



Responding to the Opioid Epidemic: Legal Developments and FDA's Role

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According to the [Centers for Disease Control and Prevention](#), “115 Americans die every day from an opioid overdose,” and deaths from prescription opioids have more than quadrupled since 1999. The epidemic’s origins are complex, with fingers pointed at [pharmaceutical manufacturers](#) and [distributors](#), [addicts and dealers](#), [health care professionals](#), and [insurance companies](#). Like the causes of the opioid epidemic, any solutions to the problem will likely involve many actors, [including the federal government](#). The Food and Drug Administration (FDA)—the executive agency [charged with protecting the public health](#) by ensuring the nation’s drug supply is safe and effective—has developed an “[opioids action plan](#),” discussed in more detail below. Nonetheless, questions remain as to what actions the agency should take and whether the agency’s existing authorities are adequate for addressing the crisis. This Sidebar provides an overview of FDA’s existing authorities, the historical context for the opioid epidemic, and the agency’s current plan for combatting the opioid epidemic, concluding with an examination of the broader legal questions concerning the crisis.

Background. [FDA is authorized](#) by the Food, Drug, and Cosmetic Act (FD&C Act) to regulate the nation’s drug supply both prior to and after marketing. Before a new drug product can be legally marketed in the United States, a manufacturer [must](#) obtain FDA approval of a new drug application (NDA). When considering an NDA, FDA conducts a risk-benefit assessment based on clinical evidence submitted by the drug manufacturer showing that the underlying product is safe and effective for its intended use. New drug applicants must also comply with labeling and manufacturing requirements, such that drug products are not [adulterated](#) or [misbranded](#). After approval, the FD&C Act requires FDA to monitor drugs to ensure that they abide by FD&C Act requirements, including prohibitions against adulteration and misbranding. Additionally, in 2007, the [Food and Drug Administration Amendments Act](#) authorized FDA to require manufacturers to undertake [Risk Evaluation and Mitigation Strategy](#) (REMS). A REMS is a safety strategy designed to manage a known or potential serious risk associated with a medicine. For example, as part of a REMS, drug manufacturers may be required to [provide certain information](#) to patients and/or health providers or [impose restrictions on a product’s distribution](#). FDA may require a

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REMS as a condition of a product's approval, or the agency may impose a REMS on a product it has already approved when new safety information arises. FDA enforces these requirements through a variety of legal measures, including [administrative actions](#), [criminal and civil penalties](#), [injunctions](#), and [product seizures](#).

FDA's task to ensure the safety and efficacy of drugs is particularly difficult with respect to regulating opioids. [Throughout recorded history](#), societies have struggled with balancing the medicinal use of opioids in pain management with the concomitant euphoric effects that have induced the substance's abuse. Sixty years ago, the head of surgery at the University of Illinois [noted](#), "we must appreciate that severe constant pain will destroy the morale of the sturdiest individual. . . But. . . we are often loathe to give liberal amounts of narcotics because the drug addiction itself may become a hideous spectacle." [As a result of these difficulties, for nearly a century](#), opioid pain medications were used in the United States primarily to treat acute and cancer-related pain. But, [studies from the 1970s](#) revealing inadequate management of chronic pain, followed by highly influential articles published in the 1980s [reporting](#) a low incidence of addictive behavior in small groups of cancer and non-cancer patients, led to a trend toward more liberal prescribing of opioids within the medical community. The shifting views on the safety and efficacy of opioids culminated in FDA's 1995 approval of Purdue Pharma's controlled-release opioid pain medication, OxyContin, the product [some](#) point to as the catalyst for the current opioid epidemic. Between [2000 and 2009](#), the medical community established new standards for pain management, which included [pain as a new vital sign](#), and prescriptions for opioids increased. By 2016, [an estimated 11.5 million](#) Americans were abusing prescription painkillers. And, in 2015 alone, [over 33,000](#) people died due to a drug overdose involving an opioid.

FDA's "Opioid Action Plan." To combat the epidemic, on February 4, 2016, [FDA announced](#) its "opioid action plan" that uses the agency's existing authorities, both pre- and post-market, to "reduc[e] the impact of opioid abuse on American families and communities." The agency's [plan](#) includes:

- consulting with an advisory committee prior to approving an NDA for an opioid without abuse-deterrent properties;
- developing additional warnings and safety information for certain opioid labeling;
- strengthening post-market requirements to require, for example, the study of the long-term effects of using extended-release/long-acting opioids;
- updating the REMs program, such as by requiring sponsors to fund continuing medical education for prescribers;
- expanding access to abuse-deterrent formulations (ADF) of opioid medications by issuing draft guidance on the agency's recommendations for approving such drugs;
- supporting better treatment for opioid abuse, such as expanding access (e.g., over-the-counter availability) to overdose treatments and opioid alternatives; and
- reassessing the risk-benefit approval framework for opioid use to account for the current understanding of the risks associated with opioid use and misuse.

FDA has since begun implementing this plan. For example, in March 2016, [FDA announced](#) that it would require enhanced safety warnings for immediate-release opioid medications related to misuse, abuse, addiction, overdose, and death. Last September, the agency [announced the extension of manufacturer-provided training requirements](#) for prescribers to other healthcare providers, such as nurses and pharmacists. And, in November the agency issued a [guidance document](#) for industry articulating the approval standards for generic opioid ADFs.

Broader Legal Issues Concerning the Opioid Epidemic. The announcement of FDA's opioid action plan takes place against the backdrop of broader legal questions arising from a wave of lawsuits concerning the opioid epidemic. A growing number of [state and local governments have filed suit](#) against

the manufacturers and distributors of opioid pain medications. On December 6, 2017, the United States Judicial Panel on Multidistrict Litigation (JPML) issued an [order](#) centralizing 64 actions that were pending in nine different federal courts in the Northern District of Ohio. In turn, that court is to [resolve any common questions](#) to all of the suits prior to any trial. The JPML has already been notified of 115 potentially related actions that may ultimately be included in the multi-district litigation (MDL).

A number of the lawsuits included in the MDL are directed at several major drug manufacturers and seek damages resulting from the opioid epidemic. The plaintiffs' legal claims are based on a wide range of federal and state laws, including state common law, such as "public nuisance, negligence, negligent misrepresentation, fraud and unjust enrichment" claims. [Manufacturers have argued in response](#) that FDA approval of the safety of a drug and its labeling preempts any state law claims contending that the drug is unsafe. Notably, in a 2009 case, *Wyeth v. Levine*, the Supreme Court held that FDA approval of a *brand-name* drug does not shield the manufacturer from liability under state tort law. However, in 2011, in *PLIVA v. Mensing* and two years later in *Mutual Pharmaceutical Co. v. Bartlett*, the Supreme Court concluded that the FD&C Act *does* preempt similar state law tort claims lodged against *generic* drug manufacturers because federal law prohibits generic drug manufacturers, unlike brand-name manufacturers, from making unilateral changes to the FDA-approved warning on a drug label. And in an earlier case, *Buckman Co. v. Plaintiffs Legal Committee*, the Court suggested, but did not definitively hold that even *violations* of the FD&C Act cannot support state common law claims. The open question for many of the opioid lawsuits is whether the Supreme Court's preemption case law forecloses the plaintiffs' common law claims.

The possibility that FDA-approval could shield opioid manufacturers from liability begs additional questions as to whether FDA can withdraw approval for certain opioid medications. [The FD&C Act](#) authorizes FDA to withdraw approval of an approved NDA when, among other things, there is new clinical evidence showing that the product is unsafe for its approved use. FDA must first provide the manufacturer with notice that the agency is proposing to withdraw approval and an opportunity for a hearing on the merits. However, the Secretary of Health and Human Services may suspend new drug approval immediately if it is determined that the product poses an immediate hazard to the public health. Although it is not a common occurrence, it has been [estimated](#) that FDA has withdrawn approval of approximately 600 new drug and abbreviated new drug applications.

FDA has signaled its willingness to withdraw approval of products with serious potential for abuse. Last June, [FDA requested](#) that Endo Pharmaceuticals recall from market Opana ER— a potent painkiller reformulated to make it difficult to crush and snort. Although the product was intended to curb opioid abuse, it reportedly led to the [largest HIV outbreak in Indiana history](#) when addicts resorted to liquidizing and injecting the drug with shared needles. Because FDA does not have mandatory recall authority over drug products— the agency can compel manufacturers of other products, such as [foods](#) and [medical devices](#) to recall— FDA's recall announcement included the proviso that if the company did not comply, FDA would begin procedures to have the product removed from market through the formal withdrawal of approval. Ultimately, the [company announced](#) in July that it would comply with FDA's request.

[FDA's regulations](#) also provide the opportunity for concerned citizens and organizations to request that the agency take certain actions, including withdrawing approval for drugs. Utilizing this authority, last August, a group of public health officials and physicians [petitioned FDA](#) to withdraw approval of ultra-high dose opioid pills and nasal sprays. Others, including the [American Academy of Pain Management](#) have argued that withdrawal of approval is too drastic a step to take and would unduly harm those with severe pain, including end-of-life patients. Under agency regulations, [FDA has 180 days to respond](#) to the petition. In so doing, the agency may have to grapple with the broad question that underlies the epidemic— how to strike the right balance between pain management and the risk of abuse. In the meantime, Members of Congress, in considering that same broad question, have introduced several bills that would, if enacted, alter the FDA's authority over opioids, including by altering the approval process

for opioid NDAs ([S. 1078](#)) and encouraging the development of opioids with abuse-deterrent technologies by altering the scope of marketing exclusivity for such products ([H.R. 2025](#)).
