

# ORANGE COUNTY REGISTER

## Abuse-deterrent opioids cross an ethical line

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The Commissioner of the Food and Drug Administration, addressing agency staff in May 2017, called the problem of opioid abuse “unquestionably, our greatest immediate challenge.” At the time, the Centers for Disease Control and Prevention had reported 33,000 opioid overdose deaths in 2015, the majority from heroin and fentanyl. Sadly, next month the CDC is expected to report much worse mortality numbers for 2016.

Among the steps the FDA is taking to combat this trend is its policy of encouraging drug makers to develop abuse-deterrent formulations of prescription opioids. The idea is to make it more difficult for opioid abusers to engage in nonmedical use of prescription opioids. In September the FDA announced it will soon issue an updated guidance document to assist manufacturers in developing an expanded spectrum of ADFs including generic versions.

Yet evidence shows that ADFs inflict harm — unintentional and intentional — on nonmedical drug users. By promoting them, the government might be crossing an ethical line, and it wouldn't be the first time the government has done so when addressing substance use and abuse.

During alcohol prohibition, ethanol was still permitted for commercial use, to make fuel, dyes, paints and other products, as well as for scientific research. To prevent black market activity, the federal government promoted abuse-deterrent formulations of commercial ethanol. By 1926 the government ordered that ethanol be denatured to include methanol (wood alcohol), benzene, as well as other poisons which could not be distilled out by bootleggers — and which could be fatal if consumed. It is estimated the federal poisoning program took roughly 10,000 lives by the end of Prohibition.

In the 1980s, the Drug Enforcement Administration engaged in a program of spraying the herbicide paraquat to wipe out domestic marijuana cultivation and deter use. This herbicide can cause severe lung damage if inhaled, as was noted in a 1985 federal environmental impact study. Georgia Gov. Frank Harris said of the death risks of spraying in his state, “They're doing something illegal and ought to get the message that it could happen to them at any time.”

Drug policy is less overtly inhumane these days, but as Mark Twain said about history, it “may not repeat itself, but it rhymes.”

Since 2010 the FDA has approved numerous ADF variants of prescription opioids, including OxyContin, Hysingla ER, Ventrela ER and Zohydro ER. All of these drugs are designed using methods that prevent them from being crushed or injected — common methods of abuse.

But other ADFs deter in a different way. Suboxone, a drug used for Medication Assisted Treatment of addiction in ways similar to methadone, combines the opioid buprenorphine with

the opioid antagonist naloxone (used to reverse overdoses). Unlike buprenorphine, naloxone is not orally absorbed. However, should an abuser inject the Suboxone, the naloxone blocks the buprenorphine and can precipitate withdrawal. Targiniq ER works the same way, only it mixes hydrocodone with naloxone. Other ADFs combine long-acting morphine with the opioid antagonist naltrexone. Withdrawal is a serious condition that can sometimes be fatal.

Then there are ADFs that use “aversion technology.” For example, Oxaydo and RoxyBond contain oxycodone and an ingredient that causes severe nasal irritation followed by nasal discharge if snorted.

Any of these ADFs can still be abused nonmedically by swallowing the pills with a glass of water. However, several studies suggest that abuse-deterrents are not only ineffective, but may be driving nonmedical users to heroin and fentanyl, including a 2017 RAND study stating efforts to disrupt the supply of OxyContin for abuse “may have the unintended consequence of increasing the use of substitute drugs, including heroin.” Also, a June 2017 National Bureau of Economic Research working paper found “there appears to have been one-for-one substitution of heroin deaths for opioid deaths. Thus it appears that the intent behind the abuse-deterrent reformulation of OxyContin was completely undone by changes in consumer behavior.” According to the Centers for Disease Control and Prevention, the predominant causes of overdose death have been fentanyl and heroin since 2015.

Abuse-deterrent opioids are either driving nonmedical users to fentanyl and heroin, increasing their risk of overdose death, or — in the case of Suboxone, Targiniq ER or Oxaydo — inflicting harm intentionally.

We physicians take an oath to “first do no harm.” If we discover that a course of treatment unintentionally makes matters worse, it is ethically forgivable as long as we then cease that treatment. What is not forgivable is the intentional, punitive, infliction of harm. Ethics demands that the government stop promoting ADF opioids.

The “immediate challenge” is to reduce the number of overdose deaths — not the opioid supply. The government should make it easier for health care practitioners to prescribe methadone, Suboxone and other forms of Medication Assisted Treatment to addicts; it should promote safe syringe programs to stem the spread of disease; encourage “Good Samaritan” laws so that overdose witnesses won’t fear arrest if they call for help; and make the antidote naloxone more widely available — even over-the-counter. This approach called “harm reduction” is the ethical way to address the overdose crisis.

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