

FDA Online Controlled Substances Summit

Opening Remarks by Robert M. Califf, M.D.

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Introduction

Good morning. I am pleased to welcome you to FDA's fourth online controlled substances summit. I want to thank the organizers for inviting me and all of you for joining this very important dialogue.

As substance use disorders and drug overdose deaths continue to ravage American families and communities, the FDA remains committed to working aggressively to respond to this ongoing public health crisis.

Addressing the illegal online availability of opioids and other controlled substances is an integral part of the FDA's overall efforts to protect the public -- including youth -- from harm associated with drugs that have abuse potential.

The proliferation of prescription drugs being sold illegally through unsafe websites and social media platforms presents unique challenges for regulators, law enforcement, policy makers, families, and others who are working to prevent these dangerous products from reaching and harming the American public.

There are significant risks associated with prescription drugs that are controlled substances, such as abuse, misuse, dependence, and serious or life-threatening adverse effects. The risks are further heightened when prescription drugs are purchased from unknown or unlicensed sources online because consumers have no assurance that the products they are buying are safe or effective. Instead, unbeknownst to the consumer, these products may be tainted with deadly fentanyl or other dangerous substances.

It is critical to have stakeholders from the public and private sector, including those from the Internet ecosystem, academia, regulatory, and other organizations, at the table to help navigate these challenges and develop strategic and effective solutions.

This summit provides a forum for stakeholders committed to preventing the sale of controlled substances through social media, unsafe websites, and other online channels to come together and discuss ways to further their individual and collective efforts to address this issue.

Controlled Substances Landscape

Curbing the drug overdose crisis remains a top priority for the FDA, and for me personally.

As you are aware, the overdose crisis is multifaceted and has evolved beyond prescription opioids. In recent years illicit opioids, largely driven by fentanyl and its analogues, have become key contributors to the overdose crisis.

Other controlled substances, including benzodiazepines and stimulants (specifically methamphetamine), are also being used simultaneously with opioids.

We are also seeing the overdose crisis exacerbated by other substances.

For example, we've seen an increasing number of overdoses connected to products containing xylazine. Xylazine is the active ingredient in veterinary medicine approved as a sedative and analgesic. While effective for animals, xylazine can cause serious and life-threatening toxicity in humans. And, distressingly, xylazine is being used in combination with opioids such as illicit fentanyl because it is reported to prolong and heighten the drug effect. In April, the White House Office of National Drug Control Policy designated fentanyl adulterated or associated with xylazine as an emerging threat to the United States.

We recently issued an alert to health care professionals warning of possible xylazine inclusion in fentanyl, heroin, and other illicit drug overdoses. Importantly, naloxone does not reverse the effects of xylazine. We've also issued an import alert to restrict the unlawful entry of xylazine drug products into the country. This action aims to prevent the drug from entering the U.S. market for illicit purposes, while maintaining availability for its legitimate uses in animals. .

FDA's previous strategies have largely focused on opioid use and overdoses. The evolving nature of the overdose crisis calls for an approach that is commensurate with new trends. For this reason, we are expanding the scope of this summit to include the illegal availability of other controlled substances online, in addition to opioids.

Overdose Prevention Strategy

In 2021, the U.S. Department of Health and Human Services announced an Overdose Prevention Strategy that supports the National Drug Control Strategy. In 2022, we announced FDA's Overdose Prevention Framework reflecting our vision to undertake impactful, creative actions to prevent drug overdoses and reduce deaths. This Framework consists of four overarching priorities that align with the Department's Strategy.

These priority areas are:

- supporting **primary prevention** by eliminating unnecessary initial exposure and inappropriate prolonged prescribing.
- encouraging **harm reduction** through innovation and education.
- advancing development of **evidence-based treatments for substance use disorders**; and
- **protecting the public from unapproved, diverted, or counterfeit drugs** presenting overdose risks.

I'd like to highlight some of the recent activities we've undertaken to advance these priorities.

Safety Labeling Changes

This spring, FDA announced new safety labeling changes for both opioid and stimulant medications.

The new safety labeling changes for opioid pain medicines include requiring several updates to the prescribing information for immediate-release and extended-release/long-acting opioid analgesics. These changes are intended to provide clarity on appropriate patient populations for opioid treatment, appropriate dosage and administration, and updated information on the risks associated with opioid use.

For stimulants, FDA is requiring sponsors of amphetamine and methylphenidate products to update and standardize prescribing information to clearly inform patients, caregivers, and health care professionals of risks associated with these medications. The updates will require consistent language addressing misuse and abuse, addiction, and overdose, as well as information about proper storage and disposal of unused medication.

As this group knows well, the prescribing environment has evolved over the past few years – including the increased use of telehealth – and so these safety labeling changes are even more important to ensure health care professionals and patients have the information they need to prescribe and use these medications appropriately.

Disposal Options

We have also made significant progress by expanding disposal options to reduce opportunities for nonmedical use, accidental exposure, and overdose.

We are requiring manufacturers of opioid analgesics dispensed in outpatient settings to make prepaid mail-back envelopes available to outpatient pharmacies and other dispensers.

In addition, FDA announced a public workshop on in-home disposal and issued a Federal Register notice requesting information and comments on this topic.

Overdose Reversal Agents

Another important part of our work in this area has been facilitating greater access to overdose reversal agents. These medications rapidly reverse the effects of opioid overdose and are a critical tool in addressing opioid overdoses.

Last September, we issued guidance intended to help address some of the obstacles in accessing naloxone that harm reduction programs identified during stakeholder engagements.

In March of this year, FDA approved the first non-prescription naloxone nasal spray. This action paves the way for this life-saving medication to be sold directly to consumers,

Furthermore, just last month, we expanded the availability of overdose reversal agents by approving nalmeferene nasal spray. This action provides another essential tool to combat the overdose crisis.

Compliance and Enforcement Efforts

Cracking down on the market for diverted prescription and illegal drugs and securing the supply chain for approved medications, including opioids and other controlled substances, remains a top priority for FDA under the fourth priority area of the Overdose Prevention Framework.

We are focused on preventing the growing problem of distribution of synthetic opioids that are entering the United States illegally.

We're continuing our surveillance, enforcement, and interdiction work, targeting illegal, unapproved, counterfeit, and potentially dangerous products. We are conducting this work at international mail facilities, express courier hubs, and ports of entry across the U.S. and have partnered with various other federal partners to extend our enforcements actions as far as possible.

For instance, FDA launched a National Operational Strategy targeting opioids and other unapproved drugs at multiple international mail facilities and several courier hubs from February through August 2022. **The operation successfully intercepted more than 390,000 tablets and capsules of unapproved drugs (including opioids) from entering U.S. commerce.** We expanded it further this year to include ports along the Mexican and Canadian borders.

FDA is also responding to the overdose crisis through efforts focused on preventing and reducing counterfeit and illegal online sales. One way we do this is by sending warning letters to online networks that operate websites marketing potentially dangerous, unapproved and misbranded controlled substances. In 2022, we issued five of these warning letters. Alarming, we frequently see websites selling unapproved and misbranded opioids with other controlled substances such as benzodiazepines, which further heightens the public health concern.

In addition, our Office of Criminal Investigations conducts criminal investigations of health care professionals tampering with opioids intended for patient use and preventing illegal online sales of opioids and counterfeit medicines on social media as well as the surface web and dark net.

We will continue to use the regulatory and enforcement tools under our authority to combat this illegal activity and protect the public from these dangerous products.

Conclusion

The FDA is committed to working with public and private organizations through high-impact partnerships to expand the scope of our efforts to reduce the availability of controlled

substances online. Strategically and effectively responding to the drug overdose crisis requires proactive engagement and coordination across diverse sectors.

This summit provides a unique opportunity for a broad range of stakeholders to collectively review the landscape and challenges associated with the availability of controlled substances online, share and build on successes, and identify what more can be done to prevent and reduce their illegal sale.

The tragic impact of the drug overdose crisis cannot be overstated. My hope is that by coming together and engaging in settings like today's summit, we can each harness our expertise, influence, and resources to come up with innovative solutions to tackle this issue head on and ultimately save lives.

Thank you.