U.S. Department of Justice

United States Attorney

Eastern District of Pennsylvania

615 Chestnut Street

Suite 1250
Philadelphia, Pennsylvania 19106-4476
(215) 861-8200

For Immediate Release

October 4, 2010

INTERNATIONAL MEDICAL DEVICE MAKER AGREES TO PLEAD GUILTY IN CONNECTION WITH SHIPMENTS OF ADULTERATED AND MISBRANDED BONE CEMENT PRODUCTS AS PART OF UNLAWFUL CLINICAL TRIALS

PHILADELPHIA –A superseding information[1] was filed today against Synthes, Inc. and Norian Corporation charging them for their involvement in conducting clinical trials of a medical device without the authorization of the FDA, announced Deputy Assistant Attorney General Ann Ravel and United States Attorney Zane David Memeger. Also filed today were guilty plea agreements executed by both companies, pursuant to which both companies agree to plead guilty to the charges in the superseding information and pay the maximum criminal monetary penalties allowed by law: $22,500,000 in the case of defendant Norian, and $669,800 in fines and forfeiture in the case of Norian's parent company, defendant Synthes. The case is assigned to the Honorable Legrome D. Davis.

The superseding information charges Norian with one felony count of conspiracy to impair and impede the lawful functions of the FDA and to commit crimes against the United States, and 110 misdemeanor counts of shipping adulterated and misbranded Norian XR in interstate commerce. The parent company, Synthes, is charged with one misdemeanor count of shipping adulterated and misbranded Norian XR in interstate commerce. As explained below, these crimes allegedly prevented the FDA from carrying out its role of supervising clinical trials of significant risk devices, and deprived patients of the safeguards provided by FDA oversight of clinical trials.

Synthes, a corporation based in West Chester, Pennsylvania, is the United States branch of a large multinational medical device manufacturer that specializes in trauma products to treat damaged human bone. Norian is a wholly owned subsidiary of Synthes, specializing in the

[1] An information is an accusation. A defendant is presumed innocent unless and until proven guilty. The filing of the superseding information does not affect the indictment previously returned by the grand jury against four former executives of Synthes, Inc.; those individual defendants have pleaded guilty and await sentencing. No sentencing dates have been set for the individual defendants.

manufacture of osteobiologic medical devices, with a principal place of business in West Chester, Pennsylvania.

The information charges that from May 2002 until fall 2004 Norian conspired with others, including Synthes and several former Synthes executives (charged in the original indictment), to conduct unauthorized clinical trials of Synthes's medical devices, Norian XR and Norian SRS,[2] in surgeries to treat vertebral compression fractures of the spine ("VCFs"), a painful condition commonly suffered by elderly individuals. These surgeries were allegedly performed despite a warning on the FDA-cleared label for Norian XR against this use, and in the face of serious medical concerns about the safety of the devices when used in the spine. According to the information, before the marketing program began, pilot studies showed the company that the bone cement reacted chemically with human blood in a test tube to cause blood clots. The research also showed, in a pig, that such cement-caused clots became lodged in the lungs. Notwithstanding this knowledge, the company allegedly proceeded to market the product for VCFs without putting it through FDA-required testing. The company, it is alleged, did not stop marketing the product until after a third patient had died on the operating table. The information further alleges that after the death of the third patient in January 2004, Norian and Synthes did not recall Norian XR from the market – which would have required them to disclose details of the three deaths to the FDA – but, instead, compounded their crimes by carrying out a coverup in which they made false statements to the FDA during an official inspection in May and June 2004.

"This case is another example of the Department of Justice working together as a team to enforce the Food, Drug, and Cosmetic Act against companies and individuals that fail to market their products in compliance with that statute," said Deputy Assistant Attorney General Ann Ravel.

"The FDA approval process exists to make sure that medical devices that are used in the United States are safe and effective," said United States Attorney Zane David Memeger. "Device manufacturers have a legal obligation not to test their devices on humans without FDA oversight. This case is especially troubling because in search of greater profits, Norian bypassed this process. Today's settlement sends a clear message to device manufacturers that deceptive and illegal practices of the type demonstrated in this case will result in serious consequences."

Summary of the Charges

The information charges that, from the beginning, the intended market for Norian XR was for an unapproved use, i.e., in surgeries to treat VCFs. According to the information, the company recognized early on that there were two possible solutions to this problem: (1) the legal solution, which was to disclose to the FDA the intended use of the product and then to try to secure FDA approval of XR for use in surgeries to treat VCFs after obtaining an investigational device exemption ("IDE") to investigate the safety and efficacy of the product; and (2) the illegal solution, which was to promote XR for use in VCFs through a limited so-called "test market,"

[2] Norian SRS and Norian XR were bone cements that were used in treating fractures.

during which the company would evaluate the safety and efficacy of the product in unapproved clinical trials and judge their success according to its own standards. The information charges that the company and its co-conspirators consciously and deliberately chose the illegal solution. That is, according to the information, the company intentionally bypassed the requirement that it obtain permission from the FDA to conduct clinical trials of the XR device on human beings for an unapproved use – permission that it knew it needed. With the so-called "test market," the company allegedly tried to save time and money by cutting out the FDA's oversight of clinical trials of its device. The information charges that the company did this for two principal reasons: to rush an XR-type bone cement to the market first, before its competitors, and to generate published studies that it could use later to convince other surgeons to use XR off-label to treat VCFs.

Starting as early as late summer 2002, the company allegedly approached selected spine surgeons and asked them to use a predecessor device, SRS, in VCF procedures as part of an initial Synthes "test market" for SRS. Despite a June 2002 plea from one of Synthes's own surgeon consultants that conducting such a "test market" would "amount to human experimentation whose only defense seems to be that it will be a small study [,]" Norian and its co-conspirators allegedly embarked on the SRS "test market." According to the information, the company taught the selected surgeons the recipe for mixing SRS with barium sulfate to make it more radiopaque, a process called "back-table mixing" (which the SRS label forbade), and trained two groups of surgeons in the use of SRS to treat VCFs. After training the two groups of surgeons as initial "test market" sites, the company allegedly enlisted these "test market site" surgeons to train other surgeons on how to use XR to treat VCFs.

According to the information, the company conducted two XR "Test Market Kick-Off" surgeon meetings, and one surgeon forum, from August of 2003 through mid-January 2004, training approximately 52 spine surgeons how to use Norian XR to treat VCFs. It is charged that, after the third person died on the operating table during a surgery in which a Norian cement was used to treat VCFs, the company cancelled the future surgeon forums. The information alleges that the company considered, but rejected, the idea of recalling or removing XR from the market, either of which actions would have required it to notify the FDA. In a Dear Doctor letter to test market surgeons, the company made no mention that Synthes had conducted a "test market" in which it had trained surgeons to use Norian XR to treat VCFs; that pilot studies showed that the Norian cements appeared to be thrombogenic agents; and that three patients had died on the operating table when spine surgeons had used Norian cements off-label to treat VCFs.

Three months later, according to the information, when the FDA conducted an unannounced inspection at the Norian plant in West Chester, focused on whether or not Norian and Synthes had conducted an unauthorized clinical trial of XR, a number of Synthes employees made materially false and misleading statements to the FDA investigator.

Penalties – Criminal and Civil

Upon conviction Norian faces a maximum possible sentence of a fine of $22,500,000, five years probation, forfeiture of $469,800 and special assessments of $14,150. Defendant Synthes faces a maximum possible sentence of a fine of $200,000, five years probation, forfeiture of $469,800 and a special assessment of $125.

Upon conviction Norian will face mandatory exclusion from Federal health care programs by the Office of Inspector General of the U.S. Department of Health and Human Services (OIG-HHS). Exclusion would mean that Norian's products would not be eligible for reimbursement under Medicare, Medicaid or other Federal health care programs. Norian's parent, Synthes, has entered a Divestiture Agreement with OIG-HHS under which it agrees to sell all Norian assets within a limited period of time. If Synthes fails to comply with the terms of the Divestiture Agreement, OIG-HHS will exclude Norian. In addition to the Divestiture Agreement, Synthes signed a five-year corporate integrity agreement (CIA) with OIG-HHS. The CIA requires Synthes to implement a compliance program designed to minimize future improper conduct. If Synthes fails to comply with the terms of either the Divestiture Agreement or the CIA, OIG-HHS could initiate an action to exclude Synthes.

"OIG investigates and excludes from Federal health care programs companies that jeopardize patients' lives. We ensure companies do not avoid exclusion by transferring assets or operations within a corporate family," said Daniel R. Levinson, Inspector General of the U.S. Department of Health and Human Services. "In this case, Synthes must fully divest Norian assets and cease Norian operations. Synthes also faces exclusion unless it complies with a Corporate Integrity Agreement requiring strict compliance with medical device regulations."

"The FDA's Office of Criminal Investigations will continue to vigorously pursue criminal prosecutions against companies that conspire to prevent the Food and Drug Administration from carrying out its lawful functions," said Thomas P. Doyle, FDA-OCI Special Agent-in-Charge. "The oversight of clinical trials is one of the most important functions that the FDA performs in order to ensure the safety of the public health. Impeding clinical oversight and introducing unsafe medical devices to the public will be prosecuted to the fullest extent of the law".

The resolution with Synthes and Norian also includes a civil settlement under the False Claims Act totaling $138,000, for causing the submission of thirty one false claims to various federal health care programs resulting from the use of the Norian XR and Norian SRS devices in vertebral compression fractures when the use of those devices was not reasonable and necessary, and when such an unapproved use was, on the Norian XR label, explicitly warned against.

This resolution is part of the Eastern District of Pennsylvania's Special Focus team Health Care Fraud initiative.

The Investigators

This case was investigated by the United States Food and Drug Administration Office of Criminal Investigations; the United States Department of Health and Human Services Office of Inspector General; the Defense Criminal Investigative Service, Department of Defense; and the Veterans' Administration Office of Inspector General. The case is being prosecuted by Assistant United States Attorneys Mary E. Crawley and Gerald B. Sullivan and Laura A. Pawloski, Associate Chief Counsel, FDA Office of Chief Counsel, with assistance from the U.S. Department of Justice, Office of Consumer Litigation. The corporate integrity agreement was negotiated by Senior Counsel Mary Riordan and Associate Counsel Geeta Kaveti in the Office of Counsel to HHS-OIG. The civil case was handled by Colin M. Huntley, a Trial Attorney in the Commercial Litigation Branch of the Department of Justice.

UNITED STATES ATTORNEY'S OFFICE
EASTERN DISTRICT, PENNSYLVANIA
Suite 1250, 615 Chestnut Street
Philadelphia, PA 19106

Contact: PATTY HARTMAN
Media Contact
215-861-8525

COPIES OF NEWS MEMOS AND RELATED DOCUMENTS CAN ALSO BE FOUND AT
http://www.usdoj.gov/usao/pae