



JOINT SAFETY STATEMENT OF THE INTERNATIONAL SOCIETY OF AESTHETIC PLASTIC SURGERY AND THE AESTHETIC SOCIETY



OFFICIAL BUSINESS

PATIENT SAFETY ADVISORY – FENTANYL COUNTERFEIT PRESCRIPTION MEDICATIONS THAT CONTAIN FENTANYL AND PATIENT SAFETY

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The purpose of this patient safety communication is to alert plastic surgeons, nurses, and patients about the risks of fentanyl-containing counterfeit prescription medications that patients can obtain outside of those prescribed by a physician, physician's assistant, or nurse practitioner and purchased at a licensed pharmacy. This becomes a patient safety issue where unintentional fentanyl overdose and death can occur. Patients are not well-educated about these risks and how to stay safe. Children and adolescents are also at risk. We believe that a conversation with patients will save lives and prevent tragedies.

This crisis has escalated to the extent that a patient safety advisory regarding the extreme danger of illicit fentanyl has been jointly developed by ISAPS and The Aesthetic Society. The purpose of this communication is to discuss this matter in the context of patient safety and how to take actionable steps to mitigate risk for patients. Additionally, we will review the pharmacology of powerful synthetic opioids, geopolitical issues, and naloxone used to treat opioid overdose.

Unlike legitimate medications that are manufactured with tight quality controls and good pharmaceutical manufacturing processes, there is no control over how much fentanyl is contained in counterfeit medications. Only two milligrams of fentanyl is considered a potential lethal dose; it's particularly dangerous for someone who does not have a tolerance to opioids.

Criminal drug networks mass-produce pills that contain fentanyl and falsely market them as legitimate prescription pills. Counterfeit pills are easily accessible and often sold on the street, social media, and e-commerce platforms, making them available to anyone with a smartphone, including minors. Many pills are physically indistinguishable by their appearance from prescription opioids such as oxycodone, hydrocodone, benzodiazepines like alprazolam, or stimulants like amphetamine and methylphenidate used for treating attention deficit disorders. They contain identical identification numbers and marks like a legitimate pill has stamped on its surface^{1,2}. Patients who seek medications in this fashion are exposed to the risk of fentanyl overdose and death.

TWO MILLIGRAMS OF PURE FENTANYL FITS ON THE POINT OF A PENCIL. IF INGESTED, THIS IS A LETHAL DOSE.

The United States Drug Enforcement Administration (US DEA) Laboratory has determined that, of the fentanyl-laced fake prescription pills analyzed in 2022, six out of ten now contain a potentially lethal dose of fentanyl. We would urge you to share a recent [US DEA press release](#) on this topic with your patients¹:

According to the United States Center for Disease Control (US CDC), 107,375 people in the United States died of drug overdoses and drug poisonings in the 12-month period ending in January 2022³. A staggering 67% of these deaths involved synthetic opioids like fentanyl. Some of these deaths were attributed to fentanyl mixed with other illicit drugs like cocaine, methamphetamine, and heroin, with many users unaware they were actually taking fentanyl. There is no data of how many of these deaths occurred after surgery from taking illicitly obtained pills containing fentanyl.



Photo Credit US DEA



Legitimate Oxycodone 30mg



Counterfeit Oxycodone 30mg

Photo Credit US DEA: <https://www.justice.gov/usao-id/pr/acting-us-attorney-warns-increasing-danger-counterfeit-prescription-opioids-containing>

Fentanyl overdoses are now the leading cause of death for individuals in the age range of 10 to 19 years in the United States. Earlier US CDC reports from 2019–2021 revealed approximately 90% of overdose deaths involved opioids, and 83.9% involved illicitly manufactured fentanyl⁴. Counterfeit pill evidence was present in 24.5% of overdose deaths. Last year there were 133 deaths of children younger than 3 who ingested fentanyl accidentally in the United States^{5,6}. Fentanyl patches have contributed to child overdoses in Australia⁷.

Educational initiatives for children, adolescents, and college students have tremendous value to help them understand the extreme risk of accidental fentanyl overdose and death⁸.

According to reports, the US DEA and the US Customs and Border Patrol (US CBP) have seized over 10,000 kg of fentanyl powder and 50.6 million tablets containing fentanyl in 2022. No statistics are available on the amount of fentanyl seized in other countries. The United States has the greatest amount of illicit fentanyl. This is reflected in the statistics cited in this advisory. This equates to approximately 379 million doses of fentanyl according to a press release by the US DEA⁹.

PHARMACOLOGY BACKGROUND OF FENTANYL

Fentanyl is a synthetic opioid first developed approximately 60 years ago. It is a relative of meperidine (phenylpiperidine series). There have been approximately 1,400 fentanyl analogs synthesized (fentalogs), some sold illicitly as designer drugs^{10,11}. Opioids like codeine, hydrocodone, oxycodone, and hydromorphone are synthesized by modifications of morphine. Heroin is diacetyl morphine sourced from opium.

Within the context of surgery, anesthesia, and acute pain management, fentanyl and two of its analogs (sufentanil and remifentanil) are used. Sufentanil is the most potent μ -receptor agonist available for clinical use. It is 5 to 10 times more potent than fentanyl and 1,000 times more potent than morphine. It has an affinity for opioid receptors 30 times greater than that of fentanyl¹².

Remifentanil is structurally unique because of its ester linkages¹³. This makes it susceptible to hydrolysis by blood esterase, resulting in rapid metabolism and rapid reduction of blood concentration during total intravenous anesthesia (TIVA). Fentanyl is additionally prescribed for malignant and non-malignant chronic pain. It is administered by injection, nasal spray, or skin patch, or absorbed through the cheek as a lozenge or tablet. Other routes of use are intrathecal and spinal anesthesia.

The onset of action of fentanyl is almost immediate when the drug is given intravenously; however, the maximal analgesic and respiratory depressant effect may not be noted for several minutes. Bioavailability depends on the route of administration. Fentanyl is capable of producing severe respiratory depression. It has also been reported to cause nausea, vomiting, dizziness, muscle rigidity, seizures, hypotension, coma, and death¹⁴.

NALOXONE

Naloxone is useful in treating both acute opioid overdose and respiratory or mental depression due to opioids. It is administered intravenously, intramuscularly, or via nasal spray. Depending on the venue, naloxone is available without a prescription as part of harm reduction initiatives in the United States and worldwide. Naloxone acts rapidly to reverse opioid overdose. Other adjunctive measures such as rescue breathing and cardiopulmonary resuscitation may be required. Prescribing naloxone should be accompanied by standard education for patients and caregivers that includes preventing, identifying, and responding to an overdose^{15,16}.

REGULATORY STATUS OF SYNTHETIC OPIOIDS

Fentanyl and fentalogs approved for clinical use like sufentanil and remifentanil are classified by virtually every drug regulatory agency worldwide as synthetic opioid narcotic drugs. The United States Food and Drug Administration (US FDA) classifies these as Class 2 Schedule drugs, those with known therapeutic effect, but with high potential for abuse. Fentalogs that are produced to evade regulatory scrutiny would be Class 1 Schedule drugs, without known medical use and high potential for abuse.

FENTANYL GEOPOLITICAL ISSUES

Mexican cartels source fentanyl precursors from Chinese suppliers which are finished in Mexico and smuggled to other countries worldwide. This is not exclusively a Chinese matter, as India has also emerged as a source of fentanyl and fentanyl precursors, where Mexican cartels have already developed networks for the distribution of synthetic opioid drugs. It is possible fentanyl and precursor production may disperse to other countries in Africa, Indonesia, Myanmar, and the European Union. Estonia has experienced a fentanyl crisis for many years. Fentanyl is frequently mixed with heroin, methamphetamine, or cocaine to increase potency^{17,18}.

Initiatives aimed at regulating the flow of fentanyl precursor chemicals and fentanyl from China has not been successful. China halted cooperation with the United States on combatting drug trafficking in 2022. Hopefully in the future the United States can delink counternarcotics policy through diplomatic channels with the Chinese government and its enforcement from the US-China global rivalry and overall state of mutual relations^{19,20}.

There is significant variation in the prevalence of illicitly manufactured opioids globally. Fentanyl is being used by individuals addicted to opioids worldwide. Heroin, methamphetamine, and cocaine often contain fentanyl, resulting in overdose and deaths. Some geographical areas tend to have less prevalence of counterfeit drugs that contain fentanyl or ways for individuals to acquire pain pills and mood-altering medications in the street or over

the internet. Other locations such as the United States has the greatest incidence of illicit fentanyl prevalence, including fake prescription pills.

According to a press release by the American Society of Anesthesiologists (October 2021), approximately 20% of patients who are opioid-naïve before surgery continue to use opioids three months after surgery. This includes all surgical specialties. For some patients, surgery, including plastic surgery, may create an unintended gateway to long-term opioid use. While the CDC notes synthetic opioids (primarily illicitly manufactured fentanyl) appear to be the main reason for the increase in mortality statistics in the United States, persistent opioid use after surgery can play a role in producing overdose and death²¹.

Surgeons should be alert to persistent opioid use and utilize alternative non-opioid pain management protocols. This strategy appears effective in helping patients recover from body contouring procedures (abdominoplasty) without reliance on opioids²².

The US DEA has a web page with a QR barcode in the [pdf document \(page 2\)](#) that patients can see actual examples of fake pills containing fentanyl along side of legitimate pills. Patients can access this useful information by scanning the barcode with their smartphone. The page with the QR barcode can be printed and placed in exam rooms and reception areas for patients to use²³.

This patient safety advisory was developed by:

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PHYSICIAN-NURSING-PATIENT EDUCATION RESOURCES

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2. <https://www.dea.gov/onepill>
3. <https://www.dea.gov/fentanylawareness>
4. Drug Overdose Deaths Among Persons Aged 10–19 Years – United States, July 2019–December 2021 | MMWR (cdc.gov)
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7. <https://www.nps.org.au/news/accidental-fentanyl-exposure-in-children-can-be-fatal>
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PATIENT SAFETY COMMUNICATIONS TO MITIGATE RISK OF FENTANYL OVERDOSE AND DEATH

- We believe that patient safety education concerning the fentanyl crisis is needed. One suggestion would consist of patient education material on your website and in pre-surgical materials regarding the risks from fake medications that contain fentanyl.
- Instruct patients to only take prescription medications that are prescribed by a physician, physician's assistant, or nurse practitioner. If prescription refills are needed, have this arranged ahead of time and never purchase them on the street, from another person, or over the internet without a prescription. This applies to all types of medications.
- Educate patients to keep all prescription medications in a safe place to prevent children from accidentally taking them or sharing with friends.
- Educate patients regarding how to take prescribed opioid pain medications for an acute event such as an injury or surgery. Patients are advised to destroy unused opioid pain pills when the need to manage pain can be accomplished with non-opioid medications such as ibuprofen or acetaminophen.
- Never trust your own eyes to determine if a pill is legitimate. The only safe medications are ones prescribed by a trusted medical professional and dispensed by a licensed pharmacist.
- Never ask for medication from another person. There is no way to verify if it is safe.
- During the COVID pandemic, many patients have developed mental health issues such as anxiety, sleep disorders, and depression. They are advised to seek medical care from their personal physician. Patients should never self-medicate with mood-altering drugs that are purchased online without a physician, physician's assistant, or nurse practitioner's prescription or obtained from another person.
- Plastic surgeons are not trained to treat mental health issues such as depression, anxiety, or sleep disorders. Be forthright with patients requesting prescriptions to treat mental health issues and refer them back to their personal physician for care.
- There are many treatment options for patients who are addicted to opioids including the drug suboxone and drug addiction rehabilitation programs.
- Fentanyl test strips have some benefits but may not be widely available²⁴.

