IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA	**:**	
v.	**:**	**CRIMINAL NO. 09-403-03 – 06**
MICHAEL D. HUGGINS **THOMAS B. HIGGINS** **RICHARD E. BOHNER** **JOHN J. WALSH**	**:**	

GOVERNMENT'S AMENDED PRESENTENCE MEMORANDUM

I. INTRODUCTION

On June 16, 2009, a grand jury sitting in the Eastern District of Pennsylvania returned a 97-count indictment against the four individual defendants, Michael D. Huggins ("Huggins"), Thomas B. Higgins ("Higgins"), Richard E. Bohner ("Bohner") and John J. Walsh ("Walsh"), and their former employer, one of the two corporate defendants. The indictment charges defendant Synthes, Incorporated ("Synthes"), a major medical device manufacturer which formerly employed the four defendants, with 44 misdemeanor counts of violating the Food, Drug and Cosmetics Act ("FDCA"), by introducing into interstate commerce adulterated and misbranded medical devices, in violation of Title 21, United States Code, Sections 331(a), 352(f)(1), 352(o), 351(f)(1)(B) and 333(a)(1). The indictment further charges defendant Norian Corporation ("Norian"), a wholly owned subsidiary of Synthes, with 52 felony violations of law. Count one alleges that defendant Norian and others participated in a dual-object conspiracy: to impair and impede the lawful functions of the Food and Drug Administration ("FDA"); and to commit offenses against the United States, all in violation of Title 18, United States Code, Section 371. Defendant Norian is further charged with 44 felony counts of introducing

adulterated and misbranded medical devices into interstate commerce with the intent to defraud, in violation of Title 21, United States Code, Sections 331(a), 352(f)(1), 352(o), 351(f)(1)(B) and 333(a)(2), and seven counts of making false statements to an FDA investigator during an official inspection, in violation of Title 18, United States Code, Section 1001.

The four individual defendants, all former corporate officials of defendant Synthes, are charged in Count 97 with the misdemeanor offense of introducing into interstate commerce medical devices that were adulterated pursuant to Title 21, United States Code, Section 351(f)(1)(B), and misbranded pursuant to Title 21, United States Code, Section 352(f), (o), in violation of Title 21, United States Code, Sections 331(a) and 333(a)(1). The charge against the individual defendants arises from defendants Synthes's and Norian's illegal test marketing and promotion of the medical devices Norian SRS and Norian XR in the United States between May 2002 and July 2004 and from the individual defendants' roles as corporate officers who bore the responsibility to prevent such crimes, yet not only failed to prevent them but, as set out in Count One of the indictment, directed the crimes, actively participated in them, and then later tried to cover them up during an FDA inspection.

The criminal activities charged in the indictment occurred over a period of four years. Factually, Count One of the indictment charges that Norian conspired with others to impair and impede the FDA in its oversight of clinical trials of significant risk devices such as Norian SRS and Norian XR, the implants at issue in this case. Count One alleges that, initially, Norian and others, knowing that SRS and XR had the potential to cause blood clots, lied to the FDA about the true intended use for XR, which was to treat vertebral compression fractures ("VCFs"), fractures of the spine often suffered by elderly people. Count One alleges that

defendants Huggins, Higgins and Bohner took intentional actions that furthered this aspect of the conspiracy. Count One charges that even after Norian XR was cleared with a label that warned that XR was "not intended for treatment of vertebral compression fractures," Norian and others marketed XR for treatment of VCFs, teaching spine surgeons how to use XR in surgeries to treat VCFs as part of their sponsorship of an unauthorized clinical trial of XR in humans. Again, Count One alleges that defendants Huggins, Higgins and Bohner took intentional actions that furthered this part of the conspiracy. Count One alleges further that in January 2004, after the third "test market" patient died on the operating table following a VCF surgery with a Norian bone cement, Norian and others refused to recall XR from the market, instead sending surgeons a misleading "dear surgeon" letter and then continuing the conspiracy by lying to the FDA during an official inspection in May and June 2004. Once again, Count One alleges numerous actions by all four individual defendants that furthered this part of the conspiracy. The manner and means section of Count One (paragraphs 81 through 93) specifies how each individual's actions furthered the conspiracy. Paragraphs 1 through 93 of Count One are incorporated into Count 97 by reference.

II. THE GUILTY PLEAS

Each of the four individual defendants pleaded guilty to Count 97 of the indictment.[1] Count 97 incorporates by reference paragraphs 1 through 93 of Count One, described above. Those paragraphs state in detail the four defendants' roles in the conspiracy.

Each of the defendants signed a plea agreement in which he admitted that at a

[1] Huggins and Walsh entered guilty pleas on July 20, 2009; Higgins entered his plea on July 23, 2009; and Bohner entered his plea on August 13, 2009.

trial, the government could prove the ultimate facts set out in the plea agreements, which are set out in full below:

a. The individual defendants, by virtue of their respective positions, were "responsible corporate officers" at various time during the events described below.

b. Synthes and its subsidiary, Norian, marketed Norian SRS and Norian XR, each of which was a medical device within the meaning of 21 U.S.C. § 321(h)(1), and a significant risk device within the meaning of 21 C.F.R. § 812(m)(1).

c. Significant risk devices cannot be clinically tested without prior approval of the FDA, which approval is given through an investigational device exemption ("IDE").

d. In the context of medical devices, clinical testing means research on one or more human subjects to determine the safety or effectiveness of the device.

e. Shipments of a medical device in interstate commerce must be accompanied by labeling bearing adequate directions for use for each of the medical device's intended uses. A manufacturer cannot market its device for a new intended use without notifying the FDA via a new 510(k) premarket notification. The failure to notify the FDA of a new intended use misbrands the device.

f. In December 2001, Norian SRS, a calcium phosphate compound, was cleared via the 510(k) process by the FDA as a bone void filler, to fill only those bony voids that were not intrinsic to the stability of the bony structure, in the extremities, spine and pelvis. The Norian SRS label stated further that SRS was not to be mixed with any other substance. In December 2002, the successor device, Norian XR, which consisted of calcium phosphate with barium sulfate added for extra radiopacity, was cleared via the Special 510(k) process by the FDA, also as a bone void filler, with an indication statement identical to that of SRS. The Norian XR label further contained a warning: "not intended for the treatment of vertebral compression fractures."

g. Earlier, but no later than May 2002, Synthes and Norian learned that the FDA was concerned over the imprecision of the spine indication in the then-current indication for use of bone void fillers, and that the FDA understood that some surgeons, as part of their practice of medicine, were using bone void fillers in the spine for load bearing indications. The FDA asked that Synthes and Norian -- in their pre-market notification to the FDA seeking clearance of Norian XR -- provide additional labeling for Norian XR that specified that load-bearing

indications, such as vertebroplasty, were not included in the product's indication for use. Defendants Synthes and Norian then promised the FDA that the companies would not promote Norian XR for vertebroplasty or other load-bearing indications without the appropriate regulatory authority. The FDA continued to request such labeling until Synthes submitted the warning against vertebral compression fracture ("VCF") use that became a part of the Norian XR label.

h. Between August 2002 and December 2002, Synthes and Norian trained spine surgeons to mix Norian SRS with barium sulfate and to use the resulting medical device in vertebroplasty-type surgeries to treat VCFs, notwithstanding that the label of Norian SRS stated that the product was not to be mixed with any other substance. This training of surgeons to mix Norian SRS with barium sulfate for the treatment of VCFs violated 21 U.S.C. §§ 351(f)(1)(B), 352(o) and 352(f)(1) because the mixing made SRS a new device that required premarket approval or clearance for this new intended use, and that lacked adequate directions for such use.

i. Between August 2003 and January 2004, Synthes and Norian trained spine surgeons to use Norian XR in vertebroplasty-type surgeries to treat VCFs, notwithstanding that the label of Norian XR warned that the product was not intended for treatment of VCFs. This training took place as part of a so-called "test market" for Norian XR. As part of the XR "test market," Synthes and Norian directed the Synthes Spine sales force to gather clinical data about surgeries that the "test market" surgeons performed, so that Synthes and Norian could document the results of surgeries to treat VCFs, in order to assess the risk level of using Norian XR to treat VCFs, and determine whether that risk level was too high. This unauthorized clinical testing of Norian XR for the treatment of VCFs violated 21 U.S.C. § 351(f)(1) because such testing of a significant risk device required the prior approval of the FDA, through an IDE.

j. Between December 2002 and January 2004, Synthes and Norian promoted Norian XR for use in vertebroplasty-type surgeries to treat VCFs, nothwithstanding that the label of Norian XR warned that the product was not intended for treatment of VCFs. The promotion of Norian XR for this additional intended use violated 21 U.S.C. § 351(f)(1), because Norian XR's labeling did not bear adequate directions for each of the device's intended uses, and in fact, warned against the intended use of treating VCFs.

Despite their ready admission that someone committed the conduct that led to Synthes's and Norian's criminal liability, at the guilty plea hearings each defendant insisted that he would not admit any of the evidentiary facts set forth in the government's guilty plea

memoranda – facts that showed that he and the other three individual defendants were the persons in question who knowingly and intentionally committed the acts that led to felony charges against Norian and misdemeanor charges against Synthes.[2] All four individual defendants were quite familiar with the facts outlined in the guilty plea memoranda, having attended a presentation of these facts with their counsel, at the United States Attorney's Office, prior to indictment. Those facts are alleged in detail in paragraphs 1 through 93 of Count One of the indictment. The great majority of these facts are found in internal Synthes and Norian documents, and a large number of those documents were authored by the four defendants.

The defendants contend that because they pleaded guilty to "a single strict liability misdemeanor violation of the Food Drug & Cosmetic Act . . . under the 'responsible corporate officer' doctrine" (Motion for Extension of Time, pp. 1-2), a crime not requiring proof of mens rea, they need not admit what they did, or the mental state with which they did it. The defendants appear to argue that because the Court accepted their pleas to the misdemeanor violations of the FDCA without any showing of mens rea, the government must agree that they acted without intent. The government does not so agree. The defendants' posture bespeaks an overly narrow view of the crime with which they were charged and to which they have pleaded guilty, and, more importantly, a misunderstanding of the government's obligation to inform the Court of the

[2]Indeed, defendants Huggins and Higgins went further, asking this Court to strike both the summary of evidence in support of the factual basis that was filed by the United States as part of its guilty plea memoranda, and the exhibits to the guilty plea memoranda. This surprising request led counsel for the government to write to counsel for Huggins and Higgins and ask whether their clients were denying the facts set forth in the government's plea memoranda, and advising counsel that if their clients were denying those facts, their clients ran the risk that the government would contend that this post-plea conduct warranted denial of the two-level adjustment for acceptance of responsibility.

pertinent facts surrounding the conviction in every criminal case. Not only are those facts crucial to the Court's proper determination of "relevant conduct" for the purposes of the Sentencing Guidelines, but they also bear upon the Court's duty to evaluate the statutory sentencing factors under 18 U.S.C. § 3553.

III. MISDEMEANOR VIOLATION OF 21 U.S.C. §§ 331(a) AND 333(a)(1)

Under the "responsible corporate officer" doctrine, which originated in cases under the Food, Drug and Cosmetic Act, if a corporate officer participates in corporate wrongdoing, knowingly approves of wrongful conduct, or even fails to prevent or correct the wrongful conduct, then the officer, as well as the corporation, is liable for misdemeanor penalties. See United States v. Dotterweich, 320 U.S. 277, 281-84 (1943); United States v. Park, 421 U.S. 658, 670-675 (1975). Here, as alleged in the indictment, the individual defendants did all three: they participated in wrongful conduct, they knowingly approved of it, and they failed to prevent or correct it.[3]

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[3] The doctrine applies when a corporation is liable for an offense because "the only way in which a corporation can act is through the individuals who act on its behalf." Dotterweich, at 281. To impose liability, the government must produce "evidence sufficient to warrant a finding by the trier of the facts that the defendant had, by reason of his position in the corporation, responsibility and authority either to prevent in the first instance, or promptly to correct, the violation complained of, and that he failed to do so." Park, 421 U.S. at 673-74 (1975).

The "responsible corporate officer" doctrine was first stated by the Supreme Court in Dotterweich, supra. In Dotterweich, the president and general manager of a drug company argued that he could not be held criminally liable for the company's violations of the Food, Drug, and Cosmetic Act. See Dotterweich, 320 U.S. at 279. The Supreme Court rejected this claim, holding that all who had "a responsible share" in the criminal conduct could be held accountable for corporate violations of the law. Id. at 284; see id. (explaining that "a corporation may commit an offense and all persons who aid and abet its commission are equally guilty").

The Court revisited the responsible corporate officer doctrine in Park, supra. In

Count One of the indictment alleges that each of the four individual defendants participated in extensive wrongdoing. Those allegations are incorporated by reference in Count 97, the count to which the defendants pleaded guilty. In addition, Count 97 charges that each defendant committed a crime based on his responsible relationship to the corporation, Synthes, that introduced and caused the introduction of the misbranded and adulterated Norian XR into interstate commerce. All of this conduct is charged as a violation of the misdemeanor provisions of 21 U.S.C. §§ 331(a) and 333(a)(1); thus, based on both the individual defendants' own acts and their positions at Synthes, the grand jury charged them with violating the misdemeanor provisions of the FDCA.

Prior to each guilty plea hearing, the United States filed a Guilty Plea Memorandum containing a summary of the evidence against each defendant. Fleshing out the relevant allegations of Count One, each summary detailed the actions taken by the individual defendants that led to the misdemeanor violations of adulteration and misbranding. At the plea hearings, each defendant strenuously objected to the summary of evidence in the government's Guilty Plea Memorandum. They argued that, because the misdemeanor violations of the FDCA charged in Count 97 do not require proof of intent, there was a sufficient factual basis for the Court to accept the individual defendants' guilty pleas without taking into account the government's proof of the defendants' intentional actions. The Court accepted the pleas; the

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elaborating on the concept of a "responsible share" in a violation that the defendant did not personally commit, the Court stated that the Government may satisfy its burden of proof by introducing "evidence sufficient to warrant a finding by the trier of the facts that the defendant had, by reason of his position in the corporation, responsibility and authority either to prevent in the first instance, or promptly to correct, the violation complained of, and that he failed to do so." Park, 421 U.S. at 673-74.

defendants demanded from the government and obtained extensive discovery; and the probation officer prepared draft Presentence Reports, to which the Court has now ordered that the defendants file their objections.

IV. RELEVANT CONDUCT

Putting aside the fact that the indictment charges each individual defendant with violating the FDCA based upon his own acts as well as his corporate position, the conduct underlying the defendants' offenses is also relevant conduct under the advisory Sentencing Guidelines, which all parties agree apply in this case. Relevant conduct under the Guidelines embodies the concept that in sentencing a defendant in a federal case, the Court is obligated to look at the entire offense, quite apart from the count of conviction. See U.S.S.G. § 1B1.3. The count of conviction is a starting point, but only a starting point. This concept of sentencing based upon the entire offense conduct, and the entire offender, is also central to the factors that the Court must consider under 18 U.S.C. § 3553(a).

The Guidelines allow for a two-point reduction in offense level if the defendant accepts responsibility for the actions that led to his criminal conviction. In order to be eligible for the reduction, the defendant must truthfully admit conduct comprising the offense of conviction, and truthfully admit or not falsely deny any additional relevant conduct for which the defendant is accountable under U.S.S.G. § 1B1.3 (Relevant Conduct). Section 1B1.3 defines relevant conduct as "all acts and omissions committed, aided, abetted, counseled, commanded, induced, procured, or willfully caused by the defendant . . . during the commission of the offense of conviction, in preparation for the offense of conviction, or in the course of attempting to avoid detection or responsibility for that offense." U.S.S.G. § 1B1.3(a)(1).

The comments to § 3E1.1 note that a "defendant who enters a guilty plea is not entitled to an adjustment under this section as a matter of right." U.S.S.G. § 3E1.1 cmt. n. 3. Rather, the Court takes a number of factors into consideration when determining whether a defendant qualifies for a reduction based on acceptance of responsibility. These include the truthful admission of the conduct comprising the offense and truthful admission of any additional relevant conduct. A court will not simply look at the guilty plea in isolation. At sentencing, the defendant bears the burden of proving that he or she is entitled to the downward adjustment. United States v. Bennett, 161 F.3d 171, 196 (3d Cir. 1998).

This issue was addressed by the Third Circuit Court of Appeals in Bennett. In Bennett, the defendant was charged with one count of bank fraud, sixteen counts of mail fraud, eighteen counts of wire fraud, one count of making false statements to the government, three counts of filing false tax returns, one count of impeding the administration of revenue laws, fifteen counts of money laundering, and twenty-seven counts of money laundering to promote unlawful activity. Id. at 175. After a plea of nolo contendere, which the court accepted as the equivalent of a guilty plea for the purpose of admitting guilt, the defendant publicly denied factual guilt and criminal intent for his actions. Id. In a press release announcing his nolo contendere plea, the defendant stated that he accepted responsibility for the crimes, but denied facts which supported his intent to commit fraud. Id. The Third Circuit refused to accept the defendant's argument that the nolo plea was, by itself, enough of a basis to support entitlement to the two-level reduction. Id. at 196. Therefore, the district court's decision not to give the defendant the two-level reduction was affirmed.

Here, the four defendants pleaded guilty to violating 21 U.S.C. § 331(a) and

§ 333(a)(1) by introducing into interstate commerce adulterated and misbranded medical devices. When the Supreme Court, in Park, applied the responsible corporate officer doctrine even in absence of criminal intent, the Court reflected the intent of Congress to "extend and stiffen the penal net," not to make affirmative acts of corporate officers irrelevant. Id. at 669.

While the responsible corporate officer doctrine permits omissions to be a valid basis for imputing criminal liability to corporate officers, omissions are not the only basis on which corporate officers can be charged with the crimes of their companies. As noted in Park, affirmative acts are a sufficient basis. Here, the evidence shows that the four defendants intentionally allowed adulterated medical devices to enter into interstate commerce. While Sections 331(a) and 333(a)(1) do not require any level of culpable mental state, the statute does not negate the relevance of such intentional acts in criminal prosecution. If the case had gone to trial, evidence that the four defendants acted intentionally would have been admissible to show that the defendants were all in positions of adequate authority to prevent the rogue clinical trial of XR, or to stop the product from being marketed without FDA allowance. The United States would also have been permitted to show that the four executives not only had knowledge of the scheme, but planned it and perpetuated it, in order to market Norian XR for the intended use of treatment of VCFs without FDA clearance or approval, and in the face of a warning against such use. The four defendants have failed to admit these acts and have denied that they acted with criminal intent.

As § 1B1.3 indicates, relevant conduct is more than the acts needed to commit the offense of conviction. Relevant conduct includes acts taken in preparation of an offense and during commission of that offense. Acts taken after the offense are also relevant conduct, so

long as those acts were taken in order to avoid detection or responsibility for the offense. Here, the United States will prove the defendants' acts in preparation for the adulterating and misbranding, acts during the adulteration and misbranding, and acts intended to cover it up later, both during and after the FDA's inspection of Norian in mid-2004.

To date, the four defendants have denied that they engaged in any intentional conduct in connection with the unauthorized clinical testing of Norian SRS or XR or the promotion of those devices without FDA approval. Rather, the defendants admit only that they were corporate executives of Synthes and that the devices were marketed to physicians in violation of 21 U.S.C. §§ 352(f), (o) and § 331(a) and § 333(a)(1). In so doing, the defendants refuse to admit the acts that show their knowledge of the illegal marketing of Norian; the acts that show their intent to continue to market Norian regardless of warnings from the FDA and deaths of three patients injected with Norian; the acts that show their preparation to violate the statute (e.g. choosing willing physicians, training those physicians on the use of their product and expecting data in return, and creating a delivery mechanism for the adulterated device); and the acts intended by them to avoid detection of, and responsibility for, the offense, when they made false statements to, and concealed facts from, an FDA investigator in mid-2004.

Reduced to its essence, the four individuals seek to transform the responsible corporate officer doctrine from a sword intended to achieve maximum adherence to the United States' food and drug safety laws into a shield insulating the genuinely culpable parties from the consequences of their own intentional wrongdoing. The defendants have entered guilty pleas. Those pleas merely acknowledged that some persons at their corporate employers committed acts of intentional wrongdoing, acts that were designed to, and did, foist adulterated and misbranded

medical devices on unsuspecting consumers. The facts as set forth in the Indictment, and as detailed in the Presentence Report, establish that this intentional misconduct was, in fact, committed by the four defendants. Although not strictly necessary for conviction, the wilful acts of the four individual defendants remain relevant conduct. Therefore, if the individual defendants persist in their refusal to acknowledge their individual roles in their employer's wrongdoing, they should not receive the benefit of the two-level reduction that the Sentencing Guidelines reserves for those defendants who accept responsibility.

V. ARGUMENT

The United States will prove at the sentencing hearing that from the beginning, the intended market for Norian was for an unapproved use, i.e., in surgeries to treat VCFs. The individual defendants recognized early on that there were two possible solutions to this problem: (1) the legal solution, which was to secure FDA approval of XR for use in vertebroplasty-type procedures to treat VCFs, via a long, costly approval process known as pre-market approval ("PMA"), after an IDE to investigate the safety and efficacy of the product; and (2) the illegal solution, which was to obtain clearance through the shorter 510(k) process by concealing the true intended use, then to promote XR for use in VCFs through limited, low-cost "test markets" during which Synthes would attempt to fly below the FDA's radar while evaluating the safety and efficacy of the products in unsupervised clinical trials and judging their success according to its own standards. Acting through these defendants, Synthes chose the illegal solution and got caught.

As set forth in detail herein, the defendants' limited "test markets" were not slow, or cautious, or careful, or motivated by patient safety. In deciding to embark on test markets for

SRS and XR in VCF surgeries, the individual defendants ignored alarming study results and patient outcomes (including deaths) and concealed them from the surgeons whom they invited to use the products. They also disregarded clear statements from the FDA that use in surgeries to treat VCFs was off-label and warnings from their own subordinates and consultants as well as outside surgeons that this conduct was illegal. The individual defendants might suggest that the SRS indication statement – and later, the XR label even despite the warning – were broad enough to encompass use in the spine and, therefore, confusing. But the evidence will show that the individual defendants were in no way confused. Not only did the XR label include a clear preclusion of the product for use in VCFs but, in dealing with Synthes, FDA was unequivocal and unwavering: SRS and XR were not approved for use in load bearing applications in the spine, specifically including surgeries for VCFs. In fact, this is exactly what Synthes told its physician customers in its February 2004 "dear surgeon" letters – signed by defendant Huggins – when it stopped the test markets. See Exhibit 76.

Any related claim of lack of notice – that the FDA gave Synthes inconsistent and confusing guidance on the meaning of its label – would be equally meritless. This claim is disproved with a single document: the February 2003 e-mail exchange between Synthes and the FDA about the meaning of the label. See Exhibit 53. In any event, it is the manufacturer's duty in the first instance to propose label language for its product to the FDA, and to understand that language. See Riegel v. Medtronic, Inc., 552 U.S. 312, 319 (2008). It is not the FDA's duty to explain to the manufacturer the meaning of its own label – the manufacturer has a legal obligation to understand it.

Because the company concealed its intended use of the XR device, FDA cleared

the device for marketing through a Special 510(k), which mandates a much more limited labeling review than a PMA. The FDA reviews labeling in a 510(k) or Special 510(k) application primarily to determine the device's intended use, and not to determine whether the warnings are adequate. In fact, the statute requires that FDA *only* consider the manufacturer's proposed labeling in making substantial equivalence determination and only require any additional statements in the labeling if the Director of the relevant review division determines that "there is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling" and that "such use could cause harm." 21 U.S.C. § 360c(1)(1)(E). If Synthes had been honest with the FDA about the intended use of the XR device, then its proposed labeling would have been subject to a more rigorous review.

Finally, the statements and actions of the individual defendants during the FDA inspection of Norian in May and June of 2004 will prove that their earlier actions were knowing, and taken with the intent to defraud the FDA as well as the surgeons to whom they promoted the Norian products off-label. The proof will show that the three defendants who had contact with the FDA investigator – Huggins, Bohner and Walsh – repeatedly attempted to mislead him about the unauthorized clinical trials that they had conducted with SRS and XR by way of the illegal "test markets." They told him that they were not aware of the test market for SRS in the spine, when they had approved it; they told him that the Norian XR test market was for approved indications, not treatment of VCFs; and while admitting that treating VCFs was off-label and, indeed, warned against by the XR label, they argued that vertebroplasty could be used for treating conditions other than VCFs, when they knew such other uses were de minimis at best and that from the beginning, Synthes had sought to capture the VCF market. The defendants' false

statements during and after the FDA inspection were made to avoid detection of their misbranding and adulteration, and to escape responsibility for that crime, and so are relevant conduct.

VI. SUMMARY OF EVIDENCE

A. The Defendants' Positions At Synthes

The four individual defendants held the following positions at Synthes:

1. defendant Huggins was hired by defendant Synthes at the end of 1994, and held the following positions from 1999 through 2005, the time period covered by the indictment:

1999 through January 2004: President of Synthes North America;

February 2004 through the end of 2005: President of Synthes Spine Division.

Out of the four individual defendants, Huggins was the highest-ranking. Further, defendant Higgins reported directly to defendant Huggins from 1999 until February 2004; defendant Bohner reported directly to defendant Huggins until February 2004; and defendant Walsh reported to defendant Huggins indirectly, through Bohner, from August 2003 until February 2004, and then directly to defendant Huggins beginning in February 2004.

2. defendant Higgins was hired by defendant Synthes in September 1991 and held the following positions from 1999 through 2005, the time period covered by the indictment:

1999 through January 2004 -- President of Synthes Spine Division.

February 2004 through May 2005 -- Senior Vice President of Global Strategy, Synthes.

May 2005 through December 2005 -- President of Synthes Biomaterials.

Further, during the relevant period, defendant Higgins was the President of the

Synthes division -- the Spine Division -- that ran the Norian SRS for the spine and Norian XR test markets and unauthorized clinical trials, reporting to defendant Huggins until the end of January 2004.

3. defendant Bohner began working at defendant Synthes in June 1997. From 1999 through 2005, the time period covered by the indictment, Bohner was Synthes's Vice President of Operations, overseeing regulatory affairs for the company, and reporting to defendant Huggins.

Further, during the relevant period, defendant Bohner was closely involved with the division of Synthes -- the Spine Division -- that ran the Norian SRS for the spine and Norian XR test markets and unauthorized clinical trials.

4. defendant Walsh was hired by defendant Synthes as a regulatory consultant in the Spine Division in June 2003; he took full time employment at Synthes in August 2003, with the title Director of Regulatory and Clinical Affairs in the Spine Division.

Further, defendant Walsh reported to defendant Bohner from August 2003 until February 2004, and then to defendant Huggins beginning in February 2004.

B. The Medical Context

At sentencing, the evidence will show that vertebral compression fractures ("VCFs") are fractures of the spine, most of which result from osteoporosis. An estimated 700,000 VCFs occur annually in the United States due to osteoporosis, and a large proportion of VCFs are painful and clinically diagnosed. The aging of the baby boomer generation makes the market for treatment of VCFs a large and lucrative one. See, e.g., Exhibit 1, binder, Vertebroplasty Market Investigation Executive Summary ("Vertebroplasty Summary"), pp. 1, 4,

10; Exhibit 1A, AO Clinical Investigations, "Vertebroplasty and Kyphoplasty: How safe and effective are they?" from defendant Huggins' file at Synthes.

In the 1980s, a surgery called vertebroplasty was developed to treat VCFs. During the surgery, a needle was inserted 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. See Exhibit 1, 1A.

Traditional vertebroplasty involved a high-pressure injection of bone cement. Kyphoplasty was a later variation on vertebroplasty, originated by a company called Kyphon, in which 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 cavity created was then filled with bone cement under lower pressure than required for traditional vertebroplasty. See Exhibit 1, 1A.

In addition to describing a traditional high-pressure injection, the term "vertebroplasty" is commonly used in a broader sense to refer to any surgery – including those involving a created vertebral cavity – in which bone cement is injected through a needle into the vertebral body in order to stabilize the fractured bone and alleviate back pain. The evidence will show that defendants Synthes and Norian and their employees often used the term "vertebroplasty" in this broader sense.

C. Synthes and Norian's Development and Marketing of Norian SRS and XR for Treatment of Vertebral Compression Fractures

Defendant Synthes purchased defendant Norian in mid-1999, approximately six

months after defendant Higgins became President of the Spine Divison. At that time, Norian manufactured and marketed two bone cements: SRS, which stands for Skeletal Repair System, and CRS, which stands for Cranial Repair System. Beginning in spring 2000, defendants Synthes and Norian conducted market research on the use of Norian bone cements to treat VCFs, and interviewed spine surgeons, neuroradiologists, and neurosurgeons who used an acrylic bone cement, polymethylmethacrylate ("PMMA"), off-label in vertebroplasty and kyphoplasty surgeries to treat VCFs. Defendants Synthes and Norian asked them whether they had used SRS in such surgeries, how SRS had performed in this indication, how to improve the use of SRS in such surgeries, and – for the many surgeons 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 of a version of SRS with radiopaque barium sulfate (SRS-R, which became XR) in vertebroplasty and kyphoplasty surgeries to treat VCFs. See Exhibit 1, Vertebroplasty Summary, pp. A-1, A-2; Exhibit 2, Facsimile Transmission from Michael Lehmicke to Nisra Thongpreda dated 2/17/00 concerning conversations with surgeons on vertebroplasty, pp. 1-6; Exhibit 3, Memorandum from Tom Higgins and Nisra Thongpreda to Hansjoerg Wyss dated 2/24/00, SRS for Spinal Applications – Action Plan Proposal.

Starting in late summer 2000, based on the surgeon interviews, research of literature, and conversations with spine surgeons performing surgeries to treat VCFs, defendant Higgins and the Spine Division began development of the Synthes Vertebroplasty System for treating VCFs. The Vertebroplasty System consisted of SRS-R, and a group of Class I

instruments[4] for approaching an osteoporotic vertebral body and injecting the Norian through a needle into the patient's back called the Cavity Creation System. In November 2000, defendant Higgins sent an e-mail to persons working on the Vertebroplasty project, demonstrating his sophisticated understanding of the two separate routes for obtaining the FDA's permission to market a medical device – approval of a PMA application and clearance of a 510(k) or Special 510(k) pre-market notification. Defendant Higgins' e-mail directed his subordinates to evaluate a particular study on osteoporotic sheep "in light of any strategy to get clearance for vertebroplasty. Although our initial strategy is to use the bone void indication, we should look at what it would take for a vertebroplasty indication. . ." See Exhibit 4, e-mail from defendant Higgins to Nisra Thongpreda, original group manager for Norian SRS-R, which became XR, dated 11/2/00.

A year later, in November 2001, at a management meeting attended by defendants Huggins and Higgins and other top Synthes officials, the Spine Division made a presentation on how Synthes could obtain the FDA's approval for use of Norian to treat VCFs. The Spine Division reported that the IDE and PMA process would take 36 months and cost Synthes at least $1 million. See Exhibit 5, 11/26/01 Management Review Board ("MRB") Minutes, pp. 2-3. The Spine Division's presentation was based upon a draft vertebroplasty clinical study outline that had been reviewed and approved by defendant Bohner in October 2001. When defendant Bohner

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[4] "Class I" refers to one of the three regulatory classes under the FDCA. All devices marketed in interstate commerce in the United States fall into one of three regulatory classes under the FDCA. 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. 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. Synthes' Cavity Creation System was a group of Class I instruments.

asked the author of the outline, Barry Sands, Group Manager of Spine Regulatory, what the company would use for a "control" in the clinical trial, Sands (who reported to Bohner), responded that the control would have to be standard medical practice – to treat non-surgically – because "[c]urrently no device controls exist. PMMA is used off-label. Thus, if we used PMMA it would be considered another experimental cohort." See Exhibit 6, e-mail chain between Sands and defendant Bohner dated 10/17/01 and 10/22/01, and attached outline of clinical study.

After this meeting, Wyss, the CEO and major shareholder of Synthes, directed that Synthes would not pursue FDA approval of Norian via an IDE and a PMA, but instead would press on with a "test market"[5] for use of an extra-radiopaque version of Norian in the spine, with the aim of trying to persuade surgeons to publish on the results of their surgeries. See Exhibit 5, p. 3. Defendants Huggins, Higgins and Bohner followed this directive, approving a test market for SRS in the spine ("Phase I"), that is, a test market for SRS mixed with barium sulfate to treat VCFs, which began in late summer 2002. The evidence shows that no later than May 2002, defendants Huggins, Higgin and Bohner were aware of, and involved in, the process of approving the test market for SRS in the spine. See, e.g., Exhibit 8, email dated 5/30/02 from defendant Huggins to defendants Higgins, Bohner and others, expressing second thoughts about the test market for SRS in the spine; Exhibit 9, time line of test market approvals, created

[5] "Test market" is a term used by the defendants to describe a limited release of a product, to determine what customers prefer regarding *approved indications*. See Exhibit 7, Synthes Product Development Test Market Policies. In this case, however, both the test market for SRS in the spine and the later XR test market were for the *unapproved* – and in the case of XR, warned-against – indication of treatment of VCFs.

5/31/02 by Norian XR product manager Josi Hamilton.[6]

On December 20, 2001, defendant Synthes obtained from the FDA 510(k) clearance for SRS as a general bone void filler, 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. See Exhibit 11, SRS label. Defendant Synthes never told the FDA that it intended to market SRS for load bearing spine use such as treating VCFs.

By May 2002, representatives of defendants Synthes and Norian had had multiple conversations with the FDA about CRS and SRS. Through those conversations, starting as early as 1999, defendants Synthes and Norian had become aware of the FDA's concerns with the products, and in particular, that the FDA was concerned about their use in the vertebral bodies. See, e.g., Exhibit 12, Synthes Minutes of Conference Call with FDA 7/8/99, p. 1, paragraph 3.[7]

Specifically, on May 8, 2002, Group Manager of Spine Regulatory Barry Sands, along with other Spine employees, had a telephone conference call with the FDA concerning the new SRS plus barium sulfate (the product eventually named XR). During the call, the FDA stated that it was concerned about the imprecision in the current indication for use, and that it understood that as part of their practice of medicine, surgeons were using bone void fillers in the

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[6] An entry from defendant Bohner's diary corroborates the time line, showing that a President's Meeting took place on the date listed in the time line. See Exhibit 80, entry from defendant Bohner's diary for 5/22/02, while an e-mail exchange between the XR product manager and defendant Bohner, also on 5/22/02, shows Bohner's awareness of , and apparent agreement to, the planned test market for SRS in the spine. See Exhibit 10, e-mail chain dated 5/22/02.

[7] The evidence shows that this conference call was attended by defendant Bohner. See Exhibit 80, entry from defendant Bohner's diary for 7/8/99.

spine for load bearing indications. The FDA asked that defendants Synthes and Norian provide additional labeling for XR that specified that load bearing indications, such as vertebroplasty, were not included in the current indication for use. On behalf of defendants Synthes and Norian, Sands promised the FDA that the companies would not promote XR for vertebroplasty or other load bearing indications without the appropriate regulatory authority. Sands expressed the belief that such labeling would create an uneven playing field, as no other manufacturers of other bone void fillers had such labeling, but the FDA continued to request such labeling until defendant Synthes submitted the warning against VCF use that became part of the Norian XR label. See Exhibit 13, Synthes minutes of conference call with FDA, Norian SRS with BaSO4, 5/8/02, copied to defendants Higgins and Bohner; Exhibit 14, Synthes consultant Harold Aberman, DVM's Handwritten Notes of Conference Call with FDA; Exhibit 15, FDA Notes of 5/8/02 Conference Call.

The evidence shows that when Sands made this promise to the FDA during the May 2002 conference call, he understood that the only way that Synthes could receive approval for load bearing spine indications such as vertebroplasty was through an IDE and a PMA application. Documents and testimony show that, prior to May 2002, Sands and others had communicated this fact to others higher up in defendant Synthes' management. See, e.g., Exhibit 16, email dated 10/22/02 to defendant Higgins concerning vertebroplasty study ("there are no FDA cleared/approved bone filling materials for this indication"); Exhibit 6 ("PMMA is used off-label.").

Emails and testimony show that by May 2002, defendant Synthes' own regulatory employees had also given Synthes management (including defendants Higgins and Bohner)

notice, and to spare, that promoting use of SRS to treat VCFs was illegal. See, e.g., Exhibit 17, email dated 8/23/00 from Group Manager of Synthes Regulatory Michael Sharp, Ph.D., to defendants Higgins and Bohner (Synthes may not promote SRS for vertebroplasty); Exhibit 18, email dated 3/19/01 from Sharp to defendant Bohner (about meeting with defendant Higgins at which Higgins was told that Synthes could not promote SRS for use in the spine). Other Synthes employees, working under defendant Higgins in the Spine Division, made this point even clearer later, in December 2002, going so far as to say that if there were any doubt, the opinion of counsel should be sought on the question. See Exhibit 19, Minutes of Meeting between Spine Professional Services Group members Timothy Hogan and Paul Gordon with Norian XR product manager Hamilton on 12/13/02. So far as the evidence shows, counsel was not consulted until January 2004, after the third patient died on the operating table during a VCF surgery in which Norian was used.

Defendants Huggins, Higgins and Bohner also received notice through the FDA's statements to another company, in the form of a Warning Letter to a competitor, showing the FDA's concerns about claims for general orthopedic devices for use in the spine. See, e.g., Exhibit 20, e-mail from Sharp to defendant Higgins and others, attaching Kyphon Warning Letter, dated 12/4/00. They also received notice from the FDA's public pronouncements, or WebAlerts, publicizing complications that had been reported related to vertebroplasty-type surgeries to treat VCFs. One WebAlert in October 2002, updated later, warned that the reported complications were related to the leakage of PMMA during surgeries to treat VCFs. See Exhibit 21, FDA Public Health Web Notification ("WebAlert") dated 10/31/02; Exhibit 22, e-mail from Defendant Huggins to Defendants Higgins and Bohner and others, attaching updated WebAlert

dated 4/4/03.

Thus, the evidence shows that, as time went on, defendants Huggins, Higgins and Bohner, like their subordinates at Synthes Spine, were increasingly on notice that the Norian bone void fillers might pose serious risks if used in the spine in humans, specifically:

-- two adverse hypotensive events occurred in February 2001 when a spine surgeon, Dr. Rick Delamarter, used CRS off-label in two kyphoplasty surgeries to treat VCFs in two patients (each time, the CRS had been carried to the operating room by a Synthes sales representative, who was present in the operating room during the surgeries). These were two of the first VCF surgeries with a Norian cement in the United States. Both patients survived but one had to spend 3 to 4 days in the hospital's intensive care unit. Defendant Synthes learned that Dr. Delamarter had previously performed about 50 VCF surgeries with PMMA without incident. Defendant Synthes filed Medical Device Reports ("MDRs") on the two Doctor Delamarter hypotensive events.[8] See Exhibits 23 and 24, MDRs. Documents show that subordinates informed defendant Huggins of the two hypotensive events,[9] and that in response Huggins directed subordinates to reel in the sales force "ASAP" concerning the use of CRS in VCF surgeries. See Exhibit 26, Huggins email dated 3/16/01.

-- at a meeting called by defendant Synthes with surgeons and researchers to try to learn the

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[8] By regulation, a device manufacturer must file an MDR with the FDA within 30 days, whenever the manufacturer learns information from any source that reasonably suggests that the manufacturer's device might have caused or contributed to a death or serious injury.

[9] Defendant Higgins learned of them no later than March 1, 2001, and defendant Bohner learned of them no later than March 16, 2001. See Exhibit 25.

cause(s) of the two hypotensive events, a meeting which defendant Higgins attended, one participant, a prominent trauma surgeon from the University of Washington, Dr. Sohail Mirza, reported that the Norian in its pre-hardened state might be interacting with blood in such a way as to cause problems. He told defendant Synthes that he believed it was critical that there be a study of the pre-hardened state of Norian before it was used in live patients because, in its pre-hardened state, Norian had the potential adversely to interact with tissues and blood in a way that hardened Norian did not. See Exhibit 27, Norian for Spine Indications Focus Group materials 4/01; Exhibit 28, Handwritten Notes of Nisra Thongpreda taken at Focus Group meeting.

-- in November 2001, at the annual Spine sales meeting, defendant Synthes invited Dr. Mirza to speak to the Spine sales force about surgeries to treat VCFs. Doctor Mirza discussed the serious complications of vertebroplasty-type surgeries to treat VCFs, including leakage of the cement into the venous system, which could cause pulmonary embolism and death. See, e.g., Exhibit 5, MRB Minutes, p. 3; Exhibit 29, Spine Annual Sales Meeting Agenda on vertebroplasty.

-- in April 2002, another surgeon published an article in Spine Journal of Bone and Joint Science concerning the death of his patient during spinal screw augmentation surgery with CRS. See Exhibit 30.

-- in May and June 2002, Dr. Mirza and his then-colleague, Dr. Jens Chapman, told defendant Synthes that they had performed preclinical pilot studies at the University of Washington with 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 "pilot studies"). The pilot studies showed that the calcium contained in 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 following injection of SRS. The surgeons also reported some of their findings from their pilot studies with SRS to the FDA via an MDR. See Exhibit 31, University of Washington letter dated 6/28/02 (copied to defendant Higgins), attached MDR and attached proposal to conduct more safety studies.

At the end of May 2002, notwithstanding the growing awareness of the serious risks posed by the Norian products when used in the spine; despite the interpretations and advice given by the FDA and defendant Synthes's own regulatory group; and contrary to the label stating that SRS was not to be mixed with any other substance, defendants Synthes and Norian approved the test market for SRS in the spine, in which the companies taught spine surgeons how to mix SRS with barium sulfate and use it in surgeries to treat VCFs. The evidence shows that prior to approval of the test market for SRS in the spine, defendant Huggins was in contact with Dr. Kenneth Lambert, a medical consultant for defendant Synthes who opposed the plan to conduct a test market for SRS in the spine, warning that it amounted to human experimentation. See Exhibit 32, emails from consultant to defendants Huggins and Higgins, and Wyss. The evidence shows further that, on May 30, 2002, after speaking with Dr. Lambert, defendant Huggins sent an email to defendants Higgins and Bohner, among others, citing his awareness of the plan and stating that he was now having second thoughts. See Exhibit 8.

Nonetheless, documents and testimony show that this blatantly illegal "test market" went forward during late summer and fall 2002, with the knowledge and approval of

defendants Huggins, Higgins and Bohner. See, e.g., Exhibit 33, memorandum from Nisra Thongpreda to defendants Huggins, Higgins and Bohner on SRS Training, dated 6/4/02; Exhibit 34, Powerpoint Presentation for SRS Training. The progress of the test market for SRS in the spine was discussed at a management meeting in September 2002, attended by defendants Huggins, Higgins and Bohner. See Exhibit 35, MRB Meeting Spine Business Plan Review Agenda dated 9/17/02, p. 2; Exhibit 36, Powerpoint Presentation on Test Market for SRS in the Spine given at 9/02 MRB Meeting. The results of the test market for SRS in the spine were also discussed later at the July 18, 2003 Safety Meeting and in the Safety Meeting materials, Exhibits 38-42 and 37, see pp. 31-32 below.

In fall 2002, defendant Synthes submitted to the FDA a Special 510(k)[10] premarket notification for XR requesting clearance for a general bone void filler indication, listing Norian as the manufacturer, and telling the FDA that XR was substantially equivalent to SRS. Notwithstanding the promise that defendants Synthes and Norian had made during the conference call with the FDA, Synthes made the submission without the language requested by the FDA, that is, without language stating that Norian XR was not intended for load bearing indications such as treating VCFs. And defendant Synthes never told the FDA that its true intended use for XR was to market it for load bearing spine use such as treating VCFs. See Exhibit 43, Norian XR 510(k) Submission dated 11/18/02.

On December 16, 2002, defendant Synthes learned that the FDA was still seeking

[10] A "Special 510(k)" is available to manufacturers who are seeking to market a modified version of their own previously cleared device. The regulations are clear, however, that this expedited process cannot be used when the proposed change or modification to the device affects the intended use of the device.

specific wording concerning "no vertebroplasty and non load bearing only"; two days later, Synthes agreed to add the warning "not intended for treatment of [VCFs]" to the XR label. See Exhibit 44, email from Synthes Regulatory Employee 12/16/02; Exhibit 45, Regulatory Sign-Off Sheet Concerning Warning dated 12/18/02.

Norian XR was cleared by the FDA on December 19, 2002, 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 specifically warning that XR was "not intended for treatment of vertebral compression fractures." Exhibit 46, Norian XR label as cleared 12/19/02. The next day, defendant Higgins sent the XR team an email congratulating them on getting XR approved, "designing such a smart plan, and executing it so well." Exhibit 47, email from defendant Higgins dated 12/20/02.

Less than a month later, on January 13, 2003, a surgeon who had participated in the test market for SRS in the spine, Dr. Barton Sachs, used SRS he had mixed with barium sulfate in a surgery using Synthes's cavity creation instruments to treat VCFs. The evidence shows that a Synthes sales consultant was present during the surgery and that the SRS was mixed with barium sulfate in the consultant's presence. After suffering a hypotensive episode, Dr. Sachs's patient died on the operating table ("the first death"). In conversations with three Synthes Spine employees, Dr. Sachs did not rule out the mixed SRS as a cause of the first death.[11] See Exhibits 49, 50 and 51, handwritten notes taken by the Synthes Spine employees

[11] The evidence shows that Bohner was fully aware that for Synthes to teach or encourage surgeons to mix barium sulfate with SRS, as had been done in the test market for SRS in the spine, was adulteration and strictly illegal. See Exhibit 48, e-mail to defendant Bohner from Spine Regulatory employee Vikki Hoffman dated 1/23/03.

(Thongpreda, Hamilton and Weikel) in conference calls with Dr. Sachs.

Even though Dr. Sachs could not rule out SRS as a cause of the first death, defendants Synthes and Norian made the decision not to file an MDR on that death. In addition, neither company had an independent medical expert review the death.

In late January 2003, following the first death, defendant Bohner emailed defendant Higgins, with a copy to defendant Huggins, urging that management notify the Spine sales force that XR should not be promoted for off-label uses. In his e-mail, Bohner argued that Higgins, as President of Spine, should send a proposed e-mail about off-label promotion to the Spine sales force. In his e-mail 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,'" showing that Bohner well understood that the treatment of VCFs was forbidden. See Exhibit 52, email from Defendant Bohner to Defendants Huggins and Higgins, dated January 28, 2003. After defendant Bohner sent his email to Higgins and Huggins, however, no communication that included both the warning label for XR, and an admonition that XR should not be promoted for off-label use, was sent to the Spine sales force.

In late February 2003, Vikki Hoffman, the Synthes regulatory employee who had handled the XR 510(k) submission, sent an email to the FDA, asking the FDA representative who had handled the clearance of 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?" Two days later, the FDA representative answered that Synthes could not, 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.

Exhibit 53, email chain between Vikki Hoffman of Synthes Spine Regulatory and FDA employee, showing that, later, this email was forwarded to defendant Walsh, on 10/16/03.

On May 28, 2003, defendant Bohner was copied on an email concerning whether Synthes should seek a vertebroplasty indication for XR from the FDA, via an IDE and a PMA. The email, written by a subordinate of Bohner's, discussed in detail the steps that would have to be taken in order for such FDA-approved clinical testing to be undertaken. See Exhibit 54, e-mail to defendant Bohner dated 5/28/03. Also on May 28, 2003, defendant Bohner interviewed defendant Walsh for the position of Director, Spine Regulatory and Clinical; Walsh took the position, in which he reported directly to Bohner.

On July 18, 2003, defendants Synthes and Norian held a "Safety Meeting" attended by defendants Huggins, Higgins, Bohner and others. The evidence shows that defendant Huggins was the most senior manager present at the Safety Meeting. According to the materials distributed at the Safety Meeting, the declared purpose of the meeting was to decide whether Norian XR was safe enough to bring to market. Safety Meeting participants heard a presentation by the XR product manager on the pilot studies, the two adverse hypotensive events that had occurred with Doctor No. 1's patients, and the first death. Notes from the meeting show that the participants also discussed defendant Synthes' failure to file an MDR on the first death, as well as the fact that there already had been three adverse events with a Norian product out of

approximately thirty-four VCF cases to date (a statistically significant figure). Faced with the choice whether to seek an IDE and a PMA, defendant Huggins, on behalf of Synthes and Norian, decided to continue the XR "test market" for use in vertebroplasty-type procedures to treat VCFs that had begun in late summer of 2002 with SRS, with the goal of having "test sites" publish results of surgeries. Materials distributed in advance of the Safety Meeting are Exhibit 37; the Powerpoint shown at the Meeting is Exhibit 38; minutes of the Safety Meeting, which show that defendants Huggins, Higgins and Bohner received them, are Exhibits 39, 49 and 41; and handwritten notes taken during the Safety Meeting by Synthes consultant, Harold Aberman, DVM, are Exhibit 42.[12]

In August 2003, defendants Huggins, Higgins and Bohner, other employees and a number of surgeons held a strategic planning meeting on XR, at which the issue of an approved clinical study of XR was raised again. The meeting minutes and participant testimony show that defendant Huggins noted that Synthes had a "poor record of PMA approvals," and that defendants Huggins and Higgins directed that the XR "test market" would continue, despite a presentation made at the meeting on vertebroplasty and XR and a recommendation by one of the doctors that an FDA study of XR be conducted to gain approval for vertebroplasty.[13] See Exhibit

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[12] Defendant Bohner also took notes of the discussion held at the Safety Meeting, in the form of a diary entry, which including the following: "Ken Lambert: thinks there's a massive cover up + many clinical problems, accuses us of not doing MDR reports." "JH [Josi Hamilton, the XR product manager]: cement leakage is main concern." "Helfet [Synthes Board of Director member, Dr. David Helfet]: after 200 to 300 patients in TM, make launch decision." "Abstract [of University of Washington research]: 'lethality . . . Norian . . . embolization' is potentially damaging." See Exhibit 80, Bohner Diary entry for 7/18/03.

[13] Defendant Bohner noted this recommendation in his diary as "IDE for vertebroplasty." See Exhibit 80, Bohner Diary entry for 8/14/03.

55, Minutes of Strategic Planning Meeting held 8/14/03.

On August 15 and 16, 2003, defendants Synthes and Norian held the first surgeon training meeting of the "test market," at which lectures and power point presentations were given to the attendees concerning the use of XR in surgeries to treat VCFs, and a cadaver lab was held during which the surgeons injected XR into the vertebral bodies of cadavers. At this surgeon training, the companies distributed notebooks to the attending spine surgeons which thanked them for participating in the XR "test market," and gave the sales consultants forms[14] for reordering XR ("test market reorder forms" or "TM forms"). Defendant Synthes also instructed its sales consultants, repeatedly, that they could not reorder XR unless they filled out the "test market" reorder forms with information about each surgery performed with XR. At the first surgeon training, the companies did not inform the trainee surgeons of the first death, the other adverse events, or the pilot study results. See Exhibit 56 (notebook distributed at first surgeon training meeting); Exhibit 57 (blank "test market" reorder form).

The evidence shows that on or about August 20, 2003, defendant Walsh became a full-time Synthes employee, with the title of Director of Regulatory and Clinical Affairs in the Spine Division, reporting to defendant Bohner. Shortly thereafter, on August 28, 2003, the Norian XR product manager e-mailed defendants Higgins, Bohner and others: "Norian XR is officially released to Test Market. We shipped to 13 Spine sites Wednesday afternoon (8/27), and have 4 cases scheduled for Friday (8/29)." See Exhibit 58. On September 10, 2003, Josi

[14] The information that Synthes requested in the "test market" reorder forms included clinical data on the warned-against indication; 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.

Hamilton, the XR product manager, e-mailed defendant Higgins that one XR test market surgeon had had two cavity creation surgeries with XR that day and that another surgeon was to have such a surgery the following day. She further forwarded to defendant Higgins a report of six other such surgeries and related shipment of product. See Exhibit 59.

Meanwhile, as the University of Washington researchers continued to conduct pre-clinical studies with the Norian product, their findings were consistent with their earlier pilot study results, and raised additional concerns, which were brought to the attention of defendant Higgins at various times during 2003. See, e.g., Exhibit 60, e-mail concerning pig lab in April 2003 showing that setting time of Norian correlated to clotting; Exhibit 61, e-mail on further tests in November 2003 showing that pigs injected with larger quantities of PMMA than the quantities of XR injected in other pigs survived, whereas the pigs injected with smaller quantities of XR had perished.

On September 19, 2003, when a spine surgeon, Dr. Paul Nottingham, used 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"). The evidence shows that a Synthes sales consultant was present during the surgery. Dr. Nottingham noted a cement leak, and believed that it was the cause of the episode, and could not rule out XR as a cause of the second death. See Exhibit 62, Minutes of 9/23/03 Meeting. Defendants Synthes and Norian filed an MDR on the second death that was vague as to the surgery and its details. Again, neither company had an independent medical expert analyze the death.

Despite the second death, defendants Synthes and Norian continued the second surgeon training meeting of the "test market" on September 19 and 20, 2003,which defendant

Higgins attended. See Exhibit 63, Norian XR Attendee List; Exhibit 64, Test Market Surgeon Training Agenda. The second training followed a format identical in substance to the first surgeon training, and again included spine surgeons selected by defendant Synthes based on their experience in performing vertebroplasty, and whose expenses to travel to and attend the training were paid for by defendant Synthes. At the second surgeon training, defendant Synthes did not inform the trainee surgeons of either of the first two deaths, the other adverse events, or the pilot study results (although the XR product manager called some surgeons later to inform them of the second death).

On September 23, 2003, defendants Huggins, Higgins, Bohner and Walsh, among others, attended a meeting focused on what defendants Synthes and Norian would do with the XR test market in the wake of the death of Dr. Nottingham's patient. The evidence shows that defendant Huggins was the most senior manager present at this meeting. See Exhibit 65, e-mail from XR product manager following up 9/23/03 meeting; Exhibit 66, agenda for 9/23/03 meeting. The evidence also shows that defendants Huggins, Higgins and Walsh attended another meeting on October 31, 2003 at which the death of Dr. Nottingham's patient and additional findings from the University of Washington were both discussed. See Exhibit 67, Colleen Flescher of Synthes Spine's handwritten notes of Meeting Held 10/31/03. The outcome of those meetings was that despite the new death and further results from the University of Washington of the same tenor, the studies on humans with Norian XR in the test market would continue.

On September 26, 2003 – as reported to defendants Huggins, Higgins, Bohner and Walsh a few days later – another spine surgeon, Dr. Lane, told the XR product manager Josi Hamilton and Dr. Aberman that he believed that XR was "potentially dewatering and causing

episodes of hypotension." He also stated that, because the Norian XR "test market" was collecting information from surgeons performing surgeries to treat VCFs, he believed that defendant Synthes was required to go to each institutional review board ("IRB") of each hospital participating in the "test market." Dr. Lane also told these Synthes representatives that, in light of the company's "test market" activities, the company should go to the FDA immediately to negotiate the removal of the warning on the XR label, "not intended for treatment of vertebral compression fractures." Dr. Lane also stated that, in his view, Synthes had risk management problems and needed more oversight of its clinical and compliance issues. The evidence shows that defendants Huggins, Higgins, Bohner and Walsh were all informed of Dr. Lane's views within days. See Exhibit 68, e-mail chain dated 10/1/03.

The evidence shows that at the end of October 2003, defendant Walsh advised Josi Hamilton, the XR product manager, that in order for Synthes to obtain the FDA's permission to market Norian XR for the treatment of VCFs, Synthes would have to have the warning, "not intended for treatment of VCFs", removed, and that the only way this could be done was through a PMA application. See Exhibit 69, e-mail from defendant Walsh dated 10/28/03.

In November 2003, while the Norian XR test market continued, defendants Bohner, Walsh, Huggins and Higgins received an initial IDE proposal concerning Norian XR, from the Norian XR project manager ("the IDE proposal"). The evidence shows that defendant Walsh reviewed the IDE proposal before it was circulated to the other defendants. See Exhibit 70, e-mail dated 11/11/03. This proposal was never shared with the FDA. After discussing the 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 that XR was 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. . . (Emphasis supplied).

Exhibit 71, Internal Synthes IDE Proposal dated [when].

At the end of December 2003, defendant Walsh approved the 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 XR's label, "not intended for treatment of [VCFs]," and notwithstanding the fact that the Technique Guide contained x-rays of VCFs, some of which were x-rays of the spine of Doctor No. 4's patient who had died on the operating table in January 2003 during a surgery to treat VCFs. See Exhibit 72, memorandum of Bonnie Kincaid Smith; Exhibit 73, Norian XR Technique Guide excerpts. Also at the end of December 2003, Synthes released XR for sale beyond the original "test market."

On January 10 and 11, 2004, defendants Synthes and Norian held the first surgeon forum, which was approved by defendants Huggins, Higgins and others, at which approximately 30 surgeons were trained to use XR to treat VCFs, and at which the companies delegated to Dr. Sachs the task of explaining the warning on XR's label, "not intended for treatment of" [VCFs].

The evidence shows that Dr. Sachs re-worded the warning, which led to questions from the surgeons in attendance. The evidence shows further that the company representatives did nothing to dispel any confusion that Dr. Sachs's presentation may have caused. In addition, the XR Technique Guide was distributed to all attendees, including the 30 surgeons.

On January 22, 2004, a spine surgeon, Dr. Hieu Ball (who at the time was Dr. Nottingham's partner) used Norian XR in a kyphoplasty surgery to treat VCFs. A hypotensive event occurred, consistent with pulmonary embolism, and the patient died on the operating table ("the third death"). Dr. Ball could not rule out Norian XR as a cause of the third death. Once again, a sales consultant was present in the operating room during the surgery that resulted in the third death. Although defendants Synthes and Norian filed an MDR on the third death, that MDR was vague as to the surgery and its details. See Exhibit 74, MDR on third death. Moreover, defendants Synthes and Norian failed to supplement that MDR when Synthes received an autopsy report, even though the autopsy report contained new information that Synthes had not put in the original MDR, that is, 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. See Exhibit 75, autopsy report.

After the third death, defendants Synthes and Norian did not recall XR from the market. A recall would have forced the companies to inform the FDA of the details of all three deaths, and led to questions by the FDA about Synthes and Norian's failure to file an MDR on the first death. Instead, defendants Synthes and Norian left XR on the market, and sent surgeons a misleading "dear surgeon" letter, signed by defendant Huggins in his capacity as President of

Synthes North America. In the "dear surgeon" letter, defendant Huggins admitted on behalf of Synthes that use of XR to treat VCFs was off-label but explained that such use was off-label because it was "intrinsic to the stability of the bony structure," while remaining silent about the warning bullet on the XR label. Defendant Huggins further omitted to state that:

-- Synthes had conducted a "test market" in which it had trained surgeons to use XR to treat VCFs;

-- the pilot studies indicated that Norian appeared to be a thrombogenic agent;[15] and

-- three patients had died on the operating table when spine surgeons had used Norian XR or its predecessor, SRS, off-label to treat VCFs.

The "dear surgeon" letter is Exhibit 76. See also, Exhibit 77, e-mails showing involvement by defendants Bohner and Walsh in the formulation of the "dear surgeon" letter. The "dear surgeon" letter proves that defendant Huggins well understood the indication statement on the XR label, what it allowed and did not allow, and how narrow that indication statement really was.

D. The FDA Inspection – May-June 2004

In May and June, 2004, the FDA conducted an unannounced inspection of the Norian plant in West Chester, PA. During the inspection, the FDA investigator reviewed documents about the test market for SRS in the spine; the later Norian XR "test market;" the three deaths; and the Safety Meeting. Synthes kept detailed daily memoranda of the inspection. See Exhibit 78. The evidence will show that, as charged in Counts two through eight of the indictment, during and after the inspection, several Synthes representatives made false statements

[15] A thrombogenic agent is one that causes blood clots.

to the FDA, in an effort 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." The persons making false and misleading statements to the FDA during the inspection included defendants Huggins and Bohner; the XR product manager; the engineer for XR; and a Compliance Manager for Regulatory Affairs.[16] In addition, defendant Walsh made a false statement to the FDA after the inspection, as part of Norian's response to the FDA's 483 findings. In these false statements, the defendants and their underlings 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.

The evidence shows that:

– on or about May 12, 2004, defendant Norian and Synthes, through the XR product manager, made false and fraudulent statements to an investigator for the FDA, in that the XR product manager denied that she had ever promoted the use of Norian XR off-label to treat VCFs;

– on or about May 19, 2004, defendant Norian and Synthes, through the Synthes director of regulatory compliance, made false and fraudulent statements to an investigator for the FDA by stating that, in August 2003, Synthes did not have a Vertebroplasty

[16] Defendant Bohner's diary entries for this period show his involvement in the FDA inspection. For example, an entry for May 27, 2004 states "FDA daily wrap up . . . MH e-mail of 5/30/02; President's Meeting of 5/22/02. 'We're so consistently bad (sloppy) that it's good' !!" Exhibit 80, Bohner diary entry for 5/27/04.

System;

– on or about May 19, 2004, defendant Norian and Synthes, through the XR product manager, made additional false and fraudulent statements to an investigator for the FDA, in that the XR product manager stated that in August 2003, Synthes did not have a Vertebroplasty System;

– on or about May 20, 2004, defendant Norian and Synthes, through defendant 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.'"

– on or about May 27, 2004, defendants Norian and Synthes, through the XR product manager, made false and fraudulent statements to an investigator for the FDA, in that the XR product manager characterized the summer 2002 "test market" for SRS in the spine as surgeons mixing SRS with barium sulfate "on their own."

– on or about June 2, 2004, defendants Norian and Synthes, through the XR engineer, made false and fraudulent statements to an investigator for the FDA, in that the XR engineer told the investigator from the FDA that he did not know the process for mixing Norian SRS with barium sulfate;

– on or about June 7, 2004, defendants Norian and Synthes, through defendant 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;

– on or about June 16, 2004, defendants Norian and Synthes, through defendant 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;

– on or about June 16, 2004, defendants Norian and Synthes, through defendant 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;

– on or about June 22, 2004, defendants Huggins, Higgins, Bohner and Walsh met with other Synthes and Norian representatives, in order to plan a response to the FDA's 483 observations made after the FDA inspection, resulting in the false claims by defendants Norian and Synthes that:

a. the Norian XR "test market" was for cleared indications, instead of 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.

– on or about July 2, 2004, in a writing submitted to the FDA on behalf of defendants Norian and Synthes, defendant Walsh admitted that an IDE would be required if

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," 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 Norian and Synthes "did not promote [Norian XR] for the[ ] off-label uses" of treating vertebral compression fractures.

VI. WITNESSES

The United States may call as witnesses some or all of the following:

A. Special Agent Mark Cavallucci, HHS

B. Captain Joseph Despins

C. Special Agent Kishara Gant, DCIS

D. Special Agent Kerry Kitzmiller, FDA

E. Dr. Kenneth Lambert

F. Dr. Sohail Mirza

G. Dr. Michael Sharp

H. Nisra Thongpreda

J. Stuart Weikel

I. Josi Hamilton Wood

VII. EXHIBITS

Exhibit	Description
1	Vertebroplasty Market Investigation Executive Summary dated 6/21/00
1A	AO Clinical Investigations, "Vertebroplasty and Kyphoplasty: How safe and effective are they?" from defendant Huggins' file at Synthes
2	Facsimile Transmission from Michael Lehmicke to Nisra Thongpreda concerning conversations with surgeons on vertebroplasty dated 2/17/00
3	Memorandum from Tom Higgins and Nisra Thongpreda to Hansjoerg Wyss, SRS for Spinal Applications – Action Plan Proposal dated 2/24/00
4	E-mail from Defendant Higgins to Nisra Thongpreda concerning strategies for obtaining FDA permission to market Norian dated 11/20/00
5	Management Review Board ("MRB") Minutes dated 11/26/01
6	E-mail Chain between Group Manager of Spine Regulatory Barry Sands and Defendant Bohner and attached outline of clinical study dated 10/17/01 and 10/22/01
7	Synthes Product Development Test Market (Field Test) Policies
8	E-mail from Defendant Huggins to Defendants Higgins, Bohner and others, expressing second thoughts about the test market for SRS in the spine, dated 5/30/02
9	Time line of SRS in Spine Test Market approvals, created by Norian XR Product Manager Josi Hamilton 5/31/02
10	E-mail exchange between defendant Bohner and Josi Hamilton, the XR product manager, dated 5/22/02
11	SRS Label as cleared 12/20/01
12	Synthes Minutes of Conference Call with FDA 7/8/99
13	Synthes Minutes of Conference Call with FDA, Norian SRS with BaSO4, 5/8/02

Exhibit	Description
14	Synthes Consultant Harold Aberman DVM's Handwritten Notes of Conference Call with FDA 5/8/02
15	FDA Notes of 5/8/02 Conference Call
16	E-mail to Defendant Higgins from Group Manager of Spine Regulatory Sands Concerning Vertebroplasty Study dated 10/22/02
17	E-mail to Defendants Higgins and Bohner from Group Manager of Synthes Regulatory Michael Sharp, Synthes May Not Promote SRS for Vertebroplasty, with response from defendant Bohner, dated 8/23/00
18	E-mail to Defendant Bohner from Group Manager of Synthes Regulatory Sharp re meeting with Defendant Higgins, dated 3/19/01
19	Minutes of Meeting with Norian XR product manager on 12/13/02
20	E-mail from Group Manager Sharp to defendant Higgins and others, attaching Kyphon Warning Letter, dated 12/4/00
21	FDA Public Health Web Notification ("WebAlert") dated 10/31/02
22	E-mail from Defendant Huggins to Defendants Higgins and Bohner and others, attaching updated WebAlert dated 4/4/03
23	MDR filed by Norian re: one of the two Doctor Delamarter hypotensive episodes
24	MDR filed by Norian re: other Doctor Delamarter hypotensive episode
25	E-mail to Defendant Bohner concerning two hypotensive episodes, dated 3/16/01
26	E-mail from Defendant Huggins to Defendant Higgins, "reel in the sales force ASAP" dated 3/16/01
27	Norian for Spine Indications Focus Group materials 4/01
28	Handwritten Notes of Nisra Thongpreda, original group manager for Norian SRS-R, which became XR, on Spine Indications Focus Group meeting

Exhibit	Description
29	Spine Annual Sales Meeting 2001 Agenda on vertebroplasty
30	Spine Journal of Bone and Joint Science Article on death of patient during spinal screw augmentation surgery with CRS, April 2002
31	Letter to Synthes from University of Washington Researchers dated 6/28/02, attached proposal to perform more safety studies, and attached MDR
32	E-mails from Dr. Kenneth Lambert, Synthes consultant, to defendants Huggins and Higgins, and Wyss, expressing concern over safety of SRS in the spine
33	Memorandum from Nisra Thongpreda to defendants Huggins, Higgins and Bohner on SRS Training, dated 6/4/02
34	Powerpoint Presentation for SRS Training
35	MRB Meeting Spine Business Plan Review Agenda dated 9/17/02
36	Powerpoint Presentation on Test Market for SRS in the Spine given at 9/02 MRB Meeting
37	Materials Distributed in Advance of Safety Meeting held 7/18/03
38	Powerpoint Presentation given at the Safety Meeting
39	Minutes of the Safety Meeting
40	Minutes of the Safety Meeting held 7/18/03 emailed to defendants Higgins and Bohner on 7/18/03
41	Minutes of the Safety Meeting held 7/18/03 emailed to defendant Huggins and others on 7/24/03, with e-mail response from Huggins to defendant Higgins and others, concerning documenting outcomes of the additional 200 or so XR “test market” cases
42	Handwritten Notes taken during the Safety Meeting by Synthes consultant, veterinarian Harold Aberman
43	Norian XR 510(k) submission dated 11/18/02

Exhibit	Description
44	E-mail from Vikki Hoffman, Synthes Spine Regulatory employee responsible for the XR submission, dated 12/16/02
45	Regulatory Sign-Off Sheet Concerning Warning dated 12/18/02
46	Norian XR label as cleared 12/19/02
47	E-mail from defendant Higgins congratulating XR team dated 12/20/02
48	E-mail to defendant Bohner from Vikki Hoffman, Synthes Spine Regulatory employee responsible for the XR submission dated 1/23/03
49	Nisra Thongpreda's handwritten notes of telephone conference call with Dr. Sachs on 1/16/03
50	Josi Hamilton's handwritten notes of telephone conference calls with Dr. Sachs on 1/13/03 and 1/16/03
51	Stuart Weikel's handwritten notes of telephone conference call with Dr. Sachs on 1/16/03
52	E-mail from Defendant Bohner to Defendants Huggins and Higgins re: announcement to employees on off-label promotion
53	E-mail chain between Vikki Hoffman, the Synthes Spine Regulatory employee responsible for the XR submission, and the FDA Employee responsible for clearance of Norian XR, forwarded to Defendant Walsh on 10/16/03
54	E-mail to defendant Bohner concerning whether Synthes should seek a vertebroplasty indication for XR from the FDA, via an IDE and a PMA dated 5/28/03
55	Minutes of Strategic Planning Meeting held 8/14/03
56	Notebook Distributed to Surgeons at First "Test Market" Training Session
57	Blank "Test Market" Reorder Form (in Notebook)
58	E-mail to defendants Higgins and Bohner from Josi Hamilton, XR product manager, re "test market" dated 8/29/03

Exhibit	Description
59	E-mail to defendant Higgins from Josi Hamilton, XR product manager, re "test market" dated 9/10/03
60	E-mail from Josi Hamilton, XR product manager, concerning pig lab in April 2003 at which defendant Higgins was present, showing that setting time of Norian correlated to clotting, dated 4/21/03
61	E-mail to defendant Higgins from Josi Hamilton, XR product manager, re: LD-50 tests on pigs in November 2003, dated 11/19/03
62	Minutes of 9/23/03 Meeting
63	Norian XR Attendee List
64	Test Market Surgeon Training Agenda from Second Surgeon Training Meeting of XR "test market"
65	E-mail to defendants Huggins, Higgins and Bohner, and others, from Josi Hamilton, XR product manager following up 9/23/03 meeting
66	Agenda for 9/23/03 Meeting
67	Colleen Flescher's handwritten notes of Meeting Held 10/31/03
68	E-mail chain from Josi Hamilton, XR product manager, sent to defendant Higgins and forwarded to defendants Bohner and Walsh, stating Dr. Lane's concerns on safety of XR and Synthes risk management
69	E-mail from defendant Walsh telling Hamilton that having FDA remove warning from XR label "would likely require a PMA" dated 10/28/03
70	E-mail from defendant Walsh telling defendant Bohner that Walsh had seen internal IDE Proposal circulated by Hamilton before she sent it to Bohner, dated 11/11/03
71	Internal Synthes IDE Proposal
72	Memorandum of Bonnie Kincaid Smith, Synthes Spine Regulatory employee objecting to Technique Guide
73	Norian XR Technique Guide excerpts

Exhibit	**Description**
74	MDR filed on the third death, that of Dr. Ball's patient
75	Autopsy Report
76	"Dear Surgeon" letter signed by defendant Huggins, dated 2/10/04
77	E-mails dated 2/5 to 2/13/04 concerning "Dear Surgeon" letter
78	Synthes Daily Memoranda of FDA Inspection, dated 5/11/04 to 6/18/04
79	Excerpts from FDA Establishment Inspection Report
80	Excerpts from Diary of Defendant Bohner
81	Evaluations of Josie Hamilton

Respectfully submitted,
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United States Attorney

/s/ Mary E. Crawley
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CERTIFICATE OF SERVICE

This is to certify that I have caused to be delivered by electronic filing to the Clerk of Court (resulting in an e-mail copy sent to counsel by the Clerk of Court), and by direct e-mail of the within memorandum to the following:

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DATED: 3/30/10