



The rapid rise of

prescription opioid abuse has spurred the FDA to call for the development of abuse-deterrent opioids.

Image Source: Flickr user Liz West

For years we have seen the headlines warning us of a rising tide in prescription opiate-related deaths, seemingly indiscriminately spilling across the country from coast to coast, infiltrating small towns and big cities alike. As prescriptions have exploded, a prolific black market emerged, and social stigma has dropped, these drugs have seen increased “environmental availability” for those seeking both legal and illegal avenues to drug procurement¹, leaving a trail of victims that include everyone from hardcore drug users to seniors who got addicted to oxycodone after surgery to college kids who buy a handful of \$25 pills of hydrocodone for Saturday night. In 2013 alone, 16,000 people died from prescription opioids, an increase of over 400% in 10 years.² That year, mounting concern regarding prescription opiate abuse spurred the FDA to call on pharmaceutical companies to create abuse-deterrent opioids, noting that the development of such drugs is “a public health priority,” as the number of overdoses and deaths continue to climb.³

By spring of 2015, the FDA released its finalized guidelines for development, evaluation, labeling, and approval of abuse deterrent drugs, promising to work with the pharmaceutical industry to bring products to market as quickly as possible to fill the need for therapeutic applications while minimizing risk of illicit use.⁴ “Development of abuse deterrent products is a priority for the FDA, and we hope this guidance will lead to more approved drugs with meaningful abuse-deterrent,” says Janet Woodcock, director of the FDA’s Center for Drug Evaluation and Research. “While abuse deterrent formulations do not make an opioid impossible to abuse and cannot wholly prevent overdose and death, they are an important part of the effort to reduce opioid misuse and abuse.” As research, development, and production of abuse-deterrent prescription opiates continue to mature and lead to advancements in pharmacological technologies, spectrophotometric color measurement can play an integral role in optimizing the success of these innovative products.

Abuse deterrent strategies that impair the crushing of opioids into fine, snortable, and soluble powder may inhibit the riskiest forms of recreational use.

Image Source: Pixabay user zephylwer0

Current Abuse Deterrent Strategies

Prescription opioids such as oxycodone, morphine, hydrocodone, and codeine can be extraordinarily effective for the treatment of pain when taken therapeutically under the guidance of a physician. In fact, they are often invaluable in allowing patients with acute, chronic, and end-of-life pain to cope with their suffering with dignity. However, the euphoric effects and addictive nature of opioids can cause many users to stray from the medical path and begin using either recreationally or to stave off unwanted side effects from withdrawal. In order to prevent abuse, addiction, and overdose, pharmaceutical companies currently focus on four abuse-deterrent strategies which may be used in concert to enhance efficacy:

Physical/Chemical Barriers

In order to intensify the drugs' effects, physically altering the state of the drug via crushing or dissolving allows users to administer the drugs by alternate means such as snorting or injecting. As such, many anti-deterrent strategies focus on disrupting the ability to manipulate the drug by physically or chemically altering the characteristics of the drug. Hysingla, a tablet form of hydrocodone, uses unique polymers that make the drug virtually impossible to crush or break while

attempts to dissolve the tablets leaves you with a gooey, sticky mess that is difficult to insert into a syringe.⁵

Extended Release (ER)

One of the earliest abuse-deterrent strategies already in use by many pharmaceutical companies is the introduction of extended-release formulations. The traditional thinking has been that addicts and recreational users will prefer the instant release (IR) of traditional prescription opioids and stay away from ER versions of the same drug. However, ER properties are typically only effective when a pill is intact; when it is crushed or dissolved, its active ingredients are available for immediate consumption, actually making them more attractive to some opiate users. Now, researchers are developing formulas that will keep the ER mechanisms intact despite physical or chemical manipulation of the drug.

Aversion Formulations

Aversion formulations are designed to deliberately induce unpleasant side effect if misused or taken in excess. Some abuse-deterrent drugs that integrate aversion characteristics will break into coarse chunks rather than a fine powder when crushed and create nasal irritation if snorted. Others produce chills, itching, or sweating when even a non-manipulated pill or capsule is taken in excess.

Opioid Antagonists

Abuse-deterrent formulations that integrate opioid antagonists are typically designed to keep the antagonist latent under normal circumstances. However, if the pill is crushed or ingested in a large dose, the antagonist is activated, blocking opioid receptors in the brain, and decreasing the efficacy of the drug.



The introduction

of dyes in certain prescription opioids may deter nasal and IV administration.

Image Source: Free Images user tijmen van dobbeburgh

Why Color Matters In Abuse-Deterrent Opioids

Initially, color may seem like a minor feature of abuse-deterrent opioids. However, as we have learned through countless color perception studies, [pharmaceutical color can have a significant impact on how users interact with medications](#) and greatly shape expectations as well as adherence. In the case of abuse deterrent drugs, the high stakes of selecting the right formulations demand the utmost attention to all aspects of the products, including aesthetic factors. Spectrophotometric color measurement may be used at various stages of the research, development, and manufacturing processes to optimize the ability to create truly effective, forward-thinking strategies for protecting the lives of individual users and public health as a whole.

Research & Development

Some researchers seek to develop visually identical abuse-deterrent versions of existing opioids to encourage patient adherence to safer medication protocols and to also potentially decrease the value of the drug on the black market; if buyers are not able to distinguish between abuse deterrent and normal versions, they cannot be sure that they're buying a usable/abusable product and may therefore be less likely to purchase the drug at all. Others believe that "a bright colorant tracer [can act] as a psychological deterrent to resist adulteration or identify abusers, such as indigo blue."⁶ In some applications, colored dyes would be formulated to dye the skin and nose should the drug be snorted. More recently, Pharmaceutical Manufacturing Research Services developed an "oral, immediate release, abuse deterrent [liquid filled capsule](#)" that incorporates hydrocodone or oxycodone along with dyes designed to deter abuse on the assumption that users will be put off by the unusual coloring.⁷ As "extraction of the dye along with the active ingredient would result in a color solution that would discourage the user from intravenous injection. Regardless of the way color is used within the abuse deterrent formulation, spectrophotometric evaluation of color ensures that you can obtain your desired results and tailor your product for a pleasing aesthetic appearance in the presence of sophisticated new chemical and physical processes.

Clinical Trials

The FDA guidelines on the evaluation abuse-deterrent opioids strongly recommend randomized, double-blind, placebo-controlled studies "generally conducted in a drug-experienced, recreational user population. The use of a pre-qualification phase to identify subjects who can reproducibly distinguish active drug from placebo is a common enrichment strategy to improve the power of the study to establish a difference between treatments."⁸ To ensure that these experienced users are not able to visually discriminate between an active pharmaceutical and a placebo, the drugs must be visually identical. Spectrophotometric color measurement allows for precise color matching and identification of even slight color variations which may be discernible to the highly trained eye of an experienced drug user, allowing for true blinding during trials.

Manufacturing

The true test of abuse-deterrent technologies is how everyday users will interact with them. In order to put all of your thoughtful design features into practice, the manufacturing process itself must consistently produce exactly the product you have envisioned, including the appropriate coloration. [Continuous monitoring of drug color throughout the manufacturing process](#) ensures that the drug stays within your chosen tolerance range, instantly alerting you to unwanted color variations that may signal process failure or, worse, compromise the abuse-deterrent qualities of the drug itself. Correct coloration is paramount to optimizing the efficacy of abuse-deterrent elements, whether the goal is to match a traditional version of the drug or to integrate new and novel dyes.

HunterLab has been a pioneer in the field of spectrophotometric color measurement for over 60 years. Our advanced instruments are highly sought after by pharmaceutical companies throughout the world to deliver the highest quality color quality control at every stage of bringing a drug to market and facilitate the introduction of safer, more advanced pharmacological therapies to improve the lives of patients. With a complete lineup of portable, benchtop, and in-line spectrophotometers to choose from, we have the tools you need to capture accurate and meaningful spectral and chromatic information regardless of whether you are working in the field, in the lab, or on a production line. As advances in abuse deterrent technologies continue to advance, you can be sure that HunterLab has the versatility, flexibility, and technical expertise to help you stay on top of a rapidly growing field. [Contact us](#) to learn more about our renowned instruments, flexible software packages, and world-class customer service.

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