

**IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA**

UNITED STATES OF AMERICA	:	CRIMINAL NO.: _____
v.	:	DATE FILED: _____
NORIAN CORPORATION	:	VIOLATIONS:
SYNTHES, INC.	:	18 U.S.C. § 371 (conspiracy – 1 count)
MICHAEL D. HUGGINS	:	18 U.S.C. § 1001 (false statements – 7
THOMAS B. HIGGINS	:	counts)
RICHARD E. BOHNER	:	21 U.S.C. §§ 331(a), 352(a) and 333(a)(2)
JOHN J. WALSH	:	(introducing into interstate commerce
		adulterated and misbranded medical
		devices with intent to defraud – 44
		counts)
		21 U.S.C. §§ 331(a), 352(a) and 333(a)(1)
		(introducing into interstate commerce
		adulterated and misbranded medical
		devices – 45 counts)
		18 U.S.C. § 2 (aiding and abetting)
		notice of forfeiture

INDICTMENT

COUNT ONE

THE GRAND JURY CHARGES:

Introduction

1. At all times relevant to this indictment:

The Defendants

- a. Synthes, Inc. (charged elsewhere in this indictment) (“Synthes”) was a business corporation organized under the laws of the State of Delaware, with its principal place of business located at West Chester, in the Eastern District of Pennsylvania. Synthes is the United States branch of a large multinational medical device manufacturing corporation which specializes in trauma products, with manufacturing facilities located in Monument, Colorado, West Chester, Pennsylvania, Elmira, New York and Tuttlingen, Germany.
- b. Defendant NORIAN CORPORATION (“NORIAN”) was a wholly owned subsidiary of Synthes, with its principal place of business located at West Chester, in the Eastern District of Pennsylvania. Prior to mid-1999, defendant NORIAN was located in Cupertino,

California and was in the business of manufacturing and selling two calcium phosphate bone cements, called Norian Cranial Repair System (“CRS”) and Norian Skeletal Repair System (“SRS”). CRS was a Class II medical device that had been cleared by the FDA to be marketed for filling defects in the skull. SRS was a Class III medical device that had been approved by the FDA to be marketed for use in the distal radius, a long bone in the arm. Synthes acquired defendant NORIAN on or about July 21, 1999, whereupon Synthes began exploring new intended uses for the Norian bone cements, with an eye toward eventually obtaining an indication for use of Norian bone cements in the spine.

c. Michael D. Huggins (charged elsewhere in this indictment)(“Huggins”) was employed by Synthes as the President of Synthes North America, a subsidiary of Synthes. In February 2004 Huggins became the President of Synthes Spine, a division of Synthes.

d. Thomas B. Higgins (charged elsewhere in this indictment)(“Higgins”) was the President of Synthes Spine, a division of Synthes, reporting to Huggins. In February 2004 Higgins left the position of President of Synthes Spine and became Senior Vice President of Global Strategy of Synthes.

e. Richard E. Bohner (charged elsewhere in this indictment)(“Bohner”) was employed by Synthes as its Vice President of Operations, reporting to Huggins.

f. John J. Walsh (charged elsewhere in this indictment)(“Walsh”) was employed by Synthes as its Director of Regulatory and Clinical Affairs, Spine Division, and reported first to Bohner and later to Huggins.

The Food and Drug Administration

2. The Food and Drug Administration (“FDA”) is an agency of the United States government responsible for protecting the health and safety of the public by assuring, among other things, that medical devices intended for use in the treatment of humans are safe and effective for their intended uses and that the labeling of such devices bear true and accurate

information. Pursuant to this statutory mandate, the FDA regulates the manufacture, labeling, and shipment in interstate commerce of any such devices.

3. Under the federal Food, Drug and Cosmetic Act (Title 21, United States Code, §§ 301-397, the "FDCA"), and pursuant to Title 21, United States Code § 321(h), the term "device" includes "an . . . implant . . . or other similar or related article . . . which is . . . intended for use in . . . the treatment or prevention of disease of man . . . or intended to affect the structure or any function of the body of man . . . which does not achieve its primary intended purposes through chemical action within or on the body of man and which is not dependent upon being metabolized for the achievement of its primary intended purposes."

4. Pursuant to the FDCA, every manufacturer of a new device is required to obtain "clearance" or "approval" from the FDA prior to marketing its device.

5. All devices marketed in interstate commerce in the United States fall into one of three regulatory classes under the FDCA. Class III devices are subject to the most stringent regulatory requirements, Class I devices to the least stringent, and Class II devices to requirements that fall in between. The classification assigned to each device is determined by the degree of regulatory control necessary to provide reasonable assurance of the safety and effectiveness of that device for its intended use.

6. Devices that were not in commercial distribution prior to May 28, 1976, when the Medical Device Amendments to the FDCA became effective, are automatically assigned to Class III by operation of law. Such Class III devices cannot legally be marketed in the United States until the manufacturer has submitted to the FDA a pre-market approval ("PMA") application and the FDA has approved that application. The FDA will not grant pre-market approval unless the information in the PMA application provides the FDA with reasonable assurance that the device is safe and effective when used according to its labeling.

7. The only ways a manufacturer can remove a device from automatic assignment to Class III, and thereby avoid the PMA process, are to obtain either an order from the FDA

reclassifying the device into Class I or Class II, or a finding by the FDA that the device is substantially equivalent to a legally marketed device (called a “predicate device”) for which pre-market approval is not required.

8. A “significant risk” device is an implant that presents a potential for serious risk to the health, safety or welfare of a human subject, or is a device that otherwise presents a potential for serious risk to the health, safety or welfare of a human subject.

9. A “clinical trial” or “clinical investigation” is a investigation or research involving one or more human subjects to determine the safety or effectiveness of a device.

10. As part of the pre-market approval or clearance process, the FDA often requires device manufacturers to submit the results of clinical trials or investigations, that is, testing on human subjects. Manufacturers of significant risk devices cannot legally conduct clinical trials or investigations in the United States without first obtaining the FDA’s permission to do so, by way of an Investigational Device Exemption (“IDE”). Before beginning a clinical trial of a significant risk device, the device manufacturer is required to obtain the FDA’s approval of the IDE, and a multi-disciplinary group of professionals with backgrounds in areas like science, medicine and bioethics called an Institutional Review Board (“IRB”) is required to approve the investigational plan and informed consent form, so that the clinical trial is properly monitored and the human subjects properly protected. In some limited circumstances, an IDE does not need to be filed if the manufacturer is conducting consumer preference testing of the device, but only if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk. The requirements of an IDE to permit clinical trials, and an IRB to oversee clinical trials, combined with the expense of planning and carrying out clinical trials, mean that obtaining pre-market approval from the FDA for a significant risk device often is a long and expensive process.

11. A manufacturer that takes the alternate route of seeking a determination of “substantial equivalence” is required to submit to the FDA “pre-market notification” (also known

as a “510(k)”) no later than ninety days before the manufacturer intends to introduce the device into interstate commerce. If the FDA makes a finding of “substantial equivalence” based on the manufacturer’s pre-market notification, the device is then “cleared” for marketing and can be marketed only for the intended use stated on the label as cleared by the FDA.

12. A manufacturer is required to file a new 510(k) for its previously cleared device if the device is to be changed or modified in a way that could significantly affect its safety or effectiveness, that is, if the manufacturer is planning a significant change to the device’s design, material, chemical composition, or manufacturing process. A new 510(k) pre-market notification is also required for a planned major change or modification in the intended use of a device.

13. If the manufacturer intends to market the device for a new or different indication for use from that cleared for the predicate device, the new 510(k) notification is required to include supporting information to show that the manufacturer has considered what consequences and effects the new use might have on the safety and effectiveness of the device.

14. Through an expedited, streamlined version of the 510(k) process, a manufacturer seeking to obtain FDA clearance to market a modified version of its own, previously cleared device can submit to the FDA a pre-market notification (also known as a “Special 510(k)”) no later than thirty days before the manufacturer intends to introduce the modified device into interstate commerce. If the FDA makes a finding that the manufacturer’s modified device is “substantially equivalent” to the manufacturer’s original device, the modified device is then cleared for marketing and can be marketed only for the intended use stated on the label as cleared by the FDA. The Special 510(k) process cannot be used when the proposed change or modification to the device affects the intended use of the device.

15. Approval of a PMA application and clearance of a 510(k) or Special 510(k) pre-market notification are separate routes for obtaining the FDA’s permission to market a medical device. Until a device obtains one of these two forms of permission, it cannot legally be distributed in interstate commerce.

16. Regardless of the route chosen by the device manufacturer in seeking the FDA's permission to market a medical device – whether by 510(k) or Special 510(k) pre-market notification, or by PMA application – the device manufacturer's application to the FDA is required to contain proposed labels and labeling sufficient to describe the device, its intended use, and the directions for its use. A device is cleared or approved by the FDA on the basis of its intended use, and the FDA-approved use is required to be included in the device's labeling.

17. The manufacturer of a medical device is not permitted to promote its device for any use other than the intended use stated on the label as cleared or approved by the FDA. A manufacturer is not permitted to promote or test market an investigational device until after the FDA has approved the device for commercial distribution, and cannot represent that the investigational device is safe and effective for the purposes for which it is being investigated.

18. A Class III device is "adulterated" if it is required to have an approved PMA application and does not have an approved PMA application in effect, or if it is required to have an approved IDE and does not have an approved IDE in effect.

19. A medical device is "misbranded" if the manufacturer of the device has failed to provide the FDA with pre-market notification of a new or non-FDA-sanctioned intended use ninety days prior to introducing the device into interstate commerce for such use.

20. A device manufacturer is required to establish and maintain records, make reports, and provide information to the FDA in order to assure that its device is not adulterated or misbranded, and otherwise to assure the safety and effectiveness of its device. In addition, a device manufacturer is required promptly to report to the FDA a removal of a medical device from the market.

21. Whenever a device manufacturer becomes aware of information from any source that reasonably suggests that the manufacturer's device might have caused or contributed to a death or serious injury, the device manufacturer is required by law to report that information to the FDA within thirty days in a report called a Medical Device Report ("MDR"). A medical

device causes or contributes to a death or serious injury when the death or serious injury was, or might have been, attributed to the medical device, or when the medical device was or may have been a factor in a death or serious injury. The FDA makes MDRs available to doctors and other members of the public through searchable databases so that the public can be aware of serious risks associated with medical devices.

22. A medical device is also “misbranded” if the manufacturer of the device fails or refuses to furnish to the FDA any material information concerning that device that is required to be reported on an MDR.

The Spine

23. The human spine is a structure made up of bone, cartilage, joints, a spinal cord, nerve roots, ligaments, tendons, muscles and a vascular system. The spinal column is a strong and flexible rod starting at the base of the skull and continuing to the pelvis. The spinal column consists of bones connected by joints and supported by ligaments, tendons and muscles. The spinal column gives a person the ability to move his or her upper body in a controlled manner. In addition, the spinal column protects the spinal cord, supports the head, provides an attachment for the ribs, and transmits most of the body’s weight to the pelvis, aided by muscles and tendons.

24. Twenty-six pieces of bone known as vertebrae stack up to form the spinal column, which is curved. The curves in the spinal column are important for balance, flexibility, stress absorption and weight distribution in the spine. The vertebrae increase in size down the spinal column to accommodate the enlarging body weight. The vertebrae group into five regions from the top to the bottom: cervical, thoracic, lumbar, sacrum and coccyx.

25. The cervical vertebrae extend from the skull to the shoulders and aid the movement of the neck and head. There are seven cervical vertebrae, referred to as C1 through C7 from top to bottom. The cervical vertebrae are followed by twelve thoracic vertebrae, from T1 at the top (at the shoulders) to T12 at the bottom (just below the rib cage). Two ribs are

connected to each thoracic vertebra, one on either side. The thoracic vertebrae are followed by five lumbar vertebrae, L1 through L5, which connect the upper spine to the pelvis. The lumbar vertebrae provide mobility and strength essential for almost all activities of daily living, such as turning, twisting and bending, and actions such as standing, walking and lifting. The sacrum, or S1, is the large irregular triangular shaped bone below the lumbar region, made of five fused bones and inserted like a wedge between the pelvis bones, held together by two joints. The coccyx is the terminal part of the spine that was commonly known as the tailbone. It comprises three vertebrae fused together.

26. With the exception of the atlas (C1), the axis (C2), the sacrum and the coccyx, each cervical, thoracic and lumbar vertebra is similarly shaped. A typical vertebra has a large vertebral body in the front and an arch of bony structures in the back (“posterior”) including two supporting pedicles and two arched laminae. The exterior vertebral body consists of very hard bone called cortical bone, with more spongy bone marrow, called cancellous bone, and blood vessels inside. The vertebral bodies support 80% of all loads applied to the spine. The main purposes of the arch of posterior bony structures are to protect the spinal cord and to enable the connection of the vertebrae to muscles and ligaments. The hollow center of the vertebra is known as the spinal canal, which contains the spinal cord, the cauda equina (in the lower spine), fat, connective tissue, and the arterial and venous supply of the spinal cord. Holes at regular levels on each side of the spinal canal below the neck form the intervertebral foramina. Under each pedicle, two spinal nerves exit the spinal cord and run through the foramen to branch out to the body.

The Spine Market

27. Osteoporosis is a disease of the bones characterized by abnormally low levels of calcium, in which the bones become fragile and more likely to break. These broken bones, known as fractures, occur in the spine, among other bones. Approximately 700,000 fractures of

the spine that are called vertebral compression fractures or VCFs occur annually in the United States due to osteoporosis; approximately 270,000 of these fractures are painful and clinically diagnosed. Most patients are treated conservatively, with bed rest, bracing and pain medicines, but some patients do not respond well to conservative treatment, and suffer serious consequences from VCFs, including loss of height, severe back pain and deformity.

28. In the early 1980s, surgeons in France developed a minimally invasive, or percutaneous, surgery called vertebroplasty to treat VCFs. During the surgery, a needle was inserted through otherwise unopened skin into the fractured vertebra through the back of the patient under general or local anesthesia with the help of image-guided X-ray. Through the needle, the surgeon injected a mixture of bone cement and a contrast agent into the vertebral body, in order to stabilize the fractured bone and alleviate back pain.

29. In the 1990s, a variation on the vertebroplasty surgery, called kyphoplasty, was developed to treat VCFs. The main difference between vertebroplasty and kyphoplasty was that in kyphoplasty a surgical instrument and a balloon were inserted into the compressed vertebral body, in order to create a cavity that elevated or expanded the fractured vertebra to its original shape. Once the instrument was withdrawn, the created cavity was filled with bone cement or a bone void filler mixture. By enlarging the fracture in this manner, kyphoplasty procedures were believed to correct deformity, restore vertebral body height, or both, as well as alleviate back pain. Enlargement of the VCF was commonly called "reduction."

30. The term "vertebroplasty," when used in a broad sense, describes any percutaneous surgery in which a mixture of bone cement and a contrast agent are injected into a vertebral body to stabilize fractured bone and alleviate back pain. The term "vertebroplasty" is also used more narrowly to describe a traditional, high-pressure percutaneous procedure in which no cavity is created prior to injection of the bone cement into the vertebral body.

31. Both vertebroplasty and kyphoplasty carry the risk of cement leaking out of the vertebral body. Traditional vertebroplasty, in which no cavity is created in the vertebra before

injection of the cement, carries the risk of cement leaking out of the vertebral body because the cement is injected at high pressure, and because, so that such high pressure injection can take place, the cement is used in a runny form. Cement leakage can cause soft tissue damage. Moreover, because many blood vessels are near the spine, cement leakage into the venous system can also cause pulmonary embolism and death.

32. An acrylic bone cement called polymethylmethacrylate or PMMA was the first substance used in vertebroplasty and kyphoplasty procedures. PMMA was much harder than bone; it was exothermic, that is, it gave off heat when injected; and it did not remodel to bone. When PMMA was used in vertebroplasty or kyphoplasty surgeries to treat VCFs, its extreme hardness could cause fractures in adjacent vertebrae. In addition, when PMMA was used in vertebroplasty or kyphoplasty surgeries to treat VCFs, PMMA's exothermic reaction could cause nerve and soft tissue damage. Most surgeons who used PMMA in vertebroplasty or kyphoplasty surgeries to treat VCFs mixed the PMMA with a contrast agent such as barium sulfate, a process known as "back-table mixing." PMMA was typically used in a less viscous (runnier) state for vertebroplasties and a more viscous state for kyphoplasties.

33. Because PMMA had drawbacks when used in vertebroplasty and kyphoplasty surgeries to treat VCFs, medical device manufacturers began exploring alternative bone cements, such as those made from calcium phosphate. Calcium phosphate bone cements were much less hard than PMMA; they were not exothermic; and over time, under ideal conditions, they would be replaced by new bone growth.

34. Prior to April 2004, during the relevant period here, no bone cement (acrylic or calcium phosphate) was cleared or approved by the FDA for use in treatment of VCFs in vertebroplasty and kyphoplasty surgeries. On or about April 1, 2004, for the first time, the FDA cleared an acrylic bone cement for use in kyphoplasty surgeries to treat VCFs.

Synthes Develops Norian XR to Treat VCFs

35. Synthes, a medical device manufacturer that had an established market presence in trauma products, had traditionally manufactured metal medical devices that are properly characterized as “hardware,” including products such as plates, rods, nails and screws. Prior to approximately June 1999, Synthes lacked a market presence in osteobiologic products. In or about June 1999, however, Synthes purchased defendant NORIAN CORPORATION, a manufacturer of bone cements based in Cupertino, California. NORIAN had developed two products, Norian SRS (Skeletal Repair System) and Norian CRS (Cranial Repair System), which were identically formulated calcium phosphate bone cements.

36. In or about the spring of 2000, Synthes Spine Division (“Synthes Spine”) employees in Product Development (“PD”) interviewed orthopedic spine surgeons, neuroradiologists, and neurosurgeons who used PMMA off-label in performing vertebroplasty and kyphoplasty surgeries to treat VCFs, inquiring as to whether they had used SRS in such surgeries, how SRS had performed in this indication, ways to improve the use of SRS in such surgeries, and – for the many interviewees who had used only PMMA – how often they might use SRS in such surgeries, among other questions. The purpose of these interviews was to create a market for the use in vertebroplasty and kyphoplasty surgeries to treat VCFs of a version of Norian SRS with radiopaque barium sulfate (“Norian SRS-R”). Norian SRS-R was the device in development at the time that defendant NORIAN and Synthes, Michael D. Huggins, Thomas B. Higgins, and Richard E. Bohner eventually brought to market as Norian XR.

37. In or about June 2000, at the direction of Thomas B. Higgins, a Synthes Spine employee known to the grand jury (Person No. 1),¹ and another person known to the grand jury (Person No. 2), summarized the results of Synthes Spine’s interviews of orthopedic spine surgeons, neuroradiologists and neurosurgeons in a Vertebroplasty Market Investigation

¹ A table describing the persons and entities referred to by number in this indictment is attached as an addendum at the conclusion of the indictment.

Executive Summary (the "Vertebroplasty Summary"), that was distributed to management of Synthes. The Vertebroplasty Summary noted that the most common indication for vertebroplasty was "overwhelmingly osteoporotic compression fractures" and, further, that the ideal material for vertebroplasty would be more radiopaque than PMMA. The Vertebroplasty Summary concluded that the use of vertebroplasty was on the rise; that the technique had tremendous potential as it filled a void in the treatment of VCFs; and that there were currently over half a million VCFs per year in the United States. The Vertebroplasty Summary stated that, among surgeons, there was "excitement about using Norian for vertebroplasties," and concluded that for Synthes the market potential was considerable.

38. In or about late summer 2000, based on the surgeon interviews, research of literature, and conversations with spine surgeons performing vertebroplasties and kyphoplasties to treat VCFs, Synthes began development of the Synthes Vertebroplasty System for treating VCFs. The Synthes Vertebroplasty System consisted of SRS-R and a group of Class I instruments for approaching an osteoporotic vertebral body and injecting SRS-R in percutaneous surgeries, called the Cavity Creation System.

39. On or about August 23, 2000, a regulatory employee of Synthes, known to the grand jury (Person No. 3), sent an email to Thomas B. Higgins and Richard E. Bohner, among others, stating that "[a]s everyone is well aware, I hope, we do not have a spine indication for Norian SRS at this time." Person No. 3's email continued that another employee "recently reviewed a vertebroplasty 'Test Market' forecast for Norian SRS and equipment sent from the spine PD. . . . Regulatory is unaware that this is even being considered. We cannot promote the use of SRS for unapproved indications, and this is especially true for use in the spine, where FDA has previously made it clear to Norian that any intra-spinal use would require additional approval. . . . We are aware that the spine PD group has been considering developing a delivery system which could be used for vertebroplasty with any substance and which would therefore only be able to be used or promoted for use with autograft or allograft at this time. Such

instruments would be Class I – Exempt. However, any suggestion on our part that the instrument could be used with SRS would be considered promotion of an unapproved use of SRS.”

40. In or about fall 2000, agents of Synthes, including Thomas B. Higgins, Person No. 1, and a Spine Product Development employee known to the grand jury (Person No. 4), held several meetings with representatives of a company that marketed a bone tamp (“Company A”), to discuss the possibility of Synthes collaborating with Company A by marketing a calcium phosphate bone cement to be used with Company A’s bone tamp and balloon system in kyphoplasty surgeries.

41. On or about October 25, 2000, Company A received a Warning Letter from the FDA, directing Company A to cease marketing its bone tamp and balloon system for use in kyphoplasty surgeries, as those devices were not cleared for a vertebroplasty indication.

42. On or about December 4, 2000, Person No. 3 sent an email to Thomas B. Higgins, among others, attaching the FDA’s Warning Letter to Company A, and informing Higgins that “this Warning Letter emphasizes FDA’s concerns about claims for general orthopedic device[s] for use in the spine[.]”

43. In or about March 2001, agents of Synthes, including Michael D. Huggins and Thomas B. Higgins, learned of two adverse events that had occurred when a spine surgeon known to the grand jury (Doctor No. 1) had used Norian CRS off-label in two percutaneous kyphoplasty surgeries to treat VCFs in two patients, and further that each time, the Norian CRS had been carried to the operating room by a Synthes sales representative, who had been present in the operating room during the surgeries.

44. In or about March 2001, Person No. 1 telephoned Doctor No. 1 to learn details of the two adverse events. Person No. 1 learned that during the first surgery, the patient experienced a severe drop in blood pressure, after which the patient took about 20 minutes to stabilize, and which resulted in the patient’s spending three or four days in the hospital’s intensive care unit. During that telephone call, Person No. 1 learned that during the second

surgery, the patient also experienced a severe drop in blood pressure (also known as a “hypotensive episode”) but did not require admission to the intensive care unit. Person No. 1 also learned during the telephone call that before the two hypotensive events with Norian CRS, Doctor No. 1 had performed 40 to 50 kyphoplasties, all with PMMA.

45. On or about April 2, 2001, because of the two hypotensive episodes suffered by the patients of Doctor No. 1, Thomas B. Higgins invited surgeons with an interest in using Norian SRS-R in the spine to treat VCFs to meet with employees of Synthes and defendant NORIAN in Cupertino, California (the “Norian Spine Focus Group”). The Norian Spine Focus Group met with Higgins and other employees of Synthes and defendant NORIAN, including Person No. 1, Person No. 4, and the president of the Osteobiologics Division of Synthes, whose identity is known to the grand jury (Person No. 5), so that Doctor No. 1 could present information about his two patients’ hypotensive episodes, and the assembled surgeons could give Synthes and defendant NORIAN and their agents their views on the possible causes of the hypotensive episodes. At that meeting, Doctor No. 1 presented information about the two hypotensive events, and a discussion followed among the surgeons concerning the possible causes of the hypotensive events. One of the surgeon participants, a prominent spine trauma surgeon known to the grand jury (Doctor No. 2), reported that the Norian cement in its pre-hardened state might be interacting with blood and causing problems. At the Norian Spine Focus Group meeting, Doctor No. 2 reported that he believed it was critical that there be a study of the pre-hardened state of Norian cement before it was used in live patients, because in its pre-hardened state, the cement had the potential to interact with tissues and blood in a way that hardened Norian cement did not.

46. On or about April 12, 2001, on behalf of Synthes, Person No. 3 caused an MDR problem report to be filed with the FDA for each of the two adverse events that had occurred when Doctor No. 1 used Norian CRS off-label in the two percutaneous kyphoplasty surgeries to treat VCFs.

47. On or about October 22, 2001, Synthes, defendant NORIAN and Richard E. Bohner learned from the head of the regulatory staff at Synthes Spine, known to the grand jury (Person No. 6), that Norian XR would not be cleared by the FDA for a vertebroplasty indication via a 510(k) pre-market notification, but could only be approved by the FDA for a vertebroplasty indication via pre-market approval (PMA), if supported by clinical trials.

48. In or about November 2001, at an annual Synthes Spine sales meeting, Synthes educated its Spine sales force on the Synthes System of providing Norian SRS-R and Cavity Creation System instruments for vertebroplasty surgeries to treat VCFs.

49. In or about November 2001, at the annual Synthes Spine sales meeting, Synthes presented Doctor No. 2 to speak to the Spine sales force about vertebroplasty and kyphoplasty surgeries to treat VCFs. Doctor No. 2 discussed the serious complications of vertebroplasty and kyphoplasty surgeries to treat VCFs, including leakage of cement into the venous system, which could cause pulmonary embolism and death.

50. In or about November 2001, officials at Synthes held a Management Review Board ("MRB") meeting. MRB meetings were quarterly meetings at which projects were presented and discussed. The fall 2001 MRB meeting was attended by Michael D. Huggins and Thomas B. Higgins, a high-ranking executive of Synthes known to the grand jury (Person No. 7), Person No. 1 and Person No. 4. At the fall 2001 MRB meeting, Person No. 1 presented a proposal for an IDE study, that is, a clinical study to obtain the FDA's approval of SRS-R in a vertebroplasty indication to treat VCFs; however, Person No. 7 decided that Synthes would not pursue an IDE study, but instead "get a few sites to perform 60-80 procedures and help them publish their clinical results."

51. In or about November 2001, based on Doctor No. 2's presentation on vertebroplasty and kyphoplasty surgeries at the annual Synthes Spine sales meeting, and the serious nature of the complications that Doctor No. 2 discussed, Person No. 7 decided that Synthes would not introduce the Cavity Creation System in March 2002 and instead directed that

a limited test market would be begun, and "at least 50 patients followed up," before deciding whether to introduce the Cavity Creation System.

52. In or about November 2001, following the fall 2001 MRB Meeting, Person No. 7 invited Doctor No. 2 to a meeting to discuss with Doctor No. 2 why he was taking such a cautious approach to vertebroplasty, which at that time was growing in popularity among spine surgeons. Doctor No. 2 explained that because hundreds of thousands of older persons had VCFs every year, vertebroplasty could change the standard of care and needed to be investigated. Doctor No. 2 explained that, in his view, clinical studies – which would be expensive and time-consuming – were needed. When Person No. 7 responded that Synthes had performed clinical studies on other devices in the past, and they had not worked, Doctor No. 2 reiterated that clinical studies, in which the investigators were independent of the party providing the investment, were essential.

53. On or about December 20, 2001, pursuant to Synthes's application, the FDA cleared Norian SRS as a general bone void filler via a 510(k) pre-market notification, with a label stating that SRS was intended to fill only bony voids that were "not intrinsic to the stability of the bony structure," in the extremities, spine and pelvis, and further warning that SRS was not to be mixed with any other substance.²

54. On or about May 8, 2002, Synthes and defendant NORIAN, through their agents, Person No. 1, Person No. 6, Person No. 8, Person No. 9 and Person No. 10, known to the grand

² The Norian cement to which barium sulphate was added to form Norian XR and that makes up Norian SRS and Norian CRS is not identical to any other calcium phosphate-based bone cement on the market. Rather, it is a unique formulation that was developed at NORIAN in the 1990s after hundreds of different formulations were tried there and rejected. The final formulation, with its limited strength characteristics, was optimized for the filling of voids in non-spinal metaphyseal bone, which is located in long bones such as the tibia and femur. Norian's unique powder blend includes calcium-based components that – at the time of use – are mixed with a sodium phosphate solution. PMMA, on the other hand, does not contain calcium. Norian XR cannot be used in traditional, high-pressure vertebroplasty procedures because it is too thick, and high pressure can cause its liquid and suspended particle components to separate/dewater. When PMMA is used in vertebral surgeries in which a cavity is created, such as the surgeries in which Norian XR was used, it is typically used in a more viscous state than the runny PMMA that is used in traditional vertebroplasty surgeries.

jury, participated in a telephone conference call with representatives of the FDA concerning Norian XR. During the conference call, the FDA representatives stated that they were concerned over the imprecision of the spine indication in the current indication for use of bone void fillers, and that they understood that surgeons, as a part of their practice of medicine, were using bone void fillers in the spine for load-bearing indications. The FDA asked that Synthes and defendant NORIAN provide additional labeling for Norian XR that specified that spinal load-bearing indications, such as vertebroplasty, were not included in the current indication for use. Synthes and NORIAN, through their agent, Person No. 6, promised the FDA that they would not promote Norian XR for vertebroplasty or other load-bearing indications without the appropriate regulatory authority. Synthes and NORIAN, through Person No. 6, added that they believed that such labeling would create an uneven playing field, as no other manufacturers of other bone void fillers had such labeling. The FDA continued to insist on such labeling.

55. In or about late June 2002, Doctor No. 2 and his colleague, another prominent surgeon known to the grand jury (Doctor No. 3), informed Synthes, defendant NORIAN and Thomas B. Higgins, among others, that they had performed pilot studies at the University of Washington with Norian SRS which showed that even small amounts of SRS could generate formation of large volumes of blood clot if SRS escaped from bone into the venous circulation (the "University of Washington studies" or the "pilot studies"). The pilot studies on human blood in test tubes showed that the calcium contained in the unique formulation of Norian SRS had a unique interaction with blood, providing both a surface on which clot could form and a chemical stimulus to clot formation. The pilot studies further showed dramatic clotting of a pig's lung veins – consistent with the human blood tests -- following injection of a small amount of SRS.³

³ By contrast, any risk of embolus that PMMA may pose comes not from how its components interact with blood – PMMA is not known to cause or accelerate blood clots – but from liquid PMMA escaping into the venous system and only then hardening (polymerizing) into a bolus that can obstruct blood flow. Any such risk is even less when PMMA is injected in a more polymerized state, as in kyphoplasty procedures.

56. On or about June 28, 2002, Doctor No. 2 and Doctor No. 3 reported some of their findings from their pilot studies with Norian SRS to the FDA on an MDR problem report form.

57. On or about October 31, 2002, the FDA issued a Public Health Web Notification ("the Web Notification") to inform the public about complications that had been reported related to vertebroplasty and kyphoplasty surgeries to treat VCFs. The Web Notification advised that the reported complications were related to the leakage of PMMA during surgeries to treat VCFs, and that those reported complications included pulmonary embolism, respiratory and cardiac failure, and death. The Web Notification stated that PMMA had not been specifically evaluated for the treatment of VCFs, and that there had been "no prospective, randomized, controlled trials to characterize the long-term safety or effectiveness" of either type of surgery to treat VCFs. The Web Notification added that doctors usually modified PMMA to use it in treating VCFs by increasing the amount of contrast agent and changing its handling properties, and that there were "no standardized formulations, biomechanical standards or safety guidelines for the types or amounts of opacifying additives used."

58. In or about November 2002, Person No. 6 informed Synthes through its employees, Person No. 1 and Person No. 4, and Thomas B. Higgins and Richard E. Bohner, of the October 31, 2002 FDA Web Notification.

59. On or about November 6, 2002, Person No. 10 sent an email to an employee of Synthes who worked in the Spine Regulatory group. The identity of this employee, who was responsible for the Norian XR Special 510(k) submission and was supervised by Person No. 6, is known to the grand jury (Person No. 11). Person No. 10's email concerned Norian XR and reminded Person No. 11 that, during the May 8, 2002 conference call with the FDA, Synthes and defendant NORIAN had promised the FDA that "the material would not be marketed for spinal indications such as vertebroplasty."

60. In or about December 2002, Person No. 12 and Person No. 13, members of Synthes's Spine Professional Services group whose identities are known to the grand jury, met

with and informed Person No. 8, the product manager for Norian XR, that Synthes could not train surgeons to use Norian XR to treat VCFs, as it would be illegal because such training would constitute “off-label” promotion of Norian XR, and unethical because the risks of Norian XR accelerating blood clot formation should it leak from the vertebral bodies into the venous system – as shown by the pilot studies – needed to be studied more closely before Norian XR was used to treat VCFs.

61. On or about December 16, 2002, Person No. 11 sent an email to Person No. 1, Person No. 4, Person No. 6, Person No. 8, Person No. 9 and Person No. 10 concerning Synthes’s Norian XR Special 510(k) pre-market notification, which Synthes had submitted on November 18, 2002 without any labeling specifying that spinal load-bearing indications, such as vertebroplasty, were not included in Norian XR’s indication for use. The email stated that “FDA is having a meeting today with regards to labeling. They are still pushing for specific wording with regards to no vertebroplasty and non load bearing only and will get back to us in a day or so with comments from the meeting.”

62. On or about December 18, 2002, Person No. 11 gave to Person No. 4, Person No. 6 and Person No. 8 an internal Synthes Regulatory Sign-Off sheet concerning Norian XR Calcium Phosphate Bone Cement, which stated “[p]lease sign below to indicate acceptance of the attached changes to page 25 of the 510k – addition of wording to the Warning section of the product insert.” The Regulatory Sign-Off sheet was attached to page 25 of the Norian XR Special 510(k) submission. Person No. 4, Person No. 6 and Person No. 8 signed the Regulatory Sign-Off sheet to indicate their acceptance of the addition of the warning language “not intended for treatment of vertebral compression fractures” on behalf of Synthes. Person No. 11 signed the Regulatory Sign-Off sheet as the person responsible for the Norian XR Special 510(k) pre-market notification.

63. On or about December 19, 2002, pursuant to Synthes’s Special 510(k) pre-market notification, the FDA cleared Norian XR as a general bone void filler, with a label stating that

XR was intended to fill only bony voids that were “not intrinsic to the stability of the bony structure” in the extremities, spine and pelvis, and further warning that XR was “not intended for treatment of vertebral compression fractures.”

64. On or about January 13, 2003, when a spine surgeon known to the grand jury (Doctor No. 4) used SRS that had been back-table mixed with barium sulfate in a surgery using the Cavity Creation instruments to treat VCFs, the patient became immediately hypotensive and died on the operating table (“the first death”). Doctor No. 4 could not rule out the back-table mixed Norian SRS as a cause of the first death. A Synthes Spine sales representative was present in the operating room during the surgery that resulted in the first death.

65. On or about January 28, 2003, Richard E. Bohner sent an email to Thomas B. Higgins, with a copy to Michael D. Huggins, urging that management send an email to the Spine sales force, notifying them that Norian XR should not be promoted for off-label uses. In his email, Bohner argued that Higgins, as President of the Spine Division, should send the proposed email about off-label promotion to the Spine sales force. In his email outlining the proposed communication to the Spine sales force, Bohner gave an example to clarify what off-label uses were forbidden: “[f]or example, the FDA has required us to include the following warning in the product insert: ‘not intended for treatment of vertebral compression fractures.’” After Bohner sent his email to Higgins and Huggins, however, no communication that included both the warning label for Norian XR and an admonition that Norian XR should not be promoted for off-label use was sent to the Spine sales force.

66. On or about February 25, 2003, Person No. 11 sent an email to the FDA, asking the FDA representative who had handled the clearance of Norian XR whether, “as long as we clearly inform surgeons that Norian XR must be used with supplemental fixation (i.e., pedicle screws), we can indicate it [XR] for compression fractures in the spine?”

67. On or about February 26, 2003, the FDA representative answered that Synthes could not do so, stating “[u]se in treating compression fractures of the spine is not a cleared use

for any of the bone void fillers (MQV product code). This indication is considered a new intended use and requires a PMA and clinical data. Even with proper fixation, the bone void filler in this situation (vertebral compression fractures) would not be used in a way that is 'non-intrinsic to the stability of the bony structure,' which is what the indication for the MQV bone void fillers require."

68. On or about February 28, 2003, Person No. 11 forwarded to Person No. 6, Person No. 8 and Person No. 9 the February 25, 2003 email that Person No. 11 had sent to the FDA, along with the email in response from the FDA.

69. On or about April 4, 2003, Michael D. Huggins forwarded an updated version of the FDA's October 31, 2002 Web Notification – concerning complications that had been reported concerning the leakage of PMMA during vertebroplasty and kyphoplasty surgeries to treat VCFs – to Thomas B. Higgins and Richard E. Bohner, as well as Person No. 8 and others.

70. On or about September 19, 2003, when a spine surgeon known to the grand jury (Doctor No. 5) used Norian XR in a surgery using Cavity Creation instruments to treat VCFs, the patient died on the operating table after suffering a hypotensive episode ("the second death"). Doctor No. 5 noted a cement leak, and believed that it was the cause of the episode, and could not rule out Norian XR as a cause of the second death. A Synthes Spine sales representative was present in the operating room during the surgery that resulted in the second death.

71. On or about September 26, 2003, Person No. 8 and Person No. 10 met with a spine surgeon known to the grand jury (Doctor No. 6), who told them that he believed that Norian XR was "potentially dehydrating and causing episodes of hypotension." Doctor No. 6 also told Person No. 8 and Person No. 10 that, because the Norian XR "test market" was collecting information from surgeons performing vertebroplasty and kyphoplasty surgeries to treat VCFs, he believed that Synthes was required to go to each IRB of each hospital participating in the "test market." Doctor No. 6 also told Person No. 8 and Person No. 10 that, in light of Synthes's "test market" activities, Synthes should go to the FDA immediately to negotiate the removal of the

warning on the Norian XR label, "not intended for treatment of vertebral compression fractures." Doctor No. 6 also told Person No. 8 and Person No. 10 that, in his view, Synthes had risk management problems and needed more oversight of its clinical and compliance issues.

72. On or about October 1, 2003, Person No. 8 sent the minutes of the September 26, 2003 meeting among Doctor No. 6, Person No. 8 and Person No. 10 to Thomas B. Higgins and a vice president of biomaterials product development known to the grand jury (Person No. 14), among others.

73. On or about October 1, 2003, Person No. 14 forwarded the minutes of the meeting between Doctor No. 6, Person No. 8 and Person No. 10 to Thomas B. Higgins and Richard E. Bohner, stating he (Person No. 14) agreed in part with Doctor No. 6's comments about Synthes's need for better risk management, and asking Bohner to raise this issue with Michael D. Huggins, among others.

74. On or about October 16, 2003, Person No. 8 forwarded to John J. Walsh the February 25, 2003 email that Person No. 11 had sent to the FDA (asking whether Norian XR could be indicated for compression fractures in the spine so long as Synthes informed surgeons that Norian XR must be used with supplemental fixation) along with the adverse response that Person No. 11 had received from the FDA.

75. On or about November 10, 2003, Michael D. Huggins sent an email to Thomas B. Higgins, John J. Walsh and others, attaching a press release from a company known to the grand jury, which company was a competitor of Synthes, and which was developing a bone void filler for use in the treatment of VCFs ("Company B"). The press release announced that Company B had obtained the FDA's permission, via an IDE, for Company B to conduct clinical trials of its bone void filler in vertebroplasty surgeries for the treatment of VCFs.

76. On or about November 10, 2003, Person No. 8 sent an email to Michael D. Huggins, Thomas B. Higgins, John J. Walsh and Richard E. Bohner, attaching Synthes's initial proposal for obtaining an IDE from the FDA so that Synthes, like Company B, might also obtain

permission to conduct clinical trials of its bone void filler in vertebroplasty surgeries for the treatment of VCFs (“the IDE proposal”). Synthes never shared the IDE proposal with the FDA. After discussing the Norian XR “test market” and the fact that two patient deaths had occurred as part of the “test market,” the IDE proposal discussed competitive activity with other products, stating:

Norian XR is the only product that the FDA required to add the [warning bullet]. From a competitive standpoint, Norian XR is at a significant disadvantage. All of our competitors are using this bullet as a selling point against Norian XR. Rightly so, many surgeons are listening.

The IDE proposal went on to state:

Currently, Norian XR is being used off-label to treat VCFs. The FDA has been very conservative regarding the treatment of VCFs and has issued numerous statements. . .cautioning companies. . .that the use of any material in vertebroplasty/kyphoplasty is off-label. The present state of the approved indication of Norian XR and the FDA bulletin puts Synthes in a compromising position. Synthes is at an increased legal risk with regards to product liability and medical malpractice. . .We recommend that Synthes pursue an IDE for the usage of Norian XR in treating VCFs. . .

77. On or about January 22, 2004, when a spine surgeon known to the grand jury (Doctor No. 7) used Norian XR in a surgery using Cavity Creation instruments to treat VCFs, the patient died on the operating table (“the third death”). A hypotensive event occurred, leading to pulmonary embolism; Doctor No. 7 could not rule out Norian XR as a cause of the third death. A Synthes Spine sales representative was present in the operating room during the surgery that resulted in the third death.

78. From on or about May 11 to on or about June 18, 2004, an investigator for the FDA conducted an unannounced on-site inspection of defendant NORIAN at the Development Center, 1230 Wilson Drive, West Chester, PA (“the FDA inspection” or “the inspection”). The FDA inspection focused on Norian XR.

79. On or about June 18, 2004, at the close of the FDA inspection, the investigator for the FDA issued to defendant NORIAN the FDA’s observations concerning the inspection (the

“483 observations”). Among other things, the FDA observed that Synthes and defendant NORJAN:

- a. did not submit an IDE application to the FDA prior to initiating the Norian XR “test market,” whose objectives included evaluating the efficacy of using Norian XR and obtaining safety data based on patient complication rates as reported to Synthes by surgeons performing vertebroplasty or kyphoplasty procedures to treat fractures of the vertebrae; and
- b. shipped Norian XR in interstate commerce for the purpose of use in vertebroplasty or kyphoplasty procedures to treat fractures of the vertebrae, an indication for which Norian XR had not been cleared or approved by the FDA.

THE CONSPIRACY

80. From in or about May 2002 through at least fall 2004, in the Eastern District of Pennsylvania and elsewhere, defendant

NORIAN CORPORATION,

together with others known and unknown to the grand jury, agreed, combined, and conspired to:

- a. defraud the United States and its agencies by impeding, impairing, and defeating the lawful functions of the FDA to protect the health and safety of the public by ensuring that medical devices marketed and distributed in the United States were safe and effective for their intended uses, that the labeling of such devices bore true and accurate information, and that clinical investigation of significant risk devices on humans was overseen by the FDA; and
- b. commit an offense against the United States with the intent to defraud or mislead, by introducing into interstate commerce an adulterated and misbranded medical device, Norian XR, for the intended use of treating VCFs through vertebroplasty and kyphoplasty procedures, when Norian XR had not received either pre-market approval or pre-market clearance for that intended use, and when the label of Norian XR bore a warning that the device

was “not intended for treatment of vertebral compression fractures,” in violation of Title 21, United States Code, Sections 331(a) and 333(a)(2); and

c. commit an offense against the United States by knowingly and willfully making materially false, fictitious, and fraudulent statements and representations and falsifying and concealing material facts in a matter within the jurisdiction of the Food and Drug Administration (“FDA”), an agency of the executive branch of the United States, in violation of Title 18, United States Code, Section 1001.

MANNER AND MEANS

It was part of the conspiracy that:

81. Defendant NORIAN, Synthes, Michael D. Huggins and Thomas B. Higgins developed Norian XR for the treatment of VCFs by adding barium sulfate to Norian SRS.

82. Despite the SRS label, which as cleared by the FDA in December 2001 stated that SRS was intended to fill only bony voids that were “not intrinsic to the stability of the bony structure,” and further warned that SRS was not to be mixed with any other substance, defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins and Richard E. Bohner approved, organized and sponsored an illegal vertebroplasty “test market” for SRS, that is, a “test market” for the use of SRS back-table mixed with barium sulfate to treat VCFs.

83. Despite the Norian XR label, which as cleared by the FDA in December 2002 stated that Norian XR was intended to fill only bony voids that were “not intrinsic to the stability of the bony structure,” and further warned that Norian XR was “not intended for treatment of vertebral compression fractures,” defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh approved, organized, sponsored and attended surgeon forums at which spine surgeons were taught how to use Norian XR to treat VCFs.

84. Defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh conducted an unauthorized clinical trial of Norian XR for the

treatment of VCFs through an illegal “test market” in which defendant NORIAN and others sold Norian XR to spine surgeons for the intended use of treating VCFs, and gathered safety and efficacy information from those surgeons concerning their use of Norian XR in vertebroplasty and kyphoplasty surgeries to treat VCFs, in order to assess the complications rate of XR and determine whether, in the defendant’s view, it was too high.

85. Defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh concealed from spine surgeons and from Synthes’s own Spine sales force the warning bullet on the Norian XR label, “not intended for treatment of vertebral compression fractures.”

86. Defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh concealed from spine surgeons and from Synthes’s own Spine sales force the pilot study test results indicating that a small amount of Norian SRS and/or Norian XR could accelerate blood clot formation if it escaped from bone into the venous circulation.

87. Defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins and Richard E. Bohner, without having medical professionals review the first death, failed and refused to file an MDR problem report concerning the first death, in order to conceal the first death from the FDA, from spine surgeons and from Synthes’s own Spine sales force.

88. Defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh introduced into interstate commerce an adulterated and misbranded medical device, Norian XR, for the intended use of treating VCFs through vertebroplasty and kyphoplasty procedures.

89. Defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh, without having medical professionals review the second or third deaths, caused to be filed MDR problem reports with the FDA concerning the second and third deaths, which reports were brief, vague and did not mention the terms “vertebroplasty,” “kyphoplasty,” or “vertebral compression fracture” in order to conceal from the FDA and spine

surgeons the fact that the second and third deaths had occurred during surgeries to treat VCFs, in which cement leakage had been noted.

90. After the third death, defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh failed and refused to recall and remove Norian XR from the market and failed and refused to notify the FDA that Norian XR might pose a significant risk to human safety, but instead unrestricted the inventory of Norian XR so that Norian XR could be purchased by any surgeon or hospital.

91. After the third death, having trained approximately fifty carefully selected spine surgeons how to use Norian XR to treat VCFs, and having unrestricted the inventory of Norian XR so that it could be purchased by any surgeon or hospital, defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh informed the Spine sales force that Norian XR was not the subject of a recall and was not being pulled from the market, all of which led to several additional off-label surgeries to treat VCFs in March and April 2004.

92. In order to lull the FDA, to impair and impede its lawful functions, including its function of overseeing device manufacturers, and to avoid FDA scrutiny into the three deaths that had occurred during the illegal "test market," during May and June 2004 defendant NORIAN, Synthes, Michael D. Huggins, Richard E. Bohner and John J. Walsh knowingly made a series of false statements to an investigator for the FDA, in which they concealed their knowledge that Norian XR and its predecessor device, Norian SRS, had each been marketed, promoted and tested on human subjects without FDA oversight for the treatment of VCFs, an intended use that had been neither cleared nor approved by the FDA.

93. In order further to lull the FDA, to impair and impede its lawful functions, including its function of overseeing device manufacturers, and to avoid FDA scrutiny into the three deaths that had occurred during the illegal "test market," during July 2004 defendant NORIAN, Synthes, Michael D. Huggins, Richard E. Bohner and John J. Walsh knowingly made

a series of false statements to the FDA in response to the FDA's observations concerning the inspection the FDA conducted in May and June 2004.

OVERT ACTS

In furtherance of the conspiracy, defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins, John J. Walsh and others known and unknown to the grand jury, committed the following overt acts in the Eastern District of Pennsylvania and elsewhere:

1. On various dates from in and about summer 2002 through fall 2002, Michael D. Huggins, Thomas B. Higgins and Richard E. Bohner conducted an illegal "test market" for use of SRS and the Cavity Creation System to treat VCFs, by:

a. directing employees of Synthes who are known and unknown to the grand jury, including Person No. 1, Person No. 8 and Person No. 9, to create a recipe for mixing SRS with barium sulfate to make it more radiopaque, a procedure commonly known as "back-table mixing;"

b. distributing the recipe for back-table mixing of SRS and barium sulfate to spine surgeons for their use in vertebroplasty and kyphoplasty surgeries to treat VCFs;

c. training spine surgeons how to use SRS that had been back-table mixed with barium sulfate in vertebroplasty and kyphoplasty surgeries to treat VCFs;

d. directing employees of Synthes including Person No. 1, Person No. 4, Person No. 8 and Person No. 9 to attend vertebroplasty and kyphoplasty surgeries in which SRS mixed with barium sulfate was used to treat VCFs; and

e. gathering safety and efficacy information from spine surgeons who were using SRS mixed with barium sulfate in vertebroplasty and kyphoplasty surgeries to treat VCFs.

2. On or about September 17, 2002, at a Spine MRB meeting, Person No. 8 made a presentation to Person No. 7, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner, and others to update them on (a) the Norian XR project; (b) the "Test Market that began in September

2002” involving use of Norian SRS in the spine; and (c) “several additional studies to be completed by [the University of Washington] Harborview in Seattle.”

3. On or about November 18, 2002, defendant NORIAN and Synthes caused Person No. 11 to submit to the FDA the 510(k) submission for Norian XR without the language requested by the FDA in the May 8, 2002 meeting, that is, without any labeling specifying that spinal load-bearing indications, such as vertebroplasty, were not included in Norian XR’s indication for use.

4. On or about January 16, 2003, Michael D. Huggins, Richard E. Bohner and Thomas B. Higgins held a meeting with Person No. 8, and others known and unknown to the grand jury, including a vice president of spine product development known to the grand jury (Person No. 15) to approve a market introduction plan for Norian XR (“the Norian XR MIP”) that described a supposed market for the use of Norian XR in the iliac crest, which is a part of the hip, when, in fact, no such market existed or plan was intended.

5. On or about January 16, 2003, at the Norian XR MIP meeting, after Person No. 8 reported to the meeting participants information regarding the January 13, 2003 death of Doctor No. 4’s patient during a surgery using the Cavity Creation instruments to treat VCFs (hereafter the “first death”), Michael D. Huggins, Thomas B. Higgins and Richard E. Bohner postponed approval of the Norian XR MIP and directed Person No. 8 to contact Doctor No. 4 to find out more information concerning the first death.

6. On or about February 10, 2003, Michael D. Huggins, Thomas B. Higgins and Richard E. Bohner reconvened the Norian XR MIP meeting with Person No. 8 and others known and unknown to the grand jury, including Person No. 15, and approved the Norian XR MIP described in the preceding two paragraphs.

7. In or about late April 2003, at a meeting of Synthes’s board of directors, Michael D. Huggins approached a trauma surgeon who was also a member of Synthes’s board of directors and who is known to the grand jury (Doctor No. 8), told Doctor No. 8 about the first death, and

about the two adverse hypotensive events that had occurred with Doctor No. 1's patients, and obtained Doctor No. 8's agreement to participate in an upcoming "Safety Meeting" concerning whether or not Norian XR was safe enough to bring to market.

8. On or about July 18, 2003, after having previously received from Person No. 8 written materials concerning the pilot studies, the two adverse hypotensive events that had occurred with Doctor No. 1's patients, and details regarding the first death, Michael D. Huggins, Thomas B. Higgins and Richard E. Bohner held a "Safety Meeting" with Person No. 8, Person No. 10 and others known to the grand jury, including Doctor No. 8 (who participated by teleconference), for the declared purpose of determining whether Norian XR was safe enough to bring to market.

9. On or about July 18, 2003, at the Safety Meeting, after hearing a presentation by Person No. 8 on the pilot studies, the two adverse hypotensive events that had occurred with Doctor No. 1's patients, and the first death, Michael D. Huggins, Thomas B. Higgins and Richard E. Bohner decided to continue the illegal Norian XR "test market" that had begun in the summer of 2002 with SRS-R, in order to assess whether the level of risk from using Norian XR to treat VCFs was acceptable, or instead, too high.

10. On or about August 14, 2003, Michael D. Huggins and Thomas B. Higgins held a strategic planning meeting attended by Doctor No. 3 and other doctors, both known and unknown to the grand jury, as well as Person No. 8, Person No. 10, Person No. 14 and Person No. 15 (the "Strategic Planning Meeting").

11. On or about August 14, 2003, at the Strategic Planning Meeting, Michael D. Huggins noted that Synthes had a "poor record of PMA approvals," and Huggins and Thomas B. Higgins directed that the illegal Norian XR "test market" would continue, despite a presentation made at the meeting by Person No. 8 on vertebroplasty and Norian XR and a recommendation by Doctor No. 3 that an FDA study of Norian XR be conducted to gain approval for vertebroplasty.

12. On or about August 15 and 16, 2003, Michael D. Huggins, Thomas B. Higgins, and Richard E. Bohner held the first surgeon training meeting of the illegal Norian XR "test market" in San Diego, California (the "San Diego surgeon training"), which included Synthes Spine sales representatives along with spine surgeons who were selected by Synthes based on their experience in performing vertebroplasty, and whose expenses to travel to and attend the training were paid for by Synthes.

13. On or about August 15 and 16, 2003, at the San Diego surgeon training organized by Michael D. Huggins, Thomas B. Higgins and Richard E. Bohner, lectures and power point presentations were given to the attendees concerning the use of Norian XR in vertebroplasty to treat VCFs, and a cadaver lab was held during which the surgeons injected Norian XR into the vertebral bodies of cadavers.

14. On or about August 15 and 16, 2003, at the San Diego surgeon training, Synthes, through Person No. 8, distributed notebooks to the attending spine surgeons and sales representatives which thanked them for participating in the Norian XR "test market." The notebooks included forms⁴ to be used in reordering Norian XR ("test market reorder forms" or "TM forms"), and contained instructions to the sales representatives that they could not reorder Norian XR unless they filled out the "test market" reorder forms with information about each surgery performed with Norian XR.

15. On or about September 16, 2003, Thomas B. Higgins invited a spine surgeon known to the grand jury (Doctor No. 9) to give a lecture to the Spine sales force at the Spine Annual Meeting, November 22-24, 2003, concerning the use of Norian XR in vertebroplasty to treat VCFs.

⁴ The information that Synthes requested in the "test market" reorder forms included whether the patient had a previous VCF; whether the bone was osteoporotic; the number of levels treated (referring to levels of the vertebrae); the age of the fracture; the percentage of compression; and whether postural reduction was attempted.

16. On or about September 19 and 20, 2003, Michael D. Huggins, Thomas B. Higgins and Richard E. Bohner held the second surgeon training meeting of the illegal Norian XR “test market” in Charlotte, North Carolina (the “Charlotte surgeon training”), which followed a format identical in substance to the San Diego surgeon training, and which again included spine surgeons selected by Synthes based on their experience in performing vertebroplasty, and whose expenses to travel to and attend the training were paid for by Synthes.

17. On or about September 23, 2003, defendant NORIAN and Synthes, through its agents, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh, held a meeting to discuss the second death, the death of Doctor No. 5’s patient, which had occurred on September 19, 2003, with others known and unknown to the grand jury, including Person No. 8, Person No. 10, and Person No. 14 (the “second death meeting”).

18. On or about September 23, 2003, at the second death meeting, after a discussion among the participants recognizing that Doctor No. 5 had “noted a cement leak during injection and feels this was the cause of the incident,” and that, according to Doctor No. 5, “the sales consultant ‘pushed’ this product on him and was unclear as to its status on the market,” Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh directed Person No. 8 to contact spine surgeons to obtain their views on the possible causes of the second death; review complications of surgeries associated with the elderly patient population; and research how many MDR problem reports had been filed concerning PMMA, vertebroplasty and kyphoplasty.

19. On or about October 15, 2003, Person No. 8 reported back to Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh that:

a. the spine surgeons had been contacted to obtain their views on the possible causes of the second death, and while “one surgeon out of 19 has decided not to use Norian XR until more information is available,” “no one is blaming Norian XR”;

b. elderly patients undergoing surgeries had “increased patient morbidity”;

and

c. numerous MDR problem reports had been filed regarding PMMA, vertebroplasty and kyphoplasty.

20. On or about October 24, 2003, defendant NORIAN and Synthes, through their agents, Person No. 8 and Person No. 15, held a meeting to plan the upcoming Norian XR surgeon training forums. At the October 24, 2003 meeting, which was attended by employees of Synthes and Doctor No. 4, Doctor No. 7 and Doctor No. 9, the participants agreed that:

a. Synthes would “target spine surgeons as the primary attendees,” and spine sales consultants would attend the forums with their surgeons, and

b. Doctor No. 4, Doctor No. 7 and Doctor No. 9 would serve as faculty chairmen for the surgeon forums, which would include both lectures and cadaver labs.

21. On or about November 22, 2003, Thomas B. Higgins caused Person No. 15 to make a presentation to the Spine sales force at the Spine Annual Meeting, concerning Norian XR, during which Person No. 15 stated that Norian XR’s approved indications included the spine but not vertebral compression fractures, but which was misleading in that Person No. 15 did not disclose or otherwise state that Norian XR’s label bore the specific warning, “not intended for treatment of vertebral compression fractures.”

22. On or about November 24, 2003, Thomas B. Higgins caused Doctor No. 9 to speak about vertebroplasty and Norian XR to the Spine sales force, at the Spine Annual Meeting.

23. On or about December 10, 2003, Richard E. Bohner wrote a memorandum for distribution to Spine sales consultants and managers, stating that Norian XR was intended only for bony voids or defects that were not intrinsic to the stability of the bony structure, and that Norian XR was intended to be placed or injected into bony voids in the extremities, spine and pelvis, and warned against off-label promotion of Norian XR, but which did not disclose or otherwise state the specific warning on Norian XR’s label, “not intended for treatment of vertebral compression fractures.”

24. On or about December 1, 2003, John J. Walsh approved the Norian XR Technique Guide for release to the Spine sales force, despite the fact that the Technique Guide did not disclose or otherwise state the specific warning on Norian XR's label, "not intended for treatment of vertebral compression fractures," and notwithstanding the fact that the Technique Guide contained x-rays of VCFs, some of which were x-rays of the spine (with depiction of injected SRS) of Doctor No. 4's patient who had died on the operating table when the doctor used SRS that had been back-table mixed with barium sulfate in a surgery to treat VCFs.

25. On or about December 31, 2003, defendant NORIAN and Synthes released Norian XR for sale beyond the initial "test market."

26. On or about January 10 and 11, 2004, Michael D. Huggins, Thomas B. Higgins, and Richard E. Bohner held the first surgeon forum following the illegal Norian XR "test market" in Dallas, Texas (the "Dallas surgeon training"), at which they delegated to Doctor No. 4 the responsibility to inform the surgeons that Norian XR's label bore the warning, "not intended for treatment of vertebral compression fractures."

27. On or about January 22, 2004, Thomas B. Higgins traveled to San Diego, California, in order to attend the upcoming San Diego surgeon forum scheduled for January 23 through 25, 2004, which surgeon forum was cancelled early in the morning of January 23, 2004 after the third death, that is, the death of Doctor No. 7's patient.

28. On or about February 12, 2004, defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh made the decision not to recall or remove Norian XR from the market, but instead to unrestrict the inventory of Norian XR, in order to continue marketing Norian XR despite their knowledge of its potentially harmful effects.

29. On or about February 10, 2004, defendant NORIAN, Synthes, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh sent or caused to be sent "dear surgeon" letters to spine surgeons, admitting that use of Norian XR to treat VCFs was off-

label but explaining that such use was off-label because it was “intrinsic to the stability of the bony structure,” and remaining silent about the warning bullet, while falsely suggesting an equivalence between Norian XR and PMMA when there was none, and further omitting to state that:

- a. Synthes had conducted a “test market” in which it had trained surgeons to use Norian XR to treat VCFs;
- b. the pilot studies showed that the Norian cements appeared to be thrombogenic agents; and
- c. three patients had died on the operating table when spine surgeons had used Norian XR off-label to treat VCFs.

These various statements and omissions were all made in order to: impair and impede the FDA’s function of preventing unauthorized clinical trials, such as the unauthorized clinical trial that defendant NORIAN and others were conducting with Norian XR; deceive the FDA concerning defendant NORIAN and others’ off-label promotion of Norian XR and the dangers posed by Norian XR; and deceive the doctors whom defendant NORIAN and others had trained on the off-label use of Norian XR as to the doctors’ liability to their patients from whom the doctors might not have obtained informed consent.

30. On or about March 24, 2004, defendant NORIAN and Synthes, through their agent, a regulatory compliance manager known to the grand jury (Person No. 16) received an autopsy report on the third death (“the autopsy report”) and forwarded the autopsy report to John J. Walsh and others known to the grand jury.⁵

⁵The autopsy report stated that the patient had a history of osteoporosis and a vertebral compression fracture, for which a kyphoplasty surgery had been performed, and that at autopsy, foreign material was found in the L2 vertebral body and in microscopic vessels of the lungs. Despite the new information contained in the autopsy report, which had not been reported to the FDA in the original MDR problem report, neither Synthes nor defendant NORIAN filed a supplemental MDR problem report on the third death with the FDA or recalled or removed Norian XR from the market before the FDA inspection.

31. On or about May 12, 2004, defendant NORIAN and Synthes, through Person No. 8, made false and fraudulent statements to an investigator for the FDA, in that Person 8 denied that she had ever promoted the use of Norian XR off-label to treat VCFs.

32. On or about May 19, 2004, defendant NORIAN and Synthes, through the Synthes director of regulatory compliance, whose identity is known to the grand jury (Person No. 17), and Person No. 16, made false and fraudulent statements to an investigator for the FDA by stating that, in August 2003, Synthes did not have a Vertebroplasty System.

33. On or about May 19, 2004, defendant NORIAN and Synthes, through Person No. 8, made additional false and fraudulent statements to an investigator for the FDA, in that Person No. 8 stated that in August 2003, Synthes did not have a Vertebroplasty System.

34. On or about May 20, 2004, defendant NORIAN and Synthes, through John J. Walsh, made false and fraudulent statements to an investigator for the FDA, in that Walsh caused to be presented to the FDA investigator a memorandum which stated, in part, that “[w]ith the exceptions spelled out in the Warning and Contraindications section of the Instructions for Use, the use of Norian XR in association with Vertebroplasty and Kyphoplasty does not constitute ‘off-label’ use. Many uses of Norian XR in association with Vertebroplasty and Kyphoplasty are completely appropriate and ‘on-label.’”

35. On or about May 27, 2004, defendant NORIAN and Synthes, through Person No. 8, made false and fraudulent statements to an investigator for the FDA, in that Person No. 8 characterized the summer 2002 “test market” for SRS in the spine as surgeons mixing SRS with barium sulfate “on their own.”

36. On or about June 2, 2004, defendant NORIAN and Synthes, through Person No. 9, made false and fraudulent statements to an investigator for the FDA, in that Person No. 9 told the investigator from the FDA that he did not know the process for mixing Norian SRS with barium sulfate.

37. On or about June 7, 2004, defendant NORIAN and Synthes, through Michael D. Huggins, made false and fraudulent statements to an investigator for the FDA, in that Huggins told the investigator that the Norian XR “test market” discussed at the July 18, 2003 Safety Meeting involved approved indications for Norian XR.

38. On or about June 16, 2004, defendant NORIAN and Synthes, through Richard E. Bohner, made false and fraudulent statements to an investigator for the FDA, in that Bohner told the investigator that he knew nothing about a vertebroplasty “test market” for SRS.

39. On or about June 16, 2004, defendant NORIAN and Synthes, through Richard E. Bohner, made false and fraudulent statements to an investigator for the FDA, in that Bohner told the investigator that the 34 “test market” cases discussed at the July 18, 2003 Safety Meeting involved only data that Synthes had collected from what surgeons were doing on their own, rather than a test market conducted by Synthes.

40. On or about June 22, 2004, Michael D. Huggins, Thomas B. Higgins, Richard E. Bohner and John J. Walsh met with Person No. 10, Person No. 15, Person No. 16 and Person No. 17, in order to plan a response to the FDA’s 483 observations made after the FDA inspection, resulting in the false claims by defendant NORIAN and Synthes that:

- a. the Norian XR “test market” was for cleared indications, rather than the treatment of VCFs;
- b. the “test market” was not designed to obtain safety and efficacy information from surgeons about use of Norian XR to treat VCFs; and
- c. the two “test market” surgeon training meetings and the surgeon forum had not trained surgeons how to use Norian XR to treat VCFs.

41. On or about July 2, 2004, in a writing submitted to the FDA on behalf of defendant NORIAN and Synthes, John J. Walsh admitted that an IDE would be required if defendant NORIAN and Synthes were seeking to “establish the safety and efficacy of new uses for Norian XR. . .in the treatment of vertebral compression fractures,” but falsely stated that “at

the time of the test market activities,” defendant NORIAN and Synthes “did not . . . intend to market [Norian XR] for the treatment of vertebral compression fractures. Additionally, it was never our intent to suggest, in any way, that the product should be used for such purpose,” and that, defendant NORIAN and Synthes “did not promote [Norian XR] for the[] off-label uses” of treating vertebral compression fractures.

All in violation of Title 18, United States Code, Section 371.

COUNT TWO

THE GRAND JURY FURTHER CHARGES THAT:

On or about May 12, 2004, at West Chester, in the Eastern District of Pennsylvania, defendant

NORIAN CORPORATION,

through its agent, Person No. 8, in a matter within the jurisdiction of the Food and Drug Administration ("FDA"), an agency of the executive branch of the United States, knowingly and willfully made materially false, fictitious, and fraudulent statements and representations and falsified and concealed a material fact, in that Person No. 8 told an investigator from the FDA that she had never promoted Norian XR "off-label" for the treatment of VCFs, when, as Person No. 8 knew, she had promoted Norian XR "off-label" for the treatment of VCFs on more than one occasion.

In violation of Title 18, United States Code, Section 1001.

COUNT THREE

THE GRAND JURY FURTHER CHARGES THAT:

On or about May 19, 2004, at West Chester, in the Eastern District of Pennsylvania, defendant

NORIAN CORPORATION,

through its agent, Person No. 8, in a matter within the jurisdiction of the Food and Drug Administration ("FDA"), an agency of the executive branch of the United States, knowingly and willfully made materially false, fictitious, and fraudulent statements and representations and falsified and concealed a material fact, in that Person No. 8 told an investigator from the FDA that in August 2003, Synthes did not have a Vertebroplasty System, when, as Person No. 8 knew, in August 2003, Synthes had a Vertebroplasty System consisting of Norian XR and the cavity creation instruments.

In violation of Title 18, United States Code, Section 1001.

COUNT FOUR

THE GRAND JURY FURTHER CHARGES THAT:

On or about May 27, 2004, at West Chester, in the Eastern District of Pennsylvania, defendant

NORIAN CORPORATION,

through its agent, Person No. 8, in a matter within the jurisdiction of the Food and Drug Administration ("FDA"), an agency of the executive branch of the United States, knowingly and willfully made materially false, fictitious, and fraudulent statements and representations and falsified and concealed a material fact, in that Person No. 8 told an investigator from the FDA that the summer 2002 "test market" for SRS in the spine consisted of surgeons mixing SRS with barium sulfate on their own, when, as Person No. 8 knew, the summer 2002 "test market" for SRS in the spine involved Synthes creating a recipe for mixing SRS with barium sulfate; distributing that recipe to spine surgeons for use in vertebroplasty and kyphoplasty surgeries to treat VCFs; training spine surgeons how to use SRS that had been mixed with barium sulfate in vertebroplasty and kyphoplasty surgeries to treat VCFs; directing its employees to attend vertebroplasty and kyphoplasty surgeries in which SRS mixed with barium sulfate was used to treat VCFs; and gathering safety and efficacy information from spine surgeons who were using SRS in vertebroplasty and kyphoplasty surgeries to treat VCFs.

In violation of Title 18, United States Code, Section 1001.

COUNT FIVE

THE GRAND JURY FURTHER CHARGES THAT:

On or about June 7, 2004, at West Chester, in the Eastern District of Pennsylvania, defendant

NORIAN CORPORATION,

through its agent, Michael D. Huggins, in a matter within the jurisdiction of the Food and Drug Administration ("FDA"), an agency of the executive branch of the United States, knowingly and willfully made materially false, fictitious, and fraudulent statements and representations and falsified and concealed a material fact, in that Huggins told an investigator from the FDA that the Norian XR "test market" discussed at the July 18, 2003 Safety Meeting involved approved indications for Norian XR, when, as Huggins knew, the Norian XR "test market" involved the unapproved and warned-against indication of treating VCFs.

In violation of Title 18, United States Code, Section 1001.

COUNT SIX

THE GRAND JURY FURTHER CHARGES THAT:

On or about June 16, 2004, at West Chester, in the Eastern District of Pennsylvania, defendant

NORIAN CORPORATION,

through its agent, Richard E. Bohner, in a matter within the jurisdiction of the Food and Drug Administration ("FDA"), an agency of the executive branch of the United States, knowingly and willfully made materially false, fictitious, and fraudulent statements and representations and falsified and concealed a material fact, in that Bohner told an investigator from the FDA that he knew nothing about a vertebroplasty test market for SRS when, as Bohner knew, he was aware of the vertebroplasty test market for SRS.

In violation of Title 18, United States Code, Section 1001.

COUNT SEVEN

THE GRAND JURY FURTHER CHARGES THAT:

On or about June 16, 2004, at West Chester, in the Eastern District of Pennsylvania, defendant

NORIAN CORPORATION,

through its agent, Richard E. Bohner, in a matter within the jurisdiction of the Food and Drug Administration ("FDA"), an agency of the executive branch of the United States, knowingly and willfully made materially false, fictitious, and fraudulent statements and representations and falsified and concealed a material fact, in that Bohner told an investigator from the FDA that the 34 "test market" cases discussed at the July 18, 2003 Safety Meeting involved only data that Synthes had collected from what surgeons were doing on their own, rather than a test market conducted by Synthes when, as Bohner knew, the 34 "test market" cases involved data that Synthes had collected from surgeons whom Synthes had trained to mix SRS with barium sulfate for use in treating VCFs.

In violation of Title 18, United States Code, Section 1001.

COUNT EIGHT

THE GRAND JURY FURTHER CHARGES THAT:

On or about July 2, 2004, at West Chester, in the Eastern District of Pennsylvania,
defendant

NORIAN CORPORATION,

through its agent, John J. Walsh, in a matter within the jurisdiction of the Food and Drug Administration ("FDA"), an agency of the executive branch of the United States, knowingly and willfully made materially false, fictitious, and fraudulent statements and representations and falsified and concealed a material fact, in that Walsh stated in a writing submitted to the FDA on behalf of defendant NORIAN and Synthes that "at the time of the test market activities," defendant NORIAN and Synthes "did not . . . intend to market [Norian XR] for the treatment of vertebral compression fractures. Additionally, it was never our intent to suggest, in any way, that the product should be used for such purpose," and that, defendant NORIAN and Synthes "did not promote [Norian XR] for the[] off-label uses" of treating vertebral compression fractures, when, as the defendant knew, at the time of the Norian XR "test market," defendant NORIAN and Synthes did intend to market XR for the treatment of vertebral compression fractures, and did suggest that the product should be used for that purpose, and did intend to promote the off-label use of Norian XR to treat vertebral compression fractures.

In violation of Title 18, United States Code, Section 1001.

COUNTS NINE THROUGH FIFTY-TWO

THE GRAND JURY FURTHER CHARGES THAT:

1. The allegations of paragraphs one through 93 of Count One are incorporated here.
2. On or about the dates listed below, at West Chester, in the Eastern District of Pennsylvania and elsewhere, defendant

NORIAN CORPORATION,

with the intent to defraud or mislead, introduced, and delivered for introduction into interstate commerce, and caused the introduction and delivery of for introduction into interstate commerce, the below-listed device, namely Norian XR, which was adulterated and misbranded in the following ways:

- (a) misbranded in that its labeling lacked adequate directions for use and it did not qualify for an exemption to this requirement, 21 U.S.C. § 352(f)(1);
- (b) misbranded in that it failed to provide notice as required by 21 U.S.C. § 360(k) (510(k) of the FDCA), 21 U.S.C. § 352(o); and
- (c) adulterated in that it required pre-market approval to be marketed for its intended use, 21 U.S.C. § 351(f)(1)(A);

as set out in each count below:

<u>Count</u>	<u>Ship To</u>	<u>Approximate Shipment Date</u>
9	Canyon, TX	08/27/2003
10	Plano, TX	08/27/2003
11	San Ramon, CA & Walnut Creek, CA	Between 08/27/2003 & 09/04/2003
12	San Diego, CA	08/28/2003
13	Canyon, TX & Amarillo, TX	Between 08/27/2003 & 09/15/2003

<u>Count</u>	<u>Ship To</u>	<u>Approximate Shipment Date</u>
14	Canyon, TX & Amarillo, TX	Between 08/27/2003 & 09/16/2003
15	Canyon, TX & Amarillo, TX	Between 08/27/2003 & 09/16/2003
16	San Diego, CA	Between 08/28/2003 & 09/16/2003
17	San Ramon, CA & Walnut Creek, CA	Between 8/27/03 & 09/17/2003
18	San Diego, CA	Between 08/28/2003 & 09/26/2003
19	Owings Mills, MD	Between 08/28/2003 & 09/15/2003
20	Canyon, TX & Amarillo, TX	Between 08/27/2003 & 09/16/2003
21	San Diego, CA	Between 08/28/2003 & 10/07/2003
22	Plano, TX	Between 08/27/2003 & 10/03/2003
23	San Diego, CA	Between 08/28/2003 & 10/08/2003
24	San Diego, CA	Between 08/28/2003 & 10/13/2003
25	Plano, TX	Between 08/27/2003 & 10/14/2003
26	San Diego, CA	Between 08/28/2003 & 10/15/2003
27	Houston, TX	Between 08/28/2003 & 10/24/2003
28	Auburn, IN	Between 10/10/2003 & 10/16/2003
29	Seaford, NY	Between 09/26/2003 & 10/30/2003
30	Seaford, NY	Between 09/26/2003 & 10/30/2003

<u>Count</u>	<u>Ship To</u>	<u>Approximate Shipment Date</u>
31	Mechanicsburg, PA	10/10/2003
32	Birmingham, AL	10/10/2003
33	San Diego, CA	Between 08/28/2003 & 10/31/2003
34	Auburn, IN	Between 10/10/2003 & 11/07/2003
35	Canyon, TX & Amarillo, TX	Between 08/27/2003 & 10/09/2003
36	Mechanicsburg, PA	Between 10/10/2003 & 11/05/2003
37	San Diego, CA	Between 08/28/2003 & 11/07/2003
38	Plano, TX	Between 08/27/2003 & 11/13/2003
39	Auburn, IN	Between 10/10/2003 & 11/17/2003
40	Auburn, IN	Between 10/10/2003 & 11/17/2003
41	Derby, KS	Between 08/28/2003 & 10/20/2003
42	Houston, TX	Between 08/28/2003 & 11/20/2003
43	Auburn, IN	Between 10/10/2003 & 12/04/2003
44	Mechanicsburg, PA	Between 10/10/2003 & 11/12/2003
45	Mechanicsburg, PA	Between 10/10/2003 & 11/12/2003
46	Windermere, FL	Between 09/15/2003 & 12/12/2003
47	Mechanicsburg, PA	Between 10/10/2003 & 11/15/2003

<u>Count</u>	<u>Ship To</u>	<u>Approximate Shipment Date</u>
48	Plano, TX	Between 08/27/2003 & 12/31/2003
49	Plano, TX	Between 08/27/2003 & 12/31/2003
50	San Diego, CA	Between 08/28/2003 & 12/31/2003
51	Plano, TX	01/20/2004
52	Walnut Creek, CA	Between 01/08/2004 & 01/21/2004

All in violation of Title 21, United States Code, Sections 331(a) and 333(a)(2).

COUNTS FIFTY-THREE THROUGH NINETY-SIX

THE GRAND JURY FURTHER CHARGES THAT:

1. The allegations of paragraphs one through 93 of Count One are incorporated here.
2. On or about the dates listed below, at West Chester, in the Eastern District of

Pennsylvania and elsewhere, defendant

SYNTHES, INC.,

introduced, and delivered for introduction into interstate commerce, and caused the introduction and delivery of for introduction into interstate commerce, the below-listed device, namely Norian XR, which was adulterated and misbranded in the following ways:

- (a) misbranded in that its labeling lacked adequate directions for use and it did not qualify for an exemption to this requirement, 21 U.S.C. § 352(f)(1);
- (b) misbranded in that it failed to provide notice as required by 21 U.S.C. § 360(k) (510(k) of the FDCA), 21 U.S.C. § 352(o); and
- (c) adulterated in that it required pre-market approval to be marketed for its intended use, 21 U.S.C. § 351(f)(1)(A);

as set out in each count below:

<u>Count</u>	<u>Ship To</u>	<u>Approximate Shipment Date</u>
53	Canyon, TX	08/27/2003
54	Plano, TX	08/27/2003
55	San Ramon, CA & Walnut Creek, CA	Between 08/27/2003 & 09/04/2003
56	San Diego, CA	08/28/2003
57	Canyon, TX & Amarillo, TX	Between 08/27/2003 & 09/15/2003
58	Canyon, TX & Amarillo, TX	Between 08/27/2003 & 09/16/2003

<u>Count</u>	<u>Ship To</u>	<u>Approximate Shipment Date</u>
59	Canyon, TX & Amarillo, TX	Between 08/27/2003 & 09/16/2003
60	San Diego, CA	Between 08/28/2003 & 09/16/2003
61	San Ramon, CA & Walnut Creek, CA	Between 8/27/03 & 09/17/2003
62	San Diego, CA	Between 08/28/2003 & 09/26/2003
63	Owings Mills, MD	Between 08/28/2003 & 09/15/2003
64	Canyon, TX & Amarillo, TX	Between 08/27/2003 & 09/16/2003
65	San Diego, CA	Between 08/28/2003 & 10/07/2003
66	Plano, TX	Between 08/27/2003 & 10/03/2003
67	San Diego, CA	Between 08/28/2003 & 10/08/2003
68	San Diego, CA	Between 08/28/2003 & 10/13/2003
69	Plano, TX	Between 08/27/2003 & 10/14/2003
70	San Diego, CA	Between 08/28/2003 & 10/15/2003
71	Houston, TX	Between 08/28/2003 & 10/24/2003
72	Auburn, IN	Between 10/10/2003 & 10/16/2003
73	Seaford, NY	Between 09/26/2003 & 10/30/2003
74	Seaford, NY	Between 09/26/2003 & 10/30/2003
75	Mechanicsburg, PA	10/10/2003

<u>Count</u>	<u>Ship To</u>	<u>Approximate Shipment Date</u>
76	Birmingham, AL	10/10/2003
77	San Diego, CA	Between 08/28/2003 & 10/31/2003
78	Auburn, IN	Between 10/10/2003 & 11/07/2003
79	Canyon, TX & Amarillo, TX	Between 08/27/2003 & 10/09/2003
80	Mechanicsburg, PA	Between 10/10/2003 & 11/05/2003
81	San Diego, CA	Between 08/28/2003 & 11/07/2003
82	Plano, TX	Between 08/27/2003 & 11/13/2003
83	Auburn, IN	Between 10/10/2003 & 11/17/2003
84	Auburn, IN	Between 10/10/2003 & 11/17/2003
85	Derby, KS	Between 08/28/2003 & 10/20/2003
86	Houston, TX	Between 08/28/2003 & 11/20/2003
87	Auburn, IN	Between 10/10/2003 & 12/04/2003
88	Mechanicsburg, PA	Between 10/10/2003 & 11/12/2003
89	Mechanicsburg, PA	Between 10/10/2003 & 11/12/2003
90	Windermere, FL	Between 09/15/2003 & 12/12/2003
91	Mechanicsburg, PA	Between 10/10/2003 & 11/15/2003
92	Plano, TX	Between 08/27/2003 & 12/31/2003

<u>Count</u>	<u>Ship To</u>	<u>Approximate Shipment Date</u>
93	Plano, TX	Between 08/27/2003 & 12/31/2003
94	San Diego, CA	Between 08/28/2003 & 12/31/2003
95	Plano, TX	01/20/2004
96	Walnut Creek, CA	Between 01/08/2004 & 01/21/2004

All in violation of Title 21, United States Code, Sections 331(a) and 333(a)(1).

COUNT NINETY-SEVEN

THE GRAND JURY FURTHER CHARGES THAT:

1. The allegations of paragraphs one through 93 of Count One are incorporated here.
2. Between in or about mid-1999 and fall 2004, defendants MICHAEL D.

HUGGINS, THOMAS B. HIGGINS and RICHARD E. BOHNER were senior executives of Synthes, and were responsible corporate officers of Synthes under 21 U.S.C. §§ 331(a), 333(a)(1) and 352(a) during that time period.

3. Between in or about August 2003 and fall 2004, defendant JOHN J. WALSH was a senior executive of Synthes, and was a responsible corporate officer of Synthes under 21 U.S.C. §§ 331(a), 333(a)(1) and 352(a) during that time period.

4. Between in or about August 2003 and January 21, 2004, defendants MICHAEL D. HUGGINS, THOMAS B. HIGGINS, RICHARD E. BOHNER and JOHN J. WALSH were senior executives of Synthes, and responsible corporate officers of Synthes under 21 U.S.C. §§ 331(a), 333(a)(1) and 352(a) during the time when Synthes introduced and caused the introduction into interstate commerce of quantities of Norian XR from various locations outside the Commonwealth of Pennsylvania to various locations in the United States, which were adulterated and misbranded as described in paragraph 2 of Counts Fifty-Three through Ninety-Six of this Indictment.

All in violation of Title 21, United States Code, Sections 331(a), 352(a) and 333(a)(1).

NOTICE OF FORFEITURE

1. As a result of the violations of Title 21, United States Code, Sections 331 and 333, set forth in Counts Six through Ninety-Three of this Indictment, defendants

**SYNTHES, INC., and
NORIAN CORPORATION,**

shall forfeit to the United States of America any property constituting, or derived from, proceeds obtained directly or indirectly as the result of the violations of Title 21, United States Code, Sections 331 and 333, as charged in this Indictment, including, but not limited to, the sum of \$469,800.

2. If any of the property subject to forfeiture, as a result of any act or omission of the defendants:

- a. cannot be located upon the exercise of due diligence;
- b. has been transferred or sold to, or deposited with, a third party;
- c. has been placed beyond the jurisdiction of the Court;
- d. has been substantially diminished in value; or
- e. has been commingled with other property which cannot be divided without difficulty,

it is the intent of the United States, pursuant to Title 18, United States Code, Section 982(b),

incorporating 21 U.S.C. § 853(p), to seek forfeiture of any other property of the defendants up to the value of the property subject to forfeiture.

All pursuant to Title 18, United States Code, Section 982(a)(2).

A TRUE BILL:

FOREPERSON _____


MICHAEL L. LEVY
United States Attorney

Table of Unnamed Persons and Entities in Indictment

<u>Person</u>	<u>Description</u>
1	Original group manager for Norian SRS-R, which became XR
2	Original engineer for Norian SRS-R, which became XR
3	Group Manager of Synthes Regulatory
4	Director of Product Development, Spine
5	President of Osteobiologics Division
6	Group Manager of Spine Regulatory
7	CEO and major shareholder of Synthes
8	Product manager for Norian XR
9	Engineer for Norian XR
10	Veterinarian consultant to Synthes
11	Member of Spine Regulatory responsible for Norian XR 510(k) submission; reported to Person No. 6
12	Member of Spine Professional Services Group; reported to Person No. 12
13	Manager of Spine Professional Services Group; supervisor of Person No. 11
14	Vice President of Product Development, Biomaterials
15	Vice President of Product Development, Spine
16	Compliance Manager, Regulatory Affairs
17	Director of Regulatory Compliance

<u>Doctor</u>	<u>Description</u>
1	Spine surgeon whose two patients suffered adverse hypotensive events during surgeries in which Norian CRS was used to treat VCFs, in February 2001
2	Prominent trauma surgeon and researcher invited to speak at Synthes
3	Prominent trauma surgeon and researcher; later became a Synthes consultant
4	Spine surgeon who had first patient death; later became a Synthes consultant
5	Spine surgeon who had second patient death
6	Spine surgeon who met with Person No. 7 and Person No. 9 concerning whether Norian XR was causing episodes of hypotension
7	Spine surgeon who had third patient death; later became a Synthes consultant
8	Trauma surgeon and member of Synthes board of directors
9	Spine surgeon who spoke on vertebroplasty and Norian XR at Spine Annual Meeting November 22-24, 2003

<u>Company</u>	<u>Description</u>
A	Company marketing a bone tamp that competed with Synthes to capture the VCF market
B	Company that obtained IDE from the FDA in November 2003 for clinical trial of bone void filler use to treat VCFs