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# Medicolegal Sidebar

# Corporate Malfeasance, Off-Label Use, and Surgeon Liability

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## Introduction

The federal criminal case relating to the off-label use of Norian bone void filler for vertebroplasty has been well-publicized. We examined the facts of this case to understand evolving trends in federal criminal prosecution in the healthcare industry, and to address the potential liability of orthopaedic surgeons who practice off-label use of a product, especially when consulting for the industry.

## Implications of FDA Approval

Food and Drug Administration approval of a drug or device applies only to specific applications set forth by the manufacturer. If indications are to be further expanded, the manufacturer must invest additional time and resources to satisfy necessary regulatory steps. The law is clear that without FDA approval, a manufacturer may not, in any way, promote off-label use of its product to the user surgeons.

Many legal cases have clarified that FDA approval of a drug or device pertains to regulatory compliance only, with no relation to the practice of medicine. Physicians have the discretion to use a drug or medical device in an off-label manner, if such use is of benefit to the patient. For example, an injection that is FDA approved for knee osteoarthritis might be used to treat painful shoulder arthritis, even though the label is limited to the knee joint. Such off-label use is relatively common among physicians and can help alleviate patient suffering while identifying additional safe uses of a drug or device. If so, a manufacturer can then seek approval from the FDA to expand the labeling of the product.

*Note from the Editor-in-Chief: We are pleased to introduce readers of* Clinical Orthopaedics and Related Research® *to Medicolegal Sidebar, a new quarterly column. The goal of this section is to encourage thoughtful debate about how the law and medicine interact, and how this interaction affects the practice of orthopaedic surgery. We welcome reader feedback on all of our columns and articles; please send your comments to eic@clinorthop.org.*

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While injury or harm that is related to off-label use of a medical product is not negligent in itself, the law is unclear whether there is a physician duty to disclose off-label status to the patient. Several legal cases (*Klein v Biscup*, 109 3d 855 [Ohio 1996]; *Blazoski v Cook*, 787 A.2d 910 [NJ 2002]) have held that the off-label status of a device pertains to FDA regulatory status only and is unrelated to a material risk of surgery; it is, therefore, inadmissible during medical malpractice litigation. Other legal cases, however, have reached the opposite conclusion, holding that off-label status of a drug or device may be material enough that it should be disclosed to the jury (*Corrigan v Methodist Hospital*, 885. 127 [Fla 1995]); *Shadrick v Centennial Medical Center*, WL 591179 [Tenn 1996]). Therefore, in medical malpractice lawsuits, where off-label status of a device or drug is invoked, it is possible that the court may deem such information to be admissible, such that the physician-defendant is burdened with explaining that off-label use was safe and consistent with the standard of care.

Because courts have sometimes permitted off-label status of a drug or device into medical malpractice trials, full disclosure of such status should be part of the informed consent process. Otherwise, the patient can argue that had he or she known about the intended off-label use, consent would not have been given. A related concern is that the phrase "off-label" or "not approved by the FDA" may have a negative impact on jurors. The criminal case against Synthes illustrates how corporate malfeasance can contribute to physician liability from off-label use of a product that was improperly introduced into the market and led to serious patient injury.

## Facts of the Case

Synthes is an orthopaedic device manufacturer that is probably best known for its extensive line of reconstructive equipment for trauma. In 1999, Synthes acquired Norian Inc, a small company that made bone void filler for use in the wrist, pelvis, and skull. Synthes saw an attractive market for Norian bone void filler in treating fragility fractures of the spine by injecting it into collapsed vertebral bodies; however, Norian bone void filler was not approved by the FDA for use in the spine.

To gain approval for vertebroplasty, Synthes would have had to obtain an Investigational Device Exemption from the FDA then implement lengthy and expensive clinical studies. As corporate documents and emails would later attest, company executives decided to make an end run around these regulatory hurdles by encouraging spine surgeons to use Norian for vertebroplasties.

Some corporate executives at Synthes balked at this strategy, correctly recognizing that the FDA explicitly bars companies from marketing products for off-label uses. In fact, even the mention of unapproved uses to surgeons is prohibited by the law. Even so, Synthes decided to push forward with its promotional effort and get spine surgeons to use Norian for vertebroplasty.

## Injury from Off-Label Use

According to court documents, in 2001, a spine surgeon injected Norian, with the knowledge of Synthes, into two elderly patients with vertebral compression fractures. Both patients suffered acute blood pressure collapse and required aggressive resuscitation to save their lives. By December 2001, the FDA had approved Norian for spinal use but not if Norian was mixed with other substances, as is required for vertebroplasty. With this approval, Synthes sales staff gained access to spine surgeons' operating rooms, but consistent with FDA rules, the company could not promote Norian for vertebroplasty. A few months later, animal studies suggested that Norian

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could be fatal if introduced into the bloodstream. Undeterred by all this, Synthes promoted Norian for vertebroplasty and sent literature to surgeons with instructions on how to mix Norian for injection.

Several surgeons reported success with Norian in vertebroplasty, but sporadic death related to cardiovascular collapse continued to occur. According to court documents, Synthes was not forthcoming about these adverse events to the FDA, at least in a few cases. Instead, the company conducted cadaver training sessions and brought in surgeons for all-expenses-paid meetings. In the ensuing federal investigation a few years later, several Synthes executives were charged with criminal misconduct, and ultimately four executives pled guilty to a misdemeanor under the Responsible Corporate Officer Doctrine. After complex legal wrangling, these senior executives were sentenced to jail terms, albeit for only a few months each.

## Analysis and Impact

Crime and punishment have always been complex phenomena; more so when they involve business transactions impacting the medical profession. The federal criminal case against Synthes was based upon the well-established prohibition against device and drug manufacturers marketing their products for off-label purposes. The last several years have seen multiple federal actions brought against drug manufacturers for off-label marketing of drugs, such as Paxil and Neurontin®. The medical community is generally aware that although drug companies and device manufacturers cannot market their products for off-label purposes, physicians can prescribe or implant these products for whatever clinical purposes they deem beneficial to their patients.

From a theoretical standpoint, it is difficult to establish a compelling rationale for the criminalization of manufacturer off-label marketing when doctors are free to use drugs or products for off-label purposes as they see fit. Admittedly, drug or product manufacturers have a strong fiscal incentive to market their products for any condition they can, but most astute physicians and surgeons are able to separate marketing bias from legitimate information about how a product may help patients.

The incarceration of senior corporate executives at Synthes represented an important landmark in the evolution of the application of criminal law to medicine. Traditionally, off-label violations led to civil fines rather than jail sentences. While the sentencing of the Synthes executives had no direct impact on orthopaedic surgeons, every time the federal government decides to become more aggressive in its prosecution of healthcare violations, it should send a signal to all orthopaedic surgeons to carefully assess their business practices.

As mentioned, there is a confusing distinction between the prohibition against manufacturers marketing devices for off-label use versus orthopaedic surgeons utilizing those devices in their treatments or management of their patients. This distinction may be even more confusing to jurors who may hold beliefs that off-market applications of a drug by surgeons are presumably acts of negligence, even though there may be no basis for this presumption. It is, therefore, important for any orthopaedic surgeon who is considering the off-label use of a product, device, or drug to recognize the importance of properly educating the patient about the selection.

The informed consent process has always involved two essential risks that need to be disclosed when a surgical treatment is being discussed or recommended: inherent and material risks. Inherent risks are those that can lead to patient injury, no matter how flawlessly the procedure is performed. Material risks are those that impact a patient's decision to undergo a treatment or surgery. The landmark

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medical malpractice case of *Canterbury v Spence* (464 F. 2d 772 [DC Cir, 1972]) clarified that a doctor must disclose all possible risks of a procedure that a "reasonable person" would find relevant in deciding whether or not to proceed. The language of *Canterbury* states that the test for determining whether a particular risk must be disclosed is its materiality to the patient's decision; ie, all risks potentially affecting the decision must be divulged. A risk is deemed "material" when a reasonable patient, in what the physician knows or should know to be the patient's position, would be "likely to attach significance to the risk or cluster of risks in deciding whether to forego the proposed therapy or to submit to it." *Canterbury* remains a well-established law that is cited in medical malpractice rulings to this day.

According to *Canterbury*, the materiality—the relevance of a risk—is to be judged by courts using a "reasonable person" standard. It is easy for counsel to argue that a reasonable person would want to know if an orthopaedic surgeon's recommendation includes the off-label use of a drug or device, his or her rationale for the off-label use, the clinical evidence or the basis for his or her opinion that the benefits for this off-label use outweigh the risks, and the available alternatives to off-label use. Without this discussion, the patient can argue that a nondisclosure of off-label status was material in that, had the patient known, consent for surgery would not have been given.

The effect of extensive media coverage of the Synthes criminal sanctions on the orthopaedic profession is likely to be mixed. Some will believe that sunlight is the best disinfectant, that such information should be properly aired to the public. On the other hand, the profession risks being cast in a negative light. The financial conflicts of consulting orthopaedic surgeons appear, at least as some reporters have framed them, to have helped further corporate malfeasance that led to patient injury. An already disillusioned public may believe that, far from its sacred oath to protect unwary patients, it may ultimately be all about the money for the medical profession.

The Synthes investigation and its aftermath reflected a warning to the medical device industry that jail sentences are indeed possible. Until now in similar cases, civil fines were simply regarded as a cost of doing business. Under the complex plea bargaining and legal rules of civil procedure for example, Synthes would have paid hefty fines but gained financially in getting its product before surgeons for a lucrative segment of the market. Indeed the company insiders did well when corporate giant Johnson & Johnson bought Synthes; company founder Hansjörg Wyss, already a billionaire, moved up further on the Forbes list of billionaires.

## Impact on Orthopaedic-Surgeon Defendants

For orthopaedic surgeons ensnared in the Synthes debacle, the fallout may be serious. The jail sentences were a victory for the US Justice Department as it stepped up efforts to hold individuals accountable for corporate malfeasance in violating food and drug laws. After the criminal proceedings, civil lawsuits were filed by aggrieved families against several surgeons who used Norian for vertebroplasties. It is unclear if federal criminal charges will be filed against any consulting surgeons, but the message of the Synthes case should be seen as a shot fired over the bow that federal prosecutors are serious.

As defendants in civil lawsuits will find out, off-label use will most likely be viewed as a material fact that should have been disclosed to the patient during informed consent. Jurors likely will hear testimony that surgeon-defendants were paid by Synthes for using Norian in a manner not approved by the FDA. In the face of loss of life and in view of these facts, the malpractice defense here may be a

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real challenge, and financial settlement may well be the preferred option.

Criminal proceedings against surgeons, should any materialize, would be an expensive proposition. Malpractice insurance does not cover the costs of criminal defense, and legal costs related to defending white-collar crime can be significant. The collateral effects of criminal proceedings on hospital privileging, Medicare payment eligibility and related professional matters may have lasting impacts on a surgeon's career.

Off-label use is a privilege granted to doctors; a privilege based on the perceived trust and ethics attached to the medical profession. The most damaging outcome of cases like the Synthes case is related to an erosion of this public trust. A disillusioned public will turn to the government for protection from doctors who appear to help promote harmful products for financial gain. If so, "off-label" may come to mean a clear warning for future doctors to abide by the letter of the law rather than the spirit of the law, thereby restricting physician discretion and sound judgment in the practice of medicine.