers from exposure to counterfeit, stolen, intentionally adulterated or otherwise harmful drugs. As we approach the 2023 deadline for implementing this law, we are improving detection and removal of such drugs from the supply chain.

In June, FDA issued four guidance documents to assist trading partners in complying with the DSCSA to achieve a safer, more secure and more trusted drug supply chain. FDA highlighted this accomplishment with an [FDA in Brief](#) statement by Donald Ashley.

- Revised final guidance [Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification](#)
- Revised draft guidance [Definitions of Suspect Product and Illegitimate Product for Verification Obligations Under the Drug Supply Chain Security Act](#)

- Final guidance [\*Product Identifiers Under the Drug Supply Chain Security Act Questions and Answers\*](#)
- Draft guidance [\*Enhanced Drug Distribution Security at the Package Level Under the Drug Supply Chain Security Act\*](#)

To help industry understand their DSCSA requirements, we hosted two educational webinars. We presented an [FDA Drug Topics Webinar on Enhanced Drug Distribution Security: 2023 and Beyond](#) in June. This webinar provided updates on implementation of supply chain security requirements under DSCSA and described requirements that go into effect in 2023 for enhanced drug distribution security. Also in October, our DSCSA team provided a CDER Small Business and Industry Assistance webinar on [enhanced drug distribution security in 2023 under the DSCSA](#) to more than 1,000 attendees.

In November, we hosted a virtual public meeting to hear input from members of the pharmaceutical distribution supply chain and other interested stakeholders on FDA's implementation of the enhanced drug distribution security provisions of the DSCSA. We have posted the meeting materials and recording of the [public meeting](#).



## Shielding Patients and Consumers from Unsafe Drug Products

### Products with Hidden Drug Ingredients

We [alerted](#) consumers of 31 tainted [weight loss](#) and [sexual enhancement](#) products purchased through Amazon, Walmart.com and other sites after FDA laboratory testing identified hidden drug ingredients. These hidden ingredients may interact with other drugs consumers are taking, or they may be associated with serious side effects. For example, sexual enhancement drugs can lead to dangerously low blood pressure in patients taking nitrates for heart conditions. Also, when taken together, Prozac and sibutramine, a drug found in weight loss supplements, can result in changes in blood pressure, hallucinations, seizures and even coma. FDA removed sibutramine from the U.S. market due to its serious cardiovascular risks. We urged consumers to avoid these products and worked with online marketplaces and other retailers to ensure these products were removed from the market.

Among our 2021 [notifications](#) were nine posted in December on potentially dangerous sexual enhancement products sold on Walmart.com. FDA laboratory analysis found that these products contained sildenafil or tadalafil, the active ingredients in FDA-approved prescription drugs used to treat erectile dysfunction.

In addition to these alerts, we issued an updated [FDA press release](#) and a revised [FDA Consumer Update](#) on these products to ensure consumer awareness about the dangers of these products marketed as dietary supplements or conventional foods with hidden drug ingredients.

In 2020, the FDA purchased and tested 26 male enhancement and weight loss products directly fulfilled by Amazon. Our testing revealed that they all contained hidden drug products. We alerted consumers of the risks of these products and urged Amazon to remove them from its marketplace. On July 26, we issued an [untitled letter](#) to Amazon, notifying the online retailer about its distribution of sexual enhancement and weight loss products in violation of the Food, Drug, and Cosmetic Act.

## Alerting Companies and Consumers About CBD Health Fraud

The prevalence of CBD products has risen rapidly in recent years with the legalization of hemp production in the United States. While there is significant interest in potential health benefits of CBD, FDA has [approved](#) it only for treating a rare and severe form of epilepsy. Many companies have begun marketing CBD-containing products with unproven claims that it treats a variety of conditions from pain to cancer.

In 2021, we continued to send warning letters to firms illegally selling CBD products with unsubstantiated claims to treat serious diseases, such as cardiovascular disease, cancer, multiple sclerosis, rheumatoid arthritis and autism.

Our February 2021 warning letter to [BioCBDPlus](#) cited the firm for selling CBD vaping products with claims for lowering cholesterol and cardiovascular disease risk. The firm also promoted other CBD products to treat autism in children and PTSD in adults. It further said that these products can protect against Alzheimer's, Parkinson's, epilepsy and rheumatoid arthritis. In March, we issued a warning letter to [Cannafyl](#) for selling CBD products with claims that they can help treat epilepsy, ALS, multiple sclerosis, dementia and schizophrenia. The firm also claimed that CBD can inhibit cancer growth. In July we joined with the Center for Food Safety and Applied Nutrition and the Center for Veterinary Medicine to issue a warning letter to [BioSpectrum CBD](#) for selling topical and nasal spray CBD products for pain relief and anxiety as well as gummy worms and dog treats containing CBD.

In addition, we sent warning letters to [Honest Globe Inc.](#) and [Biolyte Laboratories](#) for selling various over-the-counter drugs labeled as containing CBD. The FDA has not approved any OTC drugs containing CBD, and none of these products meet the requirements to be legally marketed without an approved new drug application. Honest Globe did not manufacture its products in compliance with current good manufacturing practice and made unsubstantiated claims that the products could treat pain, inflammation, neuropathy, and anxiety, depression and high blood pressure. Biolyte also violated current good manufacturing regulations and sold CBD cream for treatment of muscle and joint pain. In March, FDA issued a [press release](#) on these warning letters to alert consumers about the risks of using these products.

## Alerting Patients and Health Care Professionals to Benzene and Nitrosamine-Related Recalls

In December, due to concern about benzene in hand sanitizer, as well as in sunscreens, over-the-counter antifungal treatments and deodorants, the FDA [alerted drug manufacturers](#) about the risk of benzene contamination from drug components and other potential risk factors. Benzene is a known human carcinogen that causes leukemia and other blood disorders. We asked manufacturers to assess the risk of benzene contamination in certain products, such as those manufactured with hydrocarbons. We also recommended testing products with an identified risk for benzene and taking appropriate action as needed.

Benzene contamination may be related to inactive ingredients such as carbomers (thickening agents), isobutane (a spray propellant), or other drug components made from hydrocarbons. We will continue to work with industry to prevent drugs with benzene contamination from reaching consumers, coordinating recalls of contaminated products and alerting consumers of products they should not use.

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### Coordinated nine benzene-related drug recall events

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### Coordinated seven nitrosamine-related drug recall events

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### 2021 benzene-associated recalls

- hand sanitizers – April 28, May 10, Oct. 4 and Oct. 26
  - sunscreens – July 14 and Sept. 30
  - antifungal foot sprays – Oct. 1 and Nov. 17
  - aerosol deodorant and hygiene products – Nov. 23
- 

In 2021, we also continued to coordinate recalls of drugs containing potentially cancer-causing substances called nitrosamines. We have been working to protect consumers from exposure to nitrosamine impurities since mid-2018 when FDA became aware of their presence in the antacid ranitidine (Zantac). Since then, nitrosamines have been found in blood pressure medications (valsartan, losartan and irbesartan), the diabetes drug metformin, and the tuberculosis drugs rifampin and rifapentine. In addition, in 2021, we [alerted](#) the public of Pfizer's voluntary recall of the smoking cessation drug varenicline (Chantix) due to the presence of unacceptable nitrosamine levels.

### Shielding Patients from Potentially Unsafe Homeopathic Medicines

Parents seeking an over-the-counter treatment for a young child's cough or cold face a dizzying array of treatment options on drug store shelves, including homeopathic medicines. While the symptoms worry parents and caregivers, they usually do not cause serious complications. To provide parents and caregivers with factual information to guide treatment choices, we worked with the FDA Office of External Affairs and the CDER Communications Office to develop a consumer-friendly article reflecting the latest scientific and pharmaceutical knowledge. On Oct. 28, FDA published the consumer update article, [Should You Give Kids Medicine for Coughs and Colds?](#), along with a new [video in English](#) and [Spanish](#) which gives advice to parents on the risks of homeopathic remedies for young children.

### Shielding Patients from Poor Quality Unapproved Porcine Thyroid Drug Products

Hundreds of consumer inquiries led us to develop with the CDER Communications Office and FDA Office of External Affairs a consumer update article, [Older Therapies Aren't Necessarily Better for Thyroid Hormone Replacement](#), about why a drug to treat hypothyroidism, porcine thyroid, is frequently recalled and has a risk of making patients sick. Manufacturing porcine thyroid from pig glands tends to be a complex process and may result in safety, effectiveness and quality issues due to inconsistencies in the amount of the active ingredient per tablet. This inconsistent dosage can lead to hypo- or hyperthyroidism and has resulted in drug recalls.



## Proactively Promoting Compliance

FDA's ability to fulfill its mission depends very much on keeping industry and our regulatory partners informed and updated about emerging issues as well as new policy, guidance and regulations. In fact, a key goal in our strategic plan is to proactively promote compliance through clear communication and collaboration with all stakeholders. To accomplish this, we sponsor and participate in numerous outreach activities and educational opportunities every year to proactively promote compliance. Although the COVID-19 pandemic has reduced in person interaction, we are using online collaboration tools for successful virtual outreach. We highlight several events below, but this is by no means an exhaustive list.

While the pandemic kept us busy in 2021, we also conducted numerous industry and stakeholder outreach efforts not directly related to COVID-19. To do so, we took advantage of online platforms to allow tens of thousands of stakeholders to access our information in real-time and after the fact without risking coronavirus exposure. Here are a few examples:

- [CDER Compliance Conference](#) hosted by CDER SBIA — Jan. 14
- Pharmacy Compounding Advisory Committee Meeting — June 9
- Third Annual Online Opioid Summit — Sept. 9
- Compounding Quality Center of Excellence conference on Sept. 14–15
- CDER SBIA webinar on [enhanced drug distribution security in 2023 under the DSCSA](#) — Oct. 5

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### Stakeholder engagement and outreach:

- Held more than 102 meetings with stakeholders, including regulatory meetings with industry, listening sessions with various stakeholder associations and trainings
  - Presented at more than 75 conferences, including three international conferences
  - Held three public meetings
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Issued 11 draft and final guidance documents and *Federal Register* notices across compliance programs

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Issued 31 [immediate public notifications](#) regarding fraudulent health products

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- Annual public workshop on [Electronic Drug Registration and Listing Using CDER Direct](#) — Oct. 13
- Intergovernmental Working Meeting on Drug Compounding — Oct. 26–27
- Public meeting on Enhanced Drug Distribution Security at the Package Level Under the Drug Supply Chain Security Act — Nov. 16

## Cosponsoring the Annual Parenteral Drug Association (PDA)/FDA Joint Regulatory Conference

We co-sponsored the [30th annual FDA/PDA conference](#) from Sept. 27–29, providing a forum for discussing the latest challenges and opportunities in drug manufacturing and quality. Major topics this year included aging facilities, supply chain reliability, process validation lifecycle, raw material quality, supplier relationships, overcoming pandemic challenges and quality risk management.

We presented case studies to promote approaches that support sustainable CGMP compliance as the foundation for consistent quality and supply. We also discussed our ongoing international collaboration efforts that improve quality and benefit patients.

## Hosting a Registration and Listing Workshop for Industry Stakeholders

On Oct. 13, our Drug Registration and Listing Branch, in collaboration with CDER's Small Business and Industry Assistance office, held its annual public workshop on [Electronic Drug Registration and Listing Using CDER Direct](#). This annual workshop features basic instruction on the submission process and error prevention, raises awareness of emerging compliance issues, and emphasizes the importance and necessity of providing complete and accurate registration and listing data. The event drew 3,567 viewers (1,609 online and 1,958 YouTube real-time playbacks). Registrants represented 91 countries, the top five being India, Canada, China, Egypt and Mexico.



## Supporting Global Collaborations to Enhance Compliance

Our Office of Scientific Investigations (OSI) shared 54 bioresearch inspection reports and participated in five remote bioresearch inspections with our global partners in 2021. These collaborative programs served as valuable alternatives to onsite inspections due to COVID travel restrictions. For the first time ever, we also exclusively used European Medicines Agency inspection information to support the assessment of clinical trial conduct and data reliability for a new drug application.

To support our global collaborations, OSI also published an [article](#) in *Clinical Pharmacology and Therapeutics* in collaboration with the UK Medicines and Healthcare Products Regulatory Agency (MHRA) in August 2021. It focuses on tackling challenging data integrity topics in response to the 2020 joint Good Clinical Practice symposium that OSI co-hosted with MHRA.

In international capacity building, four OSI staff members helped train assessors of clinical trial applications in Uganda in a virtual training course from April 19–20. The course, Assessment of Clinical Trial Applications, was held by the Uganda National Drug Authority.

Our Office of Drug Security, Integrity and Response implemented an important process improvement that enhances global compliance and saves significant time and expense associated with printing and mailing drug export certificates. We transitioned to issuing electronic certificates for pharmaceutical products (eCPPs) as downloadable PDFs through the CDER Export Certification Application and Tracking System (eCATS). This saves FDA from printing and mailing approximately 20,000 export certificates per year. For more information, see [Modernization of the FDA CDER Export Certification Program](#) on our Human Drug Exports website.



## Risk-Based Regulatory and Compliance Actions

Most pharmaceutical firms work hard to achieve compliance with FDA rules and regulations. When they do not, we use a risk-based regulatory approach to take action and protect patients and consumers. In 2021, we completed numerous actions across our compliance programs.

### Compliance by the Numbers

- Issued 149 warning letters across compliance programs
- Issued 101 facility [inspection classification letters](#)
- Obtained injunctions against [Premier Pharmacy Labs](#) and [Fusion Health and Vitality](#) in collaboration with FDA's Office of Chief Counsel and the Department of Justice
- Good clinical practice: Oversaw inspections and issued clinical inspection summaries for more than 122 new drug applications and biologics license applications
- Issued 26 ClinicalTrials.gov pre-notice of noncompliance letters and three notices of noncompliance

- Issued 10 [online advisory letters](#) to companies distributing products with fraudulent serious disease claims
- Conducted 47 bioresearch monitoring [remote regulatory assessments](#)
- Assisted in the prevention and mitigation of drug shortages for 59 different medications
- Number of drug-related recalls we oversaw:
  - Class I: 57 events, totaling 138 drug products
  - Class II: 170 events, totaling 800 drug products
  - Class III: 63 events, totaling 100 drug products
- Issued 15 [Certificates of Confidentiality](#) to protect the privacy of human subject research participants

## Proactively Keeping Dangerous Medicines from Entering the U.S. Supply Chain

We collaborated with the FDA Office of Regulatory Affairs to issue [import alerts](#) to help prevent violative drugs from legally entering the U.S. Highlights of our work on import alerts in 2021 include:

- Added all facilities producing hand sanitizer in Mexico to [import alert 62-08](#) to prevent products that appear to be in violation from entering the U.S. until the agency is able to review the products' safety.
- Added 17 facilities to [import alert 66-40](#), which lists manufacturing facilities that, based on an FDA inspection, are not operating in conformity with CGMP requirements.
- Added or updated 57 companies to [import alert 66-41](#), which lists products for which we have sufficient evidence to demonstrate that a product appears to be an unapproved new drug.
- Added seven facilities to [import alert 66-79](#) which lists companies and their products that appear to be adulterated because the companies have refused to permit FDA to inspect the facility.
- Added 13 facilities to [import alert 66-78](#), which lists manufacturers of drugs at risk for adulteration based on FDA analytical sample results demonstrating violations of the Federal Food, Drug and Cosmetic Act.
- Added one product to [import alert 54-16](#) which lists products marketed as dietary supplements and promoted for sexual enhancement, weight loss and muscle building, and contain undeclared active pharmaceutical ingredients.



## Looking Ahead

In 2022, we will continue promoting voluntary compliance and taking risk-based compliance and enforcement actions to shield patients from unsafe and poor-quality medicine. We look forward to continuing work on our key priority initiatives to fulfill our mission as well as continuing our response to the COVID-19 pandemic.

We are fortunate to have a very committed and hard-working staff whose efforts have made incredible differences in public health through work directed by our priority initiatives. We will continue to make a difference for patients and consumers in 2022 as we focus on the following priorities:

- Supporting FDA's COVID-19 response, including by supporting development of new therapies, ensuring availability of critical medications, and protecting the public from potentially harmful products.
- Taking concrete steps to reduce the public health crisis posed by opioids and other dangerous controlled substances.
- Continuing to strengthen our compounding program and building the framework for FDA's oversight of compounded drugs.

- Fully implementing and operationalizing the Drug Supply Chain Security Act requirements for licensing wholesale drug distributors and third-party logistics providers and the enhanced drug security system by 2023.
- Conducting effective regulatory and enforcement actions targeting drugs with the greatest potential to cause harm, including emerging threats, health fraud and novel impurities.
- Conducting outreach and education focusing on Office of Compliance risk-based enforcement and compliance priorities both within FDA and with outside stakeholders.



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